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Improving the worldwide vaccination plans for COVID-19: a comparison of alternative strategies

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Declaration

I declare that this document is an original work of my own authorship and that it fulfills all the requirements of the Code of Conduct and Good Practices of the Universidade de Lisboa.

Preface

The work presented in this thesis was performed at Unidade de Epidemiologia (UEPID) of Instituto de Medicina Preventiva e Saúde Pública da Faculdade de Medicina da Universidade de Lisboa (IMP-FML) between February and October of 2022. The work was supervised by Dr. Paulo Jorge Morais Zamith Nicola, from IMP-FML and Instituto Superior Técnico and co-supervised by Prof. Dr. Mónica Duarte Correia de Oliveira, from Instituto Superior Técnico. This work was also developed within the scope of the EIT Health - Master in Technological Innovation in Health (MTiH).

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Finally, I would like to thank my family, especially my brother and my parents, for the opportunities provided and for giving me everything I required to succeed. I will never be able to thank you enough for all your love and unconditional support.

Abstract

COVID-19 appeared in December 2019 and quickly spread globally. Although a vaccination campaign started in December 2020, and despite efforts such as COVAX, access to vaccines was unequal across countries. The aim of this study is to quantify and compare the direct health impact of considering global alternative allocation strategies of the available supply of vaccines with different prioritization mechanisms: 1) Age-based demographic prioritization; 2) Case-based epidemiological prioritization; 3) Mixed demographic and epidemiological prioritization.

To achieve this goal, an analysis using country-specific epidemiological data and vaccine effectiveness estimates was performed to compute the alternative number of infections and deaths until the end of 2021 for each strategy. Sensitivity analyses varying vaccine effectiveness were additionally performed.

Among the tested strategies, epidemiological prioritization produced the best results [30.9% (23.7 to 39.6) of infections and 61.6% (50.4 to 75.8) of deaths avoided], allowing for a 5.6% reduction in mortality when compared to the observed vaccine allocation. Contrarily, demographic prioritization yielded the worst results [21.4% (16.1 to 28.5) of infections and 55.4 % (44.7 to 71.2) of deaths avoided].

This study, the first of its kind, proposes an innovative strategy for vaccine allocation that may be superior to the observed distribution, reinforcing the role and articulation of national and international health organizations. These findings have the potential to lead to new global strategies which will be of utmost importance not only for future pandemics, but also for the distribution of new vaccines for the control of SARS-CoV-2 and other viruses' genetic variants.

Keywords

COVID-19, COVID-19 Vaccination, Alternative Strategies, Prioritization Strategies, Global Access, Equity

Resumo

A COVID-19 surgiu em Dezembro de 2019 e espalhou-se rapidamente por todo o mundo. A vacinação teve início no final de 2020, e apesar de esforços como a COVAX, o acesso às vacinas foi desigual entre países. O objetivo deste estudo é quantificar e comparar o impacto direto na saúde de considerar estratégias alternativas globais de alocação da quantidade disponível de vacinas, com diferentes mecanismos de priorização: 1) Priorização demográfica baseada na idade; 2) Priorização epidemiológica baseada em infeções; 3) Priorização mista.

Desta forma, foi efetuada uma análise que utilizou dados epidemiológicos e estimativas da efetividade das vacinas para calcular o número alternativo de infeções e mortes até ao final de 2021 para cada estratégia. Uma análise de sensibilidade foi ainda realizada, variando a efetividade das vacinas.

Das estratégias testadas, a priorização epidemiológica destacou-se positivamente e evitou 30,9% (23,7 a 39,6) das infeções e 61,6% (50,4 a 75,8) das mortes, permitindo uma redução de 5,6% na mortalidade relativamente à alocação observada. Contrariamente, a priorização demográfica obteve os piores resultados, evitando 21,4% (16,1 a 28,5) das infeções e 55,4% (44,7 a 71,2) das mortes.

Em suma, este estudo propõe uma estratégia inovadora para a alocação de vacinas que pode ser superior à observada, reforçando o papel da articulação das organizações de saúde nacionais e internacionais. Estas conclusões têm o potencial de conduzir a novas estratégias globais que serão da maior importância não só para futuras pandemias, mas também para o controlo de variantes genéticas do SARS-CoV-2 e de outros vírus.

Palavras Chave

COVID-19, Vacinação da COVID-19, Estratégias Alternativas, Estratégias de Priorização, Acesso Global, Equidade

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Acronyms

ACT	Access to COVID-19 Tools
CEPI	Coalition for Epidemic Preparedness Innovations
CoVDP	COVID-19 Vaccine Delivery Partnership
COVID-19	coronavirus disease 2019
DALY	Disability-adjusted Life Year
ECDC	European Centre for Disease Prevention and Control
EU/EEA	European Union/European Economic Area
EUL	Emergency Use Listing
HIC	High Income Country
ICU	Intensive Care Unit
IFR	Infection Fatality Ratio
IP	Intellectual Property
LIC	Low Income Country
LMIC	Lower Middle Income Country
mRNA	messenger Ribonucleic Acid
NAAT	nucleic acid amplification test
NPI	Non-Pharmaceutical Intervention
NRVV	Non-Replicating Viral Vector
OWID	Our World in Data
PCR	Polymerase Chain Reaction
PPF	Population Prevented Fraction
RNA	ribonucleic acid
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2

SEIR	Susceptible-Exposed-Infected-Recovered
SIR	Susceptible-Infected-Recovered
UMIC	Upper Middle Income Country
USA	United States of America
VE	Vaccine Effectiveness
VOC	Variant of Concern
VU	Vaccine Uptake
WHO	World Health Organization
WTO	World Trade Organization
YLL	Year of Life Lost

1

Introduction

Contents

1.1 Motivation

Coronavirus disease 2019 (COVID-19) appeared in December 2019 and has quickly spread to almost every country in the world. Only 3 months later, the World Health Organization (WHO) classified this disease as a pandemic. This pandemic showed a devastating effect, not only at the health level, but also at the socio-economic level, consequence of the stringent measures implemented by national governments to attenuate the health repercussions. Due to this devastating effect, there was a need to develop a vaccination programme as quickly as possibly. Unquestionably, this effort was successful in mobilizing resources and skills, notably the scientific ability to quickly develop very effective vaccines, some with especially innovative technologies.

As a result of this effort, a vaccination campaign was able to start in December 2020. However, despite international efforts such as COVAX, access to COVID-19 vaccines among countries was extremely unequal. Although health leaders agree that a world without COVID-19 will not be possible until everyone has equal access to vaccines [1], there is no quantification of the real health impact that a global equitable distribution could have had.

Furthermore, questions about what constitutes an equitable distribution arise. Especially at the start of vaccination programmes, it is important to reflect which populations should be prioritized, as there is a very limited supply of vaccines and resources to immunize the entire population at once. This is a very debated topic on literature and by national leaders. Notwithstanding, to this date, no studies comparing prioritization strategies of vaccination exist, at a global scale.

Different COVID-19 vaccine distributions among nations, considering global access and taking into account each country's epidemiological and demographic profiles to prioritize populations, could have saved a lot of lives. It is of utmost importance to make such quantification as it may provide strong arguments towards the strengthening of international institutions in their role to provide adequate health responses to countries and communities while avoiding health inequities, whether during the current COVID-19 pandemic or in future public health threats.

1.2 Objectives

The major goal of this dissertation is to analyse the potential of alternative strategies for the allocation of vaccines against COVID-19, in order to contribute to the discussion of the improvement of the worldwide vaccination plans of the same disease. In particular, the aims are:

- Evaluation of the health direct impact of considering a global-based allocation of COVID-19 vaccines, instead of country-based;
- Assessment and comparison of the health direct effect of considering demographic, epidemiological and mixed prioritization strategies for the distribution of the available supply of vaccines.

1.3 Thesis Outline

This dissertation is structured as follows:

- **Chapter 2 - Context**

  This chapter contextualizes the problem that this study aims to address. The uneven access to COVID-19 vaccines globally in the first year of immunization is highlighted, as are the causes that led to such phenomenon and the international efforts used to mitigate this inequality.

- **Chapter 3 - Concepts and Related Work**

  The chapter introduces important concepts necessary for the understanding of the rest of this dissertation. It starts by providing key concepts regarding COVID-19 and its vaccination programme. Further, methodological approaches to evaluate the impact of vaccination programmes are discussed and a description of the currently available literature regarding the estimation of the impact of COVID-19 vaccination is provided. Additionally, this chapter introduces the subject of alternative strategies for vaccination against COVID-19. It provides a review of the current available literature on the topic and the rationale behind the strategies tested.

- **Chapter 4 - Methodology**

  Based on the literature review carried out in the previous chapter, this chapter focus on describing the chosen methods for the impact and comparison of alternative strategies. An outline of the analysis is first provided and then the required input data, as well as the mathematical formulation behind the outcomes estimation of analysis are described.

  Additionally, this chapter introduces and describes the alternative strategies of vaccination studied in the present dissertation, which are the following:

1. Global Age-based Demographic Prioritization
2. Global Case-based Epidemiological Prioritization
3. Mixed Demographic and Epidemiological Prioritization

- **Chapter 5 - Results and Discussion**

  This chapter presents the results obtained in each of the strategies of vaccination tested, including the observed. These results correspond to the number of infections and fatalities averted in each of the strategies. Then, a comparison and discussion of the differential performance between strategies is done, comparing the results obtained over time, across income groups and across age groups. Finally, the limitations of the study are addressed and a summary of the main contributions and recommendations towards the improvement of vaccine distribution strategies are provided.

- **Chapter 6 - Conclusions and Future Work**

  This chapter summarises the main conclusions of this work and proposes opportunities for further developments.

2

Context

COVID-19, a disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the seventh human coronavirus [2], appeared in December 2019 in Wuhan, Hubei Province, in China, and has now spread to nearly every country in the world. On 11 March 2020, only 3 months after its appearance, the WHO declared COVID-19 a pandemic [3]. As of 24 October 2022, there have been 624 235 272 confirmed cases of COVID-19, including 6 555 270 deaths, reported to the WHO [4].

Vaccines have proven to be of extreme importance when managing diseases, reducing illness and hospitalizations as well as other indirect effects, such as mitigating transmission, and even eradicating some diseases [5]. Additionally, as waiting for natural herd immunity would take way too long, a quick worldwide immunization program against this pandemic was seen as the finest choice to quicken the reduction of populations' health susceptibility and diminish the social and financial results of COVID-19 widespread.

Since the start of vaccine development, it was clear that in addition to COVID-19 vaccinations, there was also a need to make sure that everyone in the world had access to vaccination in order to put an end to this global public health crisis. The idea of *"No one is safe, until everyone is safe"* was the foundation upon which COVAX was developed, headed by Gavi, the Vaccine Alliance, the Coalition for Epidemic Preparedness Innovations (CEPI) and the WHO [6]. The COVAX Facility is the vaccines pillar of the Access to COVID-19 Tools (ACT) Accelerator, an international partnership to hasten the creation of COVID-19 diagnostics, treatments and vaccines as well as ensure equal access to them. This facility divides the participant countries in either funded [Low Income Countries (LICs) and Lower Middle Income Countries (LMICs)] or self-funded [Upper Middle Income Countries (UMICs) and High Income Countries (HICs)] [7] and operates as a centralized vaccine purchaser, either buying vaccines from pharmaceutical companies or receiving donations from wealthier countries [8].

On 8 December 2020, the first COVID-19 vaccine was administered to a patient in the United Kingdom [9], marking the beginning of a global immunization process. However, with the current model for vaccine distribution being based on an economical competition between countries for limited vaccines, not all countries had the same access.

Not only the financial capability of HICs has allowed them to buy an excess of extra doses of vaccinations, but also, clever negotiations between HICs and the pharmaceutical industry made things much more difficult for LICs and LMICs to acquire vaccine doses. Wealthier nations were well-equipped to bargain and quickly obtain vaccines due to long-standing partnerships between vaccine makers and HICs. Additionally, as there is no set, regulated price for the purchase of COVID-19 vaccinations, it is tragically possible for manufacturers to put money before lives [10].

The emergence of vaccine nationalism, wherein nations preferred to conduct their own bilateral advance purchase agreements with vaccine manufacturers over participation in multilateral initiatives like the COVAX Facility, as explained above, was the main threat to COVAX's proper execution of its func-

tion. This vaccine nationalism has decreased the ability of COVAX to attract sufficient participation from self-funded countries, raising important international financial backing issues, and has increased the competition for a limited supply of vaccines [7]. Therefore, even COVAX struggled to purchase any vaccines and was forced to wait and rely on voluntary donations, that were not enough to achieve its goal of having 20% of its target population vaccinated by the end of 2021 [8]. Due to the LICs shallow economic power and scarce resources, their ability to acquire and distribute these vaccines is highly limited, relying mostly on COVAX. Consequently, during 2021, the first year of distribution of vaccines against COVID-19, HICs had already fully vaccinated 70% of their population while LICs had only been able to fully vaccinate 4.3% [8].

Adding to this problematic, in August 2021 some HICs started giving their populations booster shots, while some of the world's most vulnerable people remained unprotected [11]. This was initially due to evidence of the waning effect of vaccine effectiveness, *i.e.* a decrease of the immunity granted by the vaccine against COVID-19 over time. However, preliminary evidence that three doses of mRNA vaccination neutralize against Omicron, the Variant of Concern (VOC) that emerged at the end of 2021, has accelerated the booster programme [12].

A similar situation had already happened with the swine flu pandemic of 2009, caused by the influenza A virus sub-type H1N1. Large quantities of vaccinations were pre-ordered by wealthier nations to safeguard their people, instantly raising questions about fair access to pandemic vaccines [13]. Despite attempts by the WHO, many underdeveloped nations did not get vaccines until the pandemic's acute phase had subsided, at which point they were less effective [7]. Since the pandemic did not prove to be as dangerous as previously anticipated, vaccine dosage supply did not pose a significant problem, and interest in immunization declined in many nations [13]. However, COVID-19 is more deadly than the swine flu epidemic of 2009 was. Nevertheless, the distribution of vaccines appears to be following the same pattern.

It is important to reflect on how this observed distribution of vaccines has impacted the health of the populations and whether there were alternatives that could have been more effective in that regard.

First, if the access model was dominated by market conditions, and access and vaccination times differed by country as a consequence, how did this impact countries that were left last? Could the overall health outcomes have been better if access had been equal?

Further, there were guidelines on vaccine prioritisation supported by the WHO and implemented at the national level, usually common: identification of priority and high vulnerability groups and age stratification. However, was this the strategy for the allocation of vaccines that allowed to prevent more infections and/or deaths? Could a strategy based on the population's epidemiological instead of demographic profile have been better?

Different COVID-19 vaccine distributions across nations, taking into account their epidemiological

and demographic profiles, could have led to better health outcomes. However, this quantification has not been performed. It is of utmost importance to make such quantification, not only for the distribution of new vaccines for the control of SARS-CoV-2 genetic variants, but also for vaccination endeavors of other future public health threats.

3

Concepts and Related Work

Contents

This chapter introduces important concepts necessary for this dissertation and explores the related work that has been done in this field.

First, Section 3.1, focus on COVID-19. In Section 3.1.1, an overview of the disease, including the relevant clinical and genetic aspects and a description of the main measures of detection and prevention, is presented. Then, Section 3.1.2 focus on the vaccination efforts against this disease, including vaccine development, platforms and other important concepts regarding COVID-19 vaccines.

Then, Section 3.2 explores methodological approaches to evaluate the impact of vaccination programmes. To do so, a brief summary of the effects of vaccination described in literature is first provided in Section 3.2.1. Subsequently, the most usual factors affecting vaccination impact estimates and contributing to its heterogeneity are enumerated in Sections 3.2.1.A and 3.2.1.B. Finally, an assessment of the available studies regarding the estimation of the impact of COVID-19 vaccination is done in Section 3.2.2.

At last, Section 3.3 explores the subject of alternative strategies for vaccination against COVID-19. The rationale behind a global allocation strategy is first provided in Section 3.3.1, with a focus on demographic (Section 3.3.1.A) and epidemiological (Section 3.3.1.B) prioritization. Finally, an assessment of the current available literature on the topic of comparison of strategies of vaccination against COVID-19 is done in Section 3.3.2.

3.1 COVID-19

3.1.1 Overview of the Disease

Clinical and Genetic Aspects

COVID-19 is a contagious disease caused by the virus SARS-CoV-2, the seventh human coronavirus [2]. The first case was diagnosed in December 2019 in Wuhan, Hubei Province, in China. This disease has quickly spread worldwide, resulting in the COVID-19 pandemic.

Patients infected with COVID-19 can either be asymptomatic carriers or manifest symptoms, ranging from mild to severe, and, in some cases, leading to death. The most common symptoms include cough, fever and shortness of breath [2]. The main mechanisms of transmission are the inhalation of respiratory droplets and the contact with contaminated surfaces [14].

Additionally, ribonucleic acid (RNA) viruses, like SARS-CoV-2, continuously evolve when the genome is replicated and alterations in the genetic code occur, induced by genetic mutations or viral recombination [15]. This results in the emergence of new virus strains, some of which can have increased transmissibility and/or increase in virulence and/or show a decrease in effectiveness of pharmaceutical or non-pharmaceutical interventions, in these cases called a VOC [16]. The emergence of these new

variants can cause even more pressure on healthcare systems. As of 24 October 2022, there have been four previously circulating VOCs (Alpha, Beta, Gamma, Delta) and there is one currently circulating VOC (Omicron) [16].

Detection and Preventive Interventions

COVID-19 can be detected using specific viral tests: nucleic acid amplification tests (NAATs) or antigen tests [17]. NAATs, most commonly known as Polymerase Chain Reaction (PCR) tests, are performed in a laboratory. These are usually the most reliable tests and detect viral genetic material which may lodge in the body for up to 90 days after testing positive. Antigen tests are rapid tests that produce results in 15-30 minutes. These are less reliable than NAATs and sometimes a follow-up NAAT may be recommended to confirm an antigen test result. The widely used self-tests, or at-home tests, are usually antigen tests that are manufactured to be taken anywhere without having to go to a specific testing site [17].

Given the mechanisms of transmission of this disease and coupling that with the fact that no treatment specific for COVID-19 exists [14], governments have put in practice several measures to ensure the control of the COVID-19 pandemic. These Non-Pharmaceutical Interventions (NPIs) usually consisted on: isolation of COVID-19 infected patients and high-risk contacts; the closure of schools, restaurants and others; travel restrictions; disinfection and ventilation of spaces; and finally, the promotion of hand hygiene and use of face masks. However, the most effective measures are usually the ones that cause more social and economic damage. Therefore, it is challenging for the governments to strike a balance between expanding case numbers and economically and socially viable and acceptable control measures likely to have a substantial impact [18].

The WHO defines herd immunity as *"the indirect protection from an infectious disease that happens when a population is immune either through vaccination or immunity developed through previous infection"* [19]. Ultimately, this is the end goal when dealing with a pandemic. Natural herd immunity, *i.e.,* herd immunity achieved by allowing the disease to spread, would not only take too long to be attained but is also scientifically problematic and unethical [19]. Therefore, an immunization program against this pandemic was seen as the finest choice to quicken the reduction of populations' health susceptibility and diminish the social and financial results of COVID-19 widespread.

3.1.2 Vaccination

Since the genetic sequence of SARS-CoV-2 was published on 11 January 2020 [20], a massive global effort was made to discover and produce a vaccine against COVID-19 as quickly as possible. This was achieved by mobilizing multiple resources and encouraging cooperation, also leading to both technological and process innovation. On 16 March 2020, the first COVID-19 vaccine had already entered human

clinical testing [20] and on 31 December 2020 the WHO issued its first emergency use validation for a COVID-19 vaccine [21].

A remarkable aspect of the COVID-19 vaccine research landscape is the variety of technological platforms being considered, shown in Figure 3.1. Of these vaccine platforms, the ones most used against COVID-19 are: messenger Ribonucleic Acid (mRNA), Non-Replicating Viral Vector (NRVV), Protein Subunit and Inactivated vaccines. It should be noted that the use of mRNA vaccines appear as a breakthrough technology, as it was the first time in the history of vaccionology that a nucleic acid vaccine has been approved for a public health program [22]. In fact, due to their rapid development, high level of safety and efficacy, mRNA vaccines have emerged as the leading candidates of these [23]. However, because of the mRNA instability and easy degradation, vaccines of this type require ultra-low temperatures for transportation and storage [24].

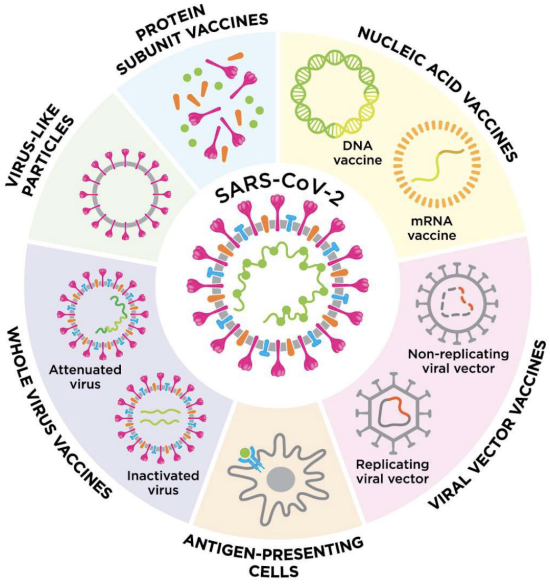


Figure 3.1: Different vaccine platforms against COVID-19 [24].

An individual receiving COVID-19 vaccination is usually considered immunized once the primary series of vaccination is completed. The primary series can range from a single dose to three doses, depending on the vaccine manufacturer and the patient's age and immune status [25]. Most vaccines are two-dose vaccines which are administered according to a characteristic time interval, that may vary between vaccine manufacturers.

Additionally, a subsequent dose, designated booster, can be administered a few months after the primary series vaccination [25]. The booster is usually administered to enhance or restore protection from vaccination which might have declined over time. This decrease in the effectiveness of vaccination over time is called waning effect.

Individuals may have an homologous vaccination schedule (when all the vaccines administered to

them are from the same manufacturer) or heterologous (when this is not the case). The rules on whether heterologous schedules can exist vary from country to country, as do the rules on what type of vaccines are given to each sub-population. Likewise, not all vaccines are available in all countries. Each country has its own sub-selection of vaccines that have been approved by the respective national governments. In addition, the WHO provides an Emergency Use Listing (EUL), which consists of a list of vaccines that demonstrate a reasonable likelihood that its quality, safety and effectiveness are acceptable and that the benefits outweigh the foreseeable risks [26].

3.2 Impact of Vaccination Programmes

3.2.1 Measuring the Impact of Vaccination

Before addressing the subject of the different effects of vaccines and vaccination programmes, as well as their impact, it is first necessary to make the distinction between vaccine efficacy and vaccine effectiveness. According to the World Health Organization [27], vaccine efficacy is measured in controlled clinical trials and is evaluated by comparing the proportion of recipients of the vaccine who acquired the "outcome of interest" (often a disease) to the proportion who also got the same outcome but received a placebo. Following the trial, the numbers of ill participants in each group are compared to determine the relative risk of contracting the disease based on whether or not the individuals had been vaccinated. This gives us the efficacy, which is a gauge of how much the vaccination decreased the likelihood of contracting the disease. On the other hand, the effectiveness of a vaccine is an indicator of how it performs in the actual world, as clinical trials are usually not a perfect reflection of the general population. Thus, effectiveness is estimated by observing how well the vaccines work to protect communities as a whole, usually measured by observational post-licensure studies [28].

Regardless, both vaccine efficacy and vaccine effectiveness (here denoted as VE) can be calculated using the same formula, shown in Equation 3.1 [28], where R denotes the risk or rate. Its the conditions in which these risks are measured that diverge between the two definitions.

$$VE = \frac{R_{unvaccinated} - R_{vaccinated}}{R_{unvaccinated}} \tag{3.1}$$

While there seems to exist a consensus among the scientific community regarding the distinction between vaccine efficacy and effectiveness and their calculation, measuring the impact of vaccination programs is not such an easy task, as the counterfactual scenario (*i.e.*, with no vaccination) cannot be observed.

In 1991, Halloran and Struchiner [29] categorized four different types of effects of interventions (in this case, vaccination). These are schematized in Figure 3.2 and enumerated below:

- **Direct Effect**: Measures the direct effect that vaccination has on the individual.
- **Indirect Effect**: Measures the effect of vaccination at the population level.
- **Total Effect**: Reflects the combination of the direct and indirect effect.
- **Overall Effect**: Evaluates the difference in outcome from an average individual from a population with a vaccination programme compared to an individual from a population without a vaccination programme.

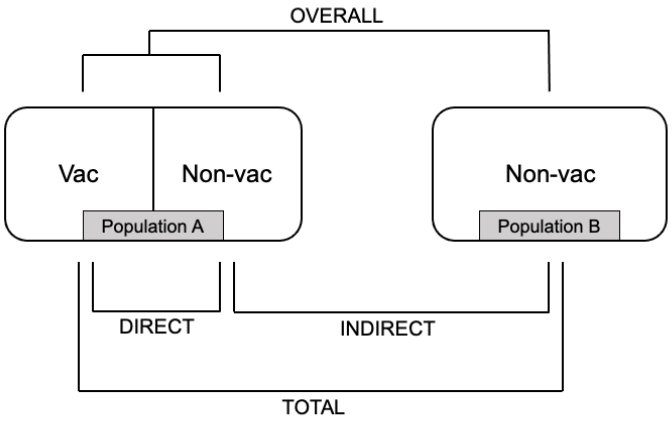


Figure 3.2: Different effects of vaccination (adapted from Halloran and Struchiner [29]).

Furthermore, epidemiology textbooks [30, 31] give one definition for the impact of a protective factor in a population, denominated Population Prevented Fraction (PPF) and defined as in Equation 3.2. According to Porta [31], the PPF can be defined as *"the proportion of the hypothetical total load of disease (in the population) that has been prevented by exposure to the factor"*.

$$PPF = p(1 - RR) \tag{3.2}$$

Where:

- p is the proportion of population exposed to protection
- RR is the relative risk (or risk ratio)

According to Hanquet et al. [28], this measure can be adapted to vaccination using the vaccine effects (here represented by VE) aforementioned. Thus, given a population with a defined vaccine coverage, VC, PPF can be written as in Equation 3.3 if the protective factor is the vaccine, whereas if the protective

factor is the vaccination programme, PPF can be written as in Equation 3.4. It is important to note that the PPF of the vaccination programme is the weighted sum of the total effect on vaccinated individuals and the indirect effect on unvaccinated individuals.

$$PPF = VE_{direct} \times VC \tag{3.3}$$

$$PPF = (VE_{total} \times VC) + (VE_{indirect} \times (1 - VC)) \tag{3.4}$$

Therefore, Hanquet et al. [28] states these four effects can be called impact, according to the concepts of public health epidemiology.

Notwithstanding, measuring the different effects of vaccination and consequently its impact is a challenging task as study designs must meet a plethora of requirements that are usually difficult to achieve [28]. In fact, even the measurement of the vaccine direct effect, or vaccine efficacy, in double-blind randomized clinical trials, is not as straightforward as it may seem due to the amount of confounding factors and biases that can exist.

To summarize the factors that can affect vaccination impact estimates, these were divided into 2 groups: intrinsic and extrinsic factors. Intrinsic factors are the ones that derive from the choice of method used to calculate the estimate, whereas extrinsic factors are usually not factored into the estimate but can still affect the perceived impact of vaccination. These factors are schematized in Figure 3.3 and described in the following sections.

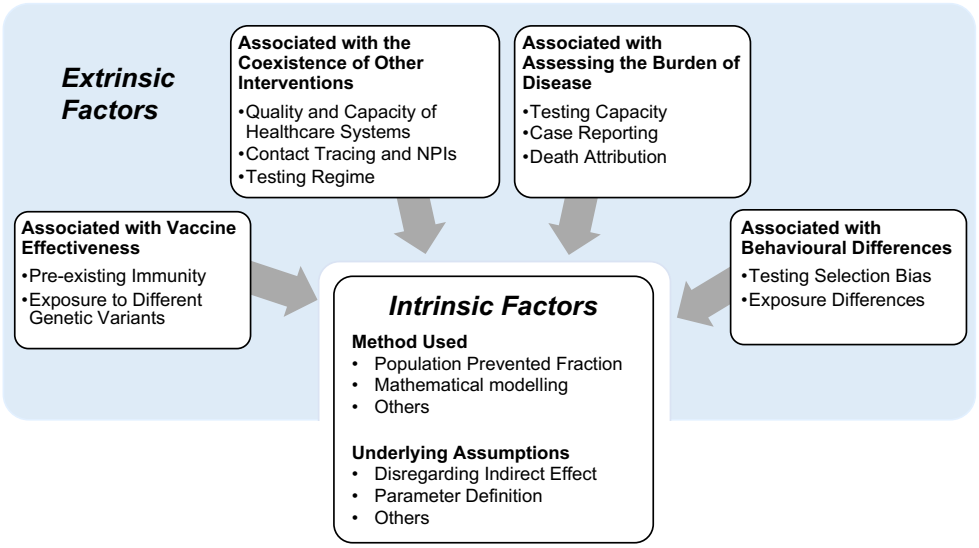


Figure 3.3: Factors affecting vaccination impact estimates.

3.2.1.A Intrinsic Factors Affecting Vaccination Impact Estimates

Directly measuring the impact of a vaccination programme is not possible as the scenario of no-vaccination cannot be observed. Therefore, the method chosen to quantify the impact of vaccination has a considerable influence in the results obtained, as do the underlying assumptions of such method. The most common methods used to estimate the impact of vaccination programmes are described below, as well as their underlying assumptions.

- **Population Prevented Fraction**

  Calculating the impact of a vaccination programme using Equation 3.4 is unfeasible as there are not many estimates available of the total and indirect effect of the vaccine. Lefebvre et al. [32] suggest that while indirect effects can be measured in retrospective studies with real-life data and in well-designed prospective studies, more research is required to identify and develop successful assessment methodologies for the analysis of this type of outcomes, as evaluating the total epidemiological impact of vaccination in a population is complex and this complexity is exacerbated by the potential of indirect effects.

  Moreover, the impact of a vaccination programme can be measured using Equation 3.3, in that case denominated the direct impact of vaccination, with the underlying assumption of disregarding the indirect effect. This method has already been used in COVID-19 vaccination impact studies, as will be seen in the next sections and was widely used to study the impact of influenza vaccination programmes by Machado et al. [33] and other authors. An approach to attenuate the limitations of this method is using vaccine effectiveness estimates, instead of vaccine efficacy. While Hanquet et al. [28] assumes that vaccine effectiveness only reflects the direct effect of the vaccine, other authors [32, 34, 35] suggest that it also captures some of the indirect effects of the vaccine, as it is measured in real-world conditions.

- **Mathematical Modelling**

  Another approach consists of using mathematical models as done by Li et al. [36] and other authors for other pathogens. These models simulate disease transmission dynamics and often model the direct effect of vaccination on vaccinated populations and the indirect effect of vaccination on both vaccinated and unvaccinated. The most commonly used models are compartmental models [37], such as Susceptible-Infected-Recovered (SIR) and its variations like Susceptible-Exposed-Infected-Recovered (SEIR), or agent-based models. Both have a predictive nature and are mostly used to forecast the evolution of the pandemic, but can also estimate the effects of public health interventions on the outcome of the disease. However, these models are based on the definition of several parameters requiring many assumptions. In fact, their accuracy and suitability for the prediction of the COVID-19 pandemic course in long-term analysis is a matter of debate [38].

Further, using this type of models for worldwide data would require an extremely complex degree of assumptions given the heterogeneity between regions.

- **Others**

  Other type of studies are proposed by Hanquet et al. [28] to study the impact of vaccination programmes. One is the comparison of pre- and post-vaccination population, unfeasible in this situation as vaccination against COVID-19 is still on-going and the comparison of disease occurrence is challenging due to the variety of NPIs that were in place before vaccination in order to control the pandemic. The other one is cluster randomized vaccination trials which is out of the scope of this study.

3.2.1.B Extrinsic Factors Affecting Vaccination Impact Estimates

Besides the intrinsic factors associated with the methodology chosen and discussed in the previous section, there are several other factors that can affect vaccination impact estimates. These factors can either over- or underestimate the perceived impact of vaccination. Therefore, when measuring the impact of vaccination programmes, as done in this study, these factors should be acknowledged and reflected upon even if they are not factored into the estimate. To simplify the discussion of these factors, the most relevant ones were divided into four categories: associated with vaccine effectiveness, associated with the coexistence of other interventions, associated with assessing the burden of disease and associated with behavioural differences. This division can be seen in Figure 3.3 and a description of each factor is provided below:

- **Pre-existing immunity**

  In individuals with some level of pre-existing immunity, vaccines may only offer little advantage, but in individuals lacking pre-existing immunity, the benefit may be significantly greater [39]. Prior infection with COVID-19 is the typical cause of pre-existing immunity. Sometimes effectiveness is adjusted to this parameter, however, since most illnesses are still unrecorded, a prior infection may not have been reported [40]. A population with high levels of pre-existing immunity will feel less the effect of the vaccine and therefore underestimate the impact of vaccination.

- **Exposure to Different Genetic Variants**

  Differences in exposure can arise from differential exposure to specific viral strains, such as the different VOCs. In fact, vaccines have genuine differences in efficacy against different VOCs [39].

- **Testing**

  - ▷ **Testing Regime**

    The national testing regime in place during the study period (including scope, eligibility, barriers of accessibility, and selection criteria related to vaccination status) can contribute to the heterogeneity of the perceived impact of vaccination across different time periods and locations [41].

  - ▷ **Testing Capacity**

    Due to variations in testing rates, epidemic curves of reported cases may not always accurately represent the underlying epidemic growth rate [42] and thus underestimate the impact of vaccination, especially in countries that lack capacity for large-scale testing, such as African countries [43].

  - ▷ **Testing Selection Bias**

    Vaccination can induce individuals in getting tested more or less frequently [39]. For example, if the vaccinated group is more health concerned and/or has greater access to testing than the unvaccinated group, they may undergo testing more frequently, reporting more cases and underestimating the impact of vaccination. In the same way, if the vaccination lessens the severity of the infection and fosters a sense of security, and if public health authorities support more frequent testing for the unvaccinated, the vaccinated group may be tested less frequently, thus reporting less infections and overestimating the impact of vaccination. In the same way, this can also impact the choice of the type of test taken, *i.e.*, the use of more sensitive tests (NAATs) as opposed to less sensitive ones (antigen), between vaccinated and unvaccinated individuals.

- **Case Reporting and Death Attribution**

  Case reporting can impact vaccine impact assessments. A significant proportion of cases are underreported in many countries [44, 45], which can happen due to a variety of reasons, such as: case definition, inadequate reporting systems, testing strategies [46], *etc.*. Substantial occurrences of underreported infections can reduce the perceived impact of vaccination [40], by not allowing to fully assess the true burden of the disease. In a similar way, death attribution can also impact vaccine impact estimates. Deaths due to COVID-19 have been undercounted in many countries, with excess mortality being over 50% of the expected annual mortality [47]. This problematic is further augmented in developing countries, that lack vital registration systems, which underestimates the burden of COVID-19 in these countries [48], and consequently, of the impact of vaccination [49]. Although the opposite can also occur, the under-ascertainment of COVID-19 cases and deaths is much more common than its overcounting [49].

- **Healthcare Systems Quality and Capacity**

  The use of other medical interventions apart from vaccination has an impact in preventing both severe diseases and deaths. Thus, in countries with better and more capacious healthcare systems, the impact of vaccination is less than in other countries with strained healthcare infrastructures and resources. Additionally, if the accessibility to healthcare providers is limited, there may be a bias towards more severe cases, as well as wealthier and more educated population groups.

- **Contact Tracing and NPIs**

  The contact tracing regime and NPIs in place during the study period can affect the perceived impact of vaccination, as these interventions are concurrent with vaccination, making the understanding of what proportion of the effect is attributable to which intervention a complex task. Additionally, NPIs can cause bias between vaccinated and unvaccinated individuals, as there may be different measures in place for these two groups [39], and also between different populations as these type of interventions are different across nations and even time-varying across pandemic waves with different transmission intensity, within the same country.

- **Exposure Differences**

  Vaccination may influence the vaccinated group to participate in more frequent, large-scale, and high-risk exposures, as they feel more protected. The value of vaccination is then lessened by this risk compensation phenomena [39].

3.2.2 State-of-the-art: Impact of COVID-19 Vaccination

At the time of writing, September 2022, only one published study was found that estimated the global impact of COVID-19 vaccination [50]. This study and other relevant ones [51–57], although at a smaller scale, will be discussed below, along with their methodological differences and limitations. The assessment of the current available literature on the measurement of the impact of COVID-19 vaccination programmes is of major significance because, even in comparison studies, these are the same methodologies used to compute the impact of alternative strategies. Table 3.1, which can be found at the end of this chapter, summarizes the main characteristics of the most relevant studies found and discussed below.

Watson et al. [50] performed the only study regarding impact of COVID-19 vaccination globally. A COVID-19 transmission model, fitted to observed mortality, was used to predict both the direct and indirect impact of the first year of vaccination against COVID-19. Although it was found that vaccination has a tremendously positive impact worldwide, the number of averted deaths varied greatly between WHO Regions and World Bank income groups. Further, due to the incompleteness of vital registration systems in some countries and the associated underreporting of COVID-19 deaths, the authors also

used model-based estimates of all-cause excess mortality to fit the model. The impact of vaccination was even higher. Although fitted to mortality, this study was limited by the fact that some key inputs had to be produced from assumptions, both due to the absence of complete data in some countries and the inherent parameter-definition nature of mathematical modelling.

A study considering 33 countries of the WHO European Region [51] was able to deal with some of the limitations experienced by Watson et al. [50] by using observed mortality as the foundation of their calculation on countries where the reporting systems are considered satisfactory. However, this study only measured the direct impact of vaccination, by using a method of calculation equivalent to the PPF to estimate the number of deaths averted in people of 60 years and older as a result of COVID-19 vaccination. The method used in this study was based on the method used by Machado et al. [33] to study the impact of influenza vaccination programmes, mentioned in Section 3.2.1. Besides only estimating the direct impact of vaccines, other assumptions were made, especially on the vaccine effectiveness domain. Vaccine effectiveness was not differentiated by vaccine manufacturer or type, was considered the same across VOCs and was assumed not to have a waning effect. Further, booster doses were not considered, as well as changes in NPIs and healthcare capacity in response to the pandemic.

These two studies [50, 51] were the only studies found that estimated the impact of COVID-19 vaccination in more than one country. Other than these, numerous other studies that estimated the impact of vaccination either at the national or regional (within-country) level were published.

Many authors have quantified the direct impact of vaccination in national settings. Sacco et al. [52] used a method similar to Meslé et al. [51] to estimate the averted cases, hospitalisations, Intensive Care Unit (ICU) admissions and deaths by COVID-19 vaccination in Italy. Yi et al. [53] and Kayano et al. [54] estimated the direct impact of vaccination in South Korea and Japan, respectively, using a similar approach. Additionally, to compare their estimate to one considering the indirect effect of the vaccine, Kayano et al. [54] conducted an analysis using a compartmental model. It was demonstrated that indirect effects would avert more cases and deaths than those attributable to direct effects by a factor of more than a hundred and thirty, respectively. This particular result is very different from the one obtained by Watson et al. [50], which is that 79% of the deaths averted were averted through direct protection, which highlights the difficulty of calculating indirect effects of vaccination.

A plethora of studies estimated or predicted the direct and indirect impact of vaccination using mathematical modelling. Most of these were conducted in the United States of America (USA). For example, both Vilches et al. [55] and Moghadas et al. [56] used age-stratified agent-based models of COVID-19 to predict the impact that a vaccination campaign could have in regions of the USA and in the whole country, respectively. Shoukat et al. [57] used a similar model to simulate a counterfactual scenario of no-vaccination and compute the events averted by vaccination in New York City, respectively.

Regardless of their methodological differences, all the studies discussed show a positive impact of

the COVID-19 vaccination programme, that varied greatly between countries and regions.

Overall, there is a general trade-off between the methodologies used to capture both the direct and indirect effect or only the direct effect of vaccination. On the one hand, authors can use mathematical modelling to forecast and speculate scenarios of either vaccination or no vaccination, capturing the direct and indirect effect. However, these studies are very limited by its assumptions on the indirect effect of vaccination. The great difference in the results obtained by Kayano et al. [54] and Watson et al. [50] regarding the relative impact of the indirect effect, in similar time-periods of the pandemic, illustrates that very well. On the other hand, authors may take a more conservative approach and aim to model with accuracy the direct impact of vaccination, assuming that the real impact of vaccination would be even higher.

Furthermore, in impact studies, it is of utmost important to represent vaccine effectiveness as accurately as possible, as the estimates are extremely dependent on this variable. Many of the studies found in literature are limited in this regard. In fact, no study has considered the waning effect of vaccination.

3.3 Comparison of Alternative Strategies of Vaccination

3.3.1 Rationale Behind a Global Equitable Strategy

A global equitable strategy is understood here as one in which vaccine distribution is not dependent on the logic of the vaccine market. In other words, it is a strategy that allocates vaccines to all countries equitably, considering a defined prioritisation strategy (addressed below), but without regard to their economic capability to purchase vaccines. There are many reasons why a global equitable strategy should be considered:

1. First and foremost, because, in a health perspective, it is morally required to defend those who are most in need, wherever they may reside.

2. Second, the protection provided by vaccination comprises other benefits apart from the direct health ones, as vaccination also battles the socioeconomic detrimental effects of COVID-19. Vaccination can relieve the strain on healthcare systems, which has an especially significant impact in LICs and LMICs, where these systems may already be more vulnerable [12]. Not only the pressure on healthcare systems but also food security, education, transport, and commerce are all impacted by vaccination inequities, particularly in these countries where infrastructures and resources may already be strained [10]. These inequities will continue to have major and long-lasting socio-economic effects in LICs and LMICs.

3. Third, since the global workforce is a necessity for the revival of the global economy, research studies indicate that COVID-19 containment is essential [58], even for HICs.

4. Finally, if the virus continues to spread around the world because of a lack of vaccinations in crucial locations, there is a greater chance that new genetic variants may evolve. These may be more contagious and/or able to resist present vaccine formulations, making them less effective for everyone. Additionally, this may cause a future COVID-19 wave that overwhelms the already vulnerable healthcare systems of countries with the least access to vaccines, such as LICs and LMICs [13].

Many authors have already addressed the subject of vaccine nationalism and the global health need for an equitable distribution of COVID-19 vaccines, especially regarding the appearance of new VOCs. On a commentary article, Rackimuthu et al. [10] stresses that the pandemic and its variants do not respect borders and that a greater opportunity for viral transmission and mutation arises from the pandemic's temporal extension due to the vast majority of the world's population being unable to get immunized. This promotes the emergence of new, concerning variants that may be more contagious and/or virulent, as Delta and Omicron.

Wagner et al. [12] also elaborates on the subject of the emergence of new variants and emphasizes that the emergence of Omicron supports modelling studies predictions that mentioned that the only effective methods for reducing the long-term burden of COVID-19 globally are those that inhibit viral transmission and evolution globally. On a previous study, Wagner et al. [59] used models of SARS-CoV-2 dynamics in two hypothetical regions (one with high access and one with low access to vaccines) and demonstrated that sharing vaccines with countries that have low access decreases overall infections and thus clinical burden and may also mitigate potential antigenic evolution.

3.3.1.A Demographic Prioritization

Essentially, the distribution of a limited supply of vaccines among nations creates complex and contentious concerns that involve various factors. Many agree that ethics plays a crucial role in this decision-making process [60]. Taking this into consideration, another issue arises: how to allocate vaccines ethically, or fairly.

To answer this question, the WHO has proposed a fair allocation framework for the distribution of vaccines through the COVAX facility [61], shown in Figure 3.4. According to this mechanism, all countries receive doses in proportion to their population, enabling every country to start by immunizing the highest priority populations, first 3% and then 20% of population. In a second phase, when 20% of population is vaccinated, vaccines should continue to be deployed to all countries to immunize additional populations according to national priorities. This mechanism was, however, only used for the portion of vaccines distributed by the COVAX facility.

Additionally, to assist countries in optimizing the use of vaccines against COVID-19, the WHO has also proposed a roadmap for prioritizing uses of COVID-19 vaccines to be deployed within each country

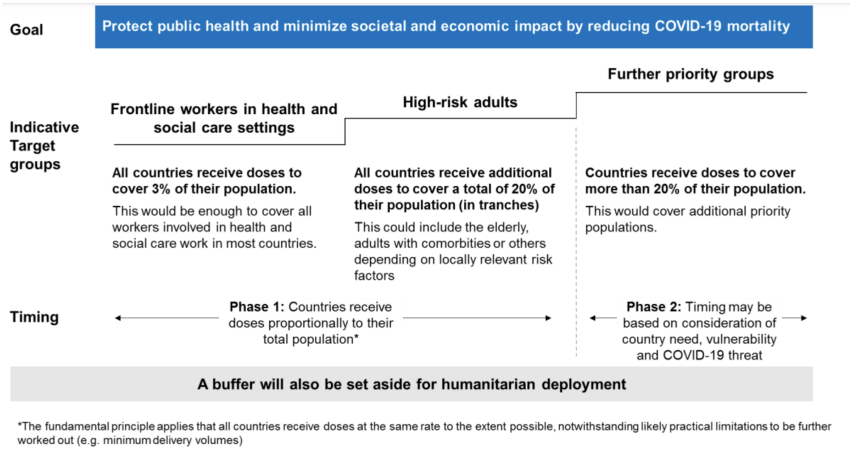


Figure 3.4: Fair allocation framework for the distribution of vaccines through the COVAX facility (retrieved from [61]).

[62]. In this roadmap, the population is divided into four groups in terms of priority: from highest to lowest. Essentially, priority populations (such as: health and other essential workers, individuals with co-morbidities or immunocompromised, older adults, *etc.*) are targeted first and then vaccination follows an age-descent order. This order according to age is based on the fact that the Infection Fatality Ratio (IFR) is estimated to form a J shape curve, with the lowest IFR occurring at 7 years of age and then showing a exponential increase with age [63].

Combining these two allocation strategies on a global scale could be an interesting option. Vaccines distributed globally using the priority-use order and allocated to each country proportionally to its population of each priority group, to account for demographic differences across countries, would ensure that the most vulnerable people in the world would be protected first. An allocation performed in such a way could have saved many lives.

3.3.1.B Epidemiological Prioritization

As mentioned in Section 3.3.1.A, the WHO has proposed a fair allocation mechanism for the distribution of COVID-19 vaccines. However, whether this mechanism is the most adequate in terms of a fair allocation of vaccines is a matter of debate. Although in Phase 2, vaccines are allocated according to threat (potential impact of COVID-19 on a country, assessed using epidemiological data) and vulnerability (the vulnerability of a country based on health systems and population factors), there is a lack of well-defined criteria in this regard.

Some authors believe that this framework, especially Phase 1, fails to account for the varying impact of COVID-19 on different countries and that it politically treats global fairness in terms of fairness among countries, instead of individuals [60, 64]. Emanuel et al. [60] developed a framework that took in consideration more variables than just the population size. It is also built in phases where the first aims

at reducing the death toll, phase 2 considers mortality but also aims at reducing economic burden and finally, phase 3 aims at reducing community transmission. Later, it was suggested that this framework could complement the one proposed by the WHO by giving priority to countries that have much greater need based on cases and premature deaths [64].

Mahajan et al. [65] also proposed a framework for the allocation of COVID-19 vaccines in India. This framework allocated vaccines to states/districts based on their expected positivity. In turn, the expected positivity is based on the total vulnerable individuals tested per day and the rate of positivity in the most recent week. The ultimate goal is to prevent the maximum number of future infections.

In short, allocating vaccines to the locations that are being the most severely hit by outbreaks of the pandemic appears as an alternative to proportional and priority group based allocation when the vaccine supply is very limited. Besides that, as the effect of NPIs is not immediate [66], such as the effect of vaccination, using vaccination as a weapon to fight local waves of the pandemic emerges as an intriguing possibility. This helps governments to avoid implementing such strict measures, hence not harming as much their economies, which is especially significant in countries that are already in a vulnerable position in this regard.

3.3.2 State-of-the-art: Comparison of Strategies of Vaccination against COVID-19

At the time of writing, September 2022, no studies were found that compared alternative scenarios for the allocation of vaccines at a global level. One study [50] attempted to model alternative global scenarios, but because more vaccines were available, it was not considered as an alternative distribution. Another study compared vaccination strategies used by different countries but did not seek to test alternative strategies [67]. On a national or regional level, several studies attempted to simulate and compare alternative strategies for the distribution of a fixed supply of vaccines [68–74]. These studies will be discussed below and a summary of their main characteristics and conclusions can be found in Table 3.2, at the end of this chapter. The discussion will be focused in the strategies tested, as the methodologies to compute the impact of vaccination programmes have already been discussed in Section 3.2.2.

In addition to estimating the impact of COVID-19 vaccination, as described in Section 3.2.2, Watson et al. [50] also evaluated how many additional deaths would be prevented by assuring that vaccination would achieve the targets set by COVAX and WHO, *i.e.*, 20% and 40% of the eligible population fully vaccinated globally, respectively. The conclusion was that 156.900 additional deaths would be averted in the first scenario and 599.300 in the second. While this is a global study, it cannot be considered as a scenario of alternative vaccination, since supply was simply increased and vaccines were not re-distributed.

Kim and Lee [67] analysed real-world epidemiological data across countries in order to evaluate the

effectiveness of different vaccination strategies, namely, the time between doses and use of different vaccine type. The authors reached the conclusion that delaying the second dose leads to better epidemiological outcomes, regarding infections and deaths, and that such affirmation is especially true for more effective vaccine types. The matter of the impact of the dosing interval in COVID-19 vaccination is very explored in the existing literature [68, 69]. The main conclusion is that bigger dosing intervals lead to better health outcomes but the waning of effectiveness after the first dose must be carefully taken into account.

Many authors have addressed the topic of demographic and epidemiological prioritization, *i.e.,* if prioritization of individuals for vaccination should be done based on their demographic characteristics (age, co-morbidities, *etc.*), on the epidemiological characteristics of their geographical location (such as COVID-19 transmissibility), or both. Zhou et al. [70] compared different strategies for vaccine allocation and hypothesized that the pandemic has a degree of spatial heterogeneity, and this must be considered, applying intervention in ”hotspots” of transmission. In fact, the strategy that achieved the best results from the ones tested, was when prioritizing both age and location. Similarly, Chapman et al. [72] also tested different strategies of vaccination in California, USA, and concluded that the scenario in which more cases, deaths and Disability-adjusted Life Years (DALYs) were avoided was when prioritizing both age and county, even considering that these authors' model only accounted for the direct effects of vaccination. Castonguay et al. [71] hypothesizes that even though the *ad hoc* principle for vaccine allocation between two areas is that of equity in distribution, there are potential economic and public health benefits in deviating from this allocation.

Another subject very debated in the existing literature is whether prioritization should be given to younger or older individuals [72–74]. There is a general consensus that the best prioritization policy depends on the goal. If the goal is to reduce the number of infections, prioritizing essential workers and overall younger individuals is a more effective strategy, whilst if the goal is to minimize mortality, prioritizing older adults and at-risk groups is more effective. In other words, there is a trade-off between minimizing infections (and thus transmission) and minimizing deaths, under different prioritization strategies [72].

Table 3.1: Summary of the main characteristics of the studies found regarding the impact of COVID-19 vaccination.

Study	Geographic Scope	Time Period	Method Type	Vaccine Effectiveness Estimate	Main Assumptions and Limitations	Outcomes
Watson et al.	Global (185 countries and territories)	First year of vaccination (8 December 2020 to 8 December 2021)	Mathematical model fitted to reported COVID-19 mortality and all-cause excess mortality	• Stratified by vaccine type (Adenovirus, Johnson&Johnson, mRNA, Subunit and Whole Virus) and VOC (Wild-Type and Delta) • Waning was not considered	No consideration of vaccine waning effectiveness and some key inputs had to be produced from assumptions: • Which types of vaccines were delivered and how they were delivered; • When new VOCs spread worldwide; • Relationship between age and IFR.	Direct and Indirect Impact: • 14.400.000 deaths prevented • 19.810.000 deaths prevented when fit to excess mortality
Meslé et al.	33 countries of the WHO European Region	December 2020 to November 2021	Calculation of Population Prevented Fraction of Direct Effect	• Not differentiated by vaccine manufacturer or type; • Considered the same across VOCs; • Waning was not considered.	• Only estimated the direct impact; • Vaccine effectiveness estimates; • Booster doses were not considered; • No consideration of changes in NPIs or healthcare capacity.	Direct Impact: • 469.186 deaths averted in people of 60+ years
Sacco et al.	Italy	January 2021 to September 2021	Calculation of Population Prevented Fraction of Direct Effect	Estimation of a Negative Binomial Generalized Linear Mixed Model with the observed number of events as a dependent variable and the vaccination status as an independent variable. Used real-life data for each event, age group and VOC.	• Only estimated the direct impact; • Vaccine effectiveness was not stratified by type; • No consideration of changes in NPIs or healthcare capacity.	Direct impact of vaccination prevented: • 445.193 cases • 79.152 hospitalizations • 9.839 ICU admissions • 22.067 deaths
Yi et al.	South Korea	13 March 2021 to 2 October 2021	Calculation of Population Prevented Fraction of Direct Effect	Calculated weekly based on the incidence rate ratio between vaccination and unvaccinated individuals	• Only estimated the direct impact; • No consideration of changes in NPIs or healthcare capacity.	Direct impact of vaccination prevented: • 46.508 cases • 3.424 severe diseases • 718 deaths
Kayano et al.	Japan	3 March 2021 to 30 November 2021	Calculation of Population Prevented Fraction of Direct Effect	Based on daily risk differences between unvaccinated and vaccinated individuals	• Only estimated the direct impact; • The averted number of hospitalizations was not consistently collected over time; • Assumption that all individuals vaccinated with a first dose received a second dose at a constant interval; • No consideration of waning immunity.	Direct impact of vaccination prevented: • 564.596 cases • 18.622 deaths
Vilches et al.	Northeastern and southern regions of USA	September 2021 to March 2022	Projective study: Age-stratified agent-based model of COVID-19 calibrated to reported incidence from the past	Derived from published studies, accounting for different vaccine types, variants, and timelines for generation of immunity after the first and second dose	• No consideration of waning immunity; • Some model parameters were considered to be constant (mean vaccine efficacies, relative transmissibilities of SARS-COV-2 variants, and the risk of outcomes with different variants)	50% increase in daily vaccine doses administered is projected to prevent a total of 30.727 hospitalizations and 11.937 deaths in the two regions, from the direct and indirect effect of vaccination.
Shoukat et al.	New York City	14 December 2020 to 15 July 2021	Age-stratified agent-based model of COVID-19 calibrated to reported incidence to simulate no vaccination	Published estimates to parameterize vaccine efficacies following each dose of vaccines against infection, symptomatic disease, and severe disease caused by the original strain.	• Underreporting of cases; • Only the contact patterns of fully vaccinated individuals were assumed to revert to pre-pandemic level; • No consideration of vaccine waning immunity;	Direct and indirect impact prevented: • 290.467 case • 48.076 hospitalizations • 8.508 deaths
Moghadas et al.	USA	300 days after start of vaccination	Projective study: Age-stratified agent-based model of COVID-19	Considered a vaccine efficacy of 95% against disease following 2 doses administered 21 days apart.	• Model parameter definition; • Poor representation of vaccine efficacy: no waning, not differentiated by type, etc..	Direct and indirect impact of vaccination reduced the overall attack rate to 4.6% from 9.0%. hospitalizations, ICU hospitalizations, and deaths decreased by 63.5%, 65.6% and 69.3%, respectively.

Table 3.2: Summary of the main characteristics of the studies found regarding the comparison of COVID-19 vaccination strategies.

Type of Strategies Tested	Study	Geographic Scope	Type of Study	Main Conclusions
Global Access: • **Achieve COVAX targets** • **Achieve WHO targets**	Watson et al.	Global	Alternative Outcomes Considering More Vaccines	• 156 900 deaths averted if COVAX targets (20% of population vaccinated) were met; • 599 300 deaths averted if WHO targets (40% of population vaccinated) were met.
Dosing Interval	Kim and Lee	Canada, United Kingdom, Israel, USA, Chile, Uruguay, United Arab Emirates, Bahrain	Comparison of Strategies Used by Different Countries	• Delaying the second dose leads to better epidemiological outcomes regarding infections and deaths; • When using less effective vaccines from other manufacturers, this is not so prominent because the marginal gain from the second dose is greater than for more effective vaccines, which are already very effective with the first dose.
	Tokuda et al.	Japan	Comparison of Alternative Strategies	• One-dose vaccination (i.e., interval extension strategy) and/or low-dose vaccination (i.e., half a dose strategy) to a higher proportion of the population obtains better results when confronted with a limited supply of vaccines compared to following manufacturers recommendations.
	Liu et al.	13 middle-income countries of Europe	Comparison of Alternative Strategies	• Optimal strategies are those that prioritise the first doses, which lead to dosing intervals longer than six months; • If considering the rapid waning of the immunity induced by the first dose, the shorter optimal dosing intervals if of 8-20 weeks.
Demographic vs. Epidemiological Prioritization	Zhou at al.	Guangzhou, China	Comparison of Alternative Strategies	• The strategy that achieved the best results from the ones tested, was when prioritizing both age and location (*i.e.,* areas with the highest herd immunity rate spreading naturally).
	Castonguay at al.	2 distinct hypothetical jurisdisctions	Optimal Allocation Assessment	• Although the principle of COVAX is that of equity in distribution, this study shows that there are potential economic and public health benefits in deviating from this allocation. The optimal distribution obtained, by contrast, is based on the principle of equity in outcomes.
	Chapman et al.	California, USA	Comparison of Alternative Strategies and Optimal Allocation Assessment	• The scenario in which more cases, deaths and DALYs were avoided was when prioritizing both age and county; • The optimal allocation strategy was also obtained and it showed that *"older individuals would still be prioritized under optimal allocation, but the proportion of individuals vaccinated would also vary considerably by county of residence, sex, race/ethnicity, and special population and comorbidity status"* .
Older vs. Younger Individuals Prioritization	Ferranna et al.	USA	Comparison of Alternative Strategies	• Even if vaccine blocks transmission, prioritising older people leads to fewer deaths; • Prioritizing essential workers leads to fewer infections and YLL. • It is recommended to use other strategies to promote equity such as prioritising specific populations at higher risk within the given groups - further fragment the population at risk level, also geographically.
	Cattaneo et al.	Lombardy region, Italy	Comparison of Alternative Strategies	• To minimize infections, the best policy is dependent on dose availability. If at least 1/3 of the population can be covered in 4 months, targeting at-risk individuals and the elderly first is recommended; otherwise, the youngest people should be vaccinated first; • To minimize overall deaths, priority is best given to at-risk groups and the elderly in all scenarios.

4

Methodology

Contents

This chapter describes the methodology proposed for the comparison of alternative scenarios of vaccination against COVID-19. An outline of this analysis is first described in Section 4.1, presenting the structure of the analysis and how each dataset interacts. Then, information regarding the input data of the analysis, its extraction, and the strategies used to deal with data incompleteness, are all reported in Section 4.2. The framework behind each of the alternative vaccination strategies considered is explained in detail in Section 4.3, with the strategies being:

1. Global Age-based Demographic Prioritization
2. Global Case-based Epidemiological Prioritization
3. Both Demographic and Epidemiological Prioritization

Subsequently, the mathematical formulation behind outcomes estimation is described in Section 4.4. Finally, a description of the uni-variate sensitivity analyses performed are reported in Section 4.5.

4.1 Analysis Outline

A graphic representation of the structure of the analysis and how each dataset interacts is shown in Figure 4.1. Blue and red arrows represent processes required to compute the impact of observed vaccination and the impact of alternative vaccination strategies, respectively. A description of this analysis outline is also provided below.

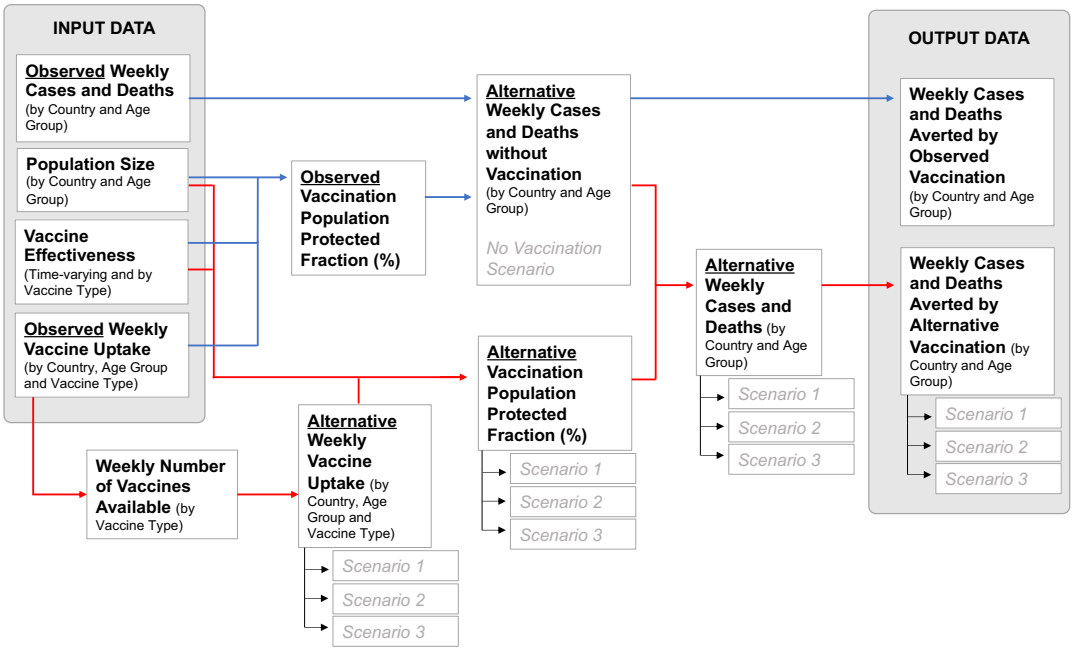


Figure 4.1: Analysis structure and data interaction.

To compare the impact of observed vaccination and of alternative scenarios of vaccination, the analysis proposed uses several data inputs. Data regarding population, Vaccine Effectiveness (VE) and Vaccine Uptake (VU) are used to compute the rate of observed protection in the population. This rate, together with the observed cases and deaths counts, allow to calculate the number of cases and deaths in a scenario of no vaccination and thus, the number of cases and deaths directly averted by observed vaccination. These calculations are explained in detail in Section 4.4.1.

To compute the impact of the alternative scenarios, an identical method is used but the number of cases and deaths in a scenario of no vaccination (computed previously) is used as the baseline. For each of the scenarios, the rate of protection in the population is calculated based on the inputs of VE and population size and the simulated alternative VU. This alternative VU is simply a re-distribution of the available vaccines, according to the framework for the allocation of vaccines that is being tested in each of the scenarios. The ”rules” for the allocation of vaccines in each scenario are explained in detail in Section 4.3. In turn, the procedure to calculate the number of averted events in alternative scenarios is explained in Section 4.4.2.

The outputs of this analysis, or study outcomes, are then the weekly number of cases and deaths averted in each scenario of vaccination, including the observed. These counts are stratified by country and age group and allow for the comparison of the direct effect of different vaccination strategies.

4.2 Input Data Extraction and Cleaning

The analysis is based on COVID-19 epidemiological and vaccination data available from public data sources. Data were collected from ISO Week 50 of 2020 (start of vaccination) until the end of 2021, for the 180 countries included. The enumeration of the countries considered, along with their classification by WHO region and income group can be found in Appendix A, Section A.1. In all datasets, data were structured by weeks and age groups (0-24, 25-49, 50-59, 60-69, 70-79, 80+), for the time period mentioned. Software R version 4.0.3 was used to perform the data cleaning.

Cases and Deaths

Data regarding cases and deaths were retrieved from two public datasets:

- WHO COVID-19 Detailed Surveillance Data [75];
- Our World in Data (OWID) COVID-19 dataset [76].

WHO data were prioritised as they allowed for weekly counts of cases and deaths by age group, whereas OWID data were not broken down by age group. OWID data were then used for countries that

were not included in the WHO dataset or where the number of cases and deaths was significantly lower in the WHO dataset compared to the OWID dataset due to the need of reporting by age group, *i.e.,* the relative difference between the two datasets compared to OWID was higher than 25% for either cases or deaths, indicating that more than 25% of cases or deaths were unreported.

In countries where WHO data were used, cases and deaths were simply grouped in the age groups considered in the study. In this process, there was a need to divide cases and deaths from the 20-29 age group. Thus, for each country, these cases and deaths were divided into the age groups 20-24 and 25-29, proportionally to the population from these age groups.

In countries where OWID data were used, it was necessary to infer the breakdown of total weekly cases and deaths by age group. For this, a weekly distribution pyramid of cases and deaths by age group for each country was required. If both the number of cases and deaths in that week was substantial in the WHO dataset, the pyramid was based on the distribution of those cases and deaths. In case that was not possible, if both the number of cases and deaths for the whole time period was substantial in the WHO dataset, the pyramid was based on the distribution of those cases and deaths. Finally, if none of these two options were viable, the distribution was based on the age and sex pyramids of cases and deaths for each WHO Region, also available in the WHO COVID-19 Detailed Surveillance Data Dashboard [75].

In the end, data regarding Cases and Deaths were organized in a table as exemplified in Table 4.1.

Table 4.1: Cases and Deaths dataset structure and example.

Country	ISO Date	Age Group	Weekly Cases	Weekly Deaths
PT	2020 W50	0-24	5644	1
...	...	...	...	...

Vaccine Uptake

Data regarding VU were retrieved from two public data sets:

- European Centre for Disease Prevention and Control (ECDC) – Data on COVID-19 vaccination in the European Union/European Economic Area (EU/EEA) [77];
- OWID COVID-19 dataset [76].

Data from the ECDC dataset were used for the 30 countries in the EU/EEA. In most countries, data were available by week, age group and vaccine manufacturer, so data were simply filtered for the time period and the age groups of the study. In 4 countries, further assumptions had to be made, such as:

- **France** - Distribution of vaccines according to vaccine manufacturer was only available for the whole population, instead of being available by age group. In each week, for each age group, vaccines were divided by vaccine manufacturer proportionally to the number of vaccines of that manufacturer given to the whole population.
- **Germany, Netherlands and Romania** - Distribution of vaccines by age group was not available. Vaccines given to the whole population were then divided by age group using the algorithm of distribution of vaccines by age group used to ”reproduce” the observed VU (Figure 4.2).

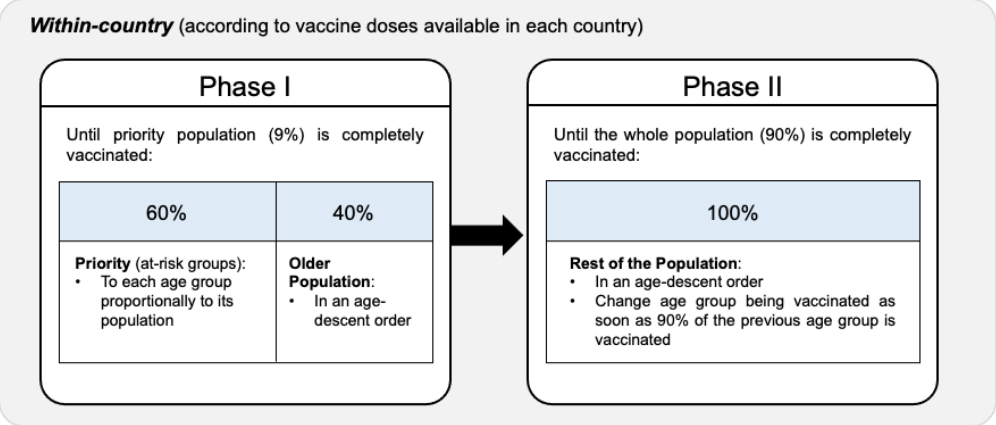


Figure 4.2: Distribution of vaccines by age group to ”reproduce” observed VU.

The framework shown in Figure 4.2 considers that priority groups (health workers, immunocompromised individuals, essential workers, *etc.*) are vaccinated first, according to the WHO SAGE Roadmap for prioritizing uses of COVID-19 vaccines [62] and that these groups comprise 9% of population, as in the first phase of the Portuguese Vaccination Plan against COVID-19 [78]. Additionally, an age group (including the priority one) was assumed completely vaccinated when 90% of its population was vaccinated, due to vaccine hesitancy.

Data from the OWID COVID-19 dataset were used for the rest of the countries and territories in the study. As this dataset had a higher degree of incompleteness, data preparation was more thorough, including the following steps:

1. Sub-setting for the time period of the study;
2. Replacement of missing values (*NA*) by the last possible value (or 0, if none) because data were organized cumulatively;
3. Change of data from cumulative to weekly by subtracting numbers from the previous week;

4. Distribution of vaccines by manufacturer as the only information available was the vaccines in use in each country in each week - they were divided equally between manufacturers;
5. Distribution of vaccines by age group using the framework described in Figure 4.2.

In the end, data regarding VU were organized in a table as exemplified in Table 4.2.

Table 4.2: Vaccine Uptake dataset structure and example.

Country	ISO Date	First Dose	Second Dose	Dose Additional 1	Dose Additional 2	Age Group	Vaccine
PT	2020 W52	176	0	0	0	0-24	Pfizer/BioNTech
...	...	...	...	...	...	...	...

Vaccine Efficacy/Effectiveness

Based on available studies [79–85] and the WHO [62], there is a substantial waning of VE in the time period of the study (*i.e.*, over the span of 1 year) if boosters are not administered, so it was considered time-varying. Hence, functions of VE according to week after vaccination, $VE(w)$, both against infection and death, were estimated based on literature [79–92]. The graphs of the functions of VE for each vaccine manufacturer/type and more information regarding VE can be found in Appendix A, Section A.2. Due to lack of data, the following assumptions had to be made to compute VE functions:

- In general, when available, real-world studies that estimated vaccine effectiveness were prioritized. When these were not available for the vaccine manufacturer or type in cause, vaccine efficacy estimates from clinical trials were used. Hence the use of the term effectiveness throughout the study.
- VE was considered the same across age groups, across countries and across COVID-19 variants.

However, the major assumption of this analysis is that only the direct effect of vaccination is considered. Although vaccine effectiveness aims to represent the real-world effect of the vaccines and some authors argue that it also captures some indirect effects [32, 34, 35], when evaluating the impact of observed vaccination, the estimate provided by this analysis is conservative as the indirect effect of vaccination is not taken into account. It is expected that the number of averted events from observed vaccination is even higher, as the vaccine also contributes to a reduction in transmission.

Countries Socio-demographic Information

The population of each country along with its age and sex distribution was retrieved from United Nations – World Population Prospects 2019 [93]. Data regarding income group classification were retrieved from The World Bank [94].

4.3 Distribution of Vaccines in Alternative Scenarios

In light of the arguments provided in Section 3.3, three alternative strategies for the global allocation of vaccines against COVID-19 are considered:

- **Strategy 1** - Global Age-based Demographic Prioritization
- **Strategy 2** - Global Case-based Epidemiological Prioritization
- **Strategy 3** - Mixed Demographic and Epidemiological Prioritization

The distribution of vaccines in these alternative scenarios, also called alternative VU matrices, were simulated using Software R version 4.0.3. The total weekly number of vaccines available was kept identical and vaccines were re-distributed according to the framework of each scenario. More details regarding how vaccines are distributed in each of the alternative scenarios considered are thereafter provided.

4.3.1 Strategy 1 - Global Age-based Demographic Prioritization

Vaccines are distributed as shown in Figure 4.2 but disregarding countries' borders. In other words, the number of vaccines available is the sum of vaccines that were given in the observed vaccination from all countries, and these are re-distributed globally. Each age group of each country receives vaccines proportionally to its population, and the vaccination follows an age-based prioritization which starts by allocating vaccines to priority (at-risk) groups and then continues in an age-descent order. Figure 4.3 schematizes this distribution.

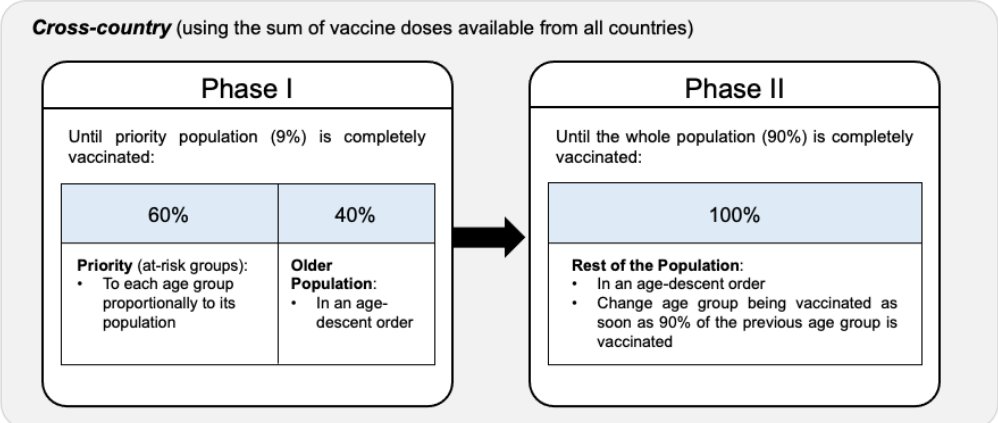


Figure 4.3: Distribution of vaccines according to Scenario 1 (Global Age-based Demographic Prioritization).

Each week, the algorithm developed for the distribution of vaccines in this scenario allocates the available supply of vaccines in the following order:

1. Second Doses: for individuals that have been administered the first dose of a two-dose primary series of vaccination;
2. Boosters: exclusively for 60+ and at-risk individuals;
3. First Doses: for the rest of the population following the rules aforementioned regarding prioritization (Figure 4.3).

This prioritization framework was based on the WHO SAGE Roadmap for prioritizing uses of COVID-19 vaccines [62]. In that document, the World Health Organization [62] states that:

"within a given priority-use group, primary series vaccination will have greater impact per dose than booster doses"

and

"across priority-use groups, increasing the booster dose coverage rate for higher priority-use groups will usually yield greater reductions in severe disease and death than use of equivalent vaccine supply to increase the primary vaccination series coverage rates of lower priority-use groups".

4.3.2 Strategy 2 - Global Case-based Epidemiological Prioritization

Each week, vaccines are allocated to countries proportionally to their number of cases from the previous week. Then, in each country, vaccines are distributed in the population in an age-descent order giving priority to at-risk groups. The distribution is schematized in Figure 4.4.

Each week, the algorithm developed for the distribution of vaccines in this scenario allocates the available supply of vaccines in the following order:

1. Second Doses: for individuals that have been administered the first dose of a two-dose primary series of vaccination;
2. First Doses: the rest of the population following the rules aforementioned regarding cross-country prioritization (Figure 4.4).

The benefits of booster doses for higher priority-use groups versus primary series doses for lower priority-use groups depends on countries' conditions [62]. As the allocation of vaccines in this scenario is especially sensible to each countries epidemiological condition, the choice of only allocating boosters after having all primary series completed was done, since the overall goal of this strategy is to allocate quick vaccination efforts (primary series) to locations where there is more COVID-19 transmission. Therefore, as in the study period there were not enough vaccines to complete all primary series vaccinations, boosters were not used.

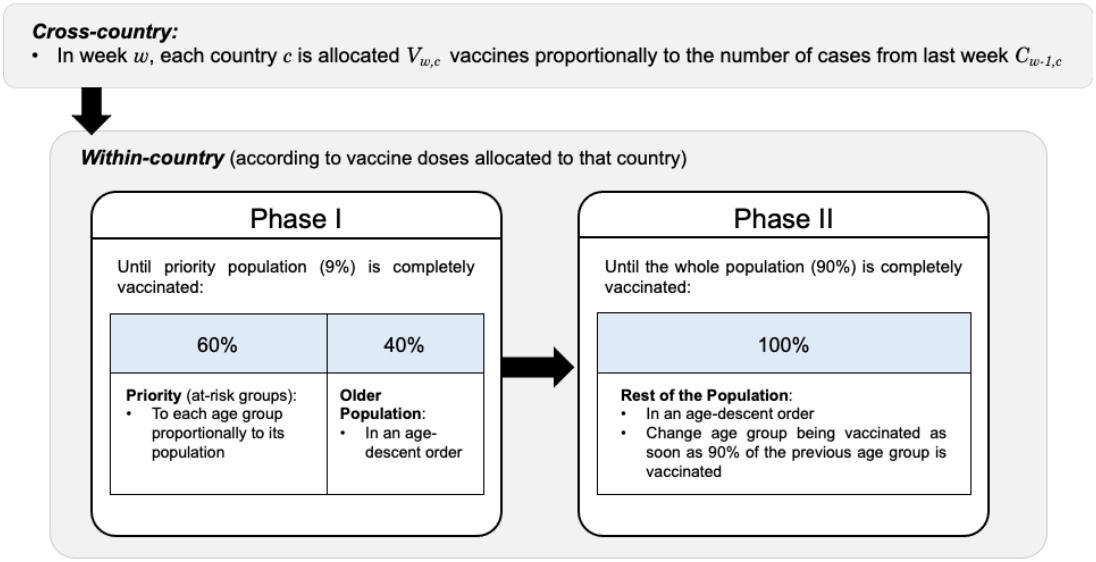


Figure 4.4: Distribution of vaccines according to Scenario 2 (Global Case-based Epidemiological Prioritization).

4.3.3 Strategy 3 - Mixed Demographic and Epidemiological Prioritization

As described in Section 3.3, the best strategies may be the ones that focus on more than one factor. In fact, immunizing high-risk populations to decrease mortality, but also targeting areas where the transmission rates of COVID-19 are high, achieved the best results in some comparison studies [70, 72]. Thus, Strategy 3 aims to cover these two dimensions by allocating 50% of vaccines according to Strategy 1 (Figure 4.3) and 50% of vaccines according to Strategy 2 (Figure 4.3) in each week (Figure 4.5).

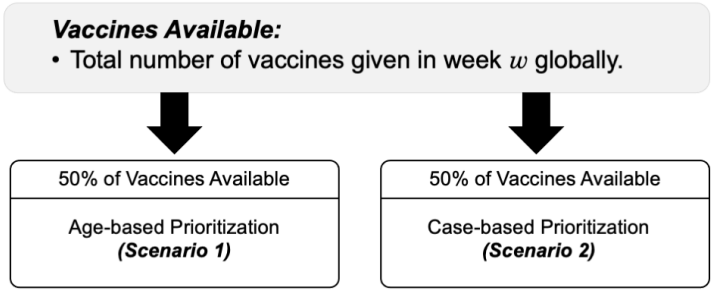


Figure 4.5: Distribution of vaccines according to Scenario 3.

4.3.4 General Considerations

Some general considerations were made when distributing vaccines that were common across all scenarios. These are discussed below.

Homologous/Heterologous Vaccination Schemes

No heterologous vaccination schemes were explored, second doses and boosters were always administered in accordance with the initial dose manufacturer, following an homologous vaccination scheme.

Time Interval Between Doses

The interval between doses varies across vaccine manufacturers and has also varied over time and different countries. Therefore, assumptions had to be made regarding this variable. As the goal of this study was not to assess the impact of varying the time interval between doses, these intervals were chosen in order to be as similar to the ones observed as possible. Consequently, as the time interval between first and second doses of the primary series of vaccination is close to 4 weeks in most vaccine manufacturers [95], this was the time interval considered for almost all vaccine manufacturers considered. The only exception was for the Oxford/AstraZeneca vaccine, since many countries were using 12-week intervals in the beginning of vaccination [96, 97]. Thus, the time interval between first and second doses of the primary series of vaccination was considered to be 12 weeks for this vaccine. Regarding boosters, when used, these were administered 6 months after the last dose of the primary series vaccination, according to the time-frame recommended by the WHO [62].

4.4 Mathematical Formulation for Outcomes Estimation

4.4.1 Impact of COVID-19 Vaccination

To measure the direct worldwide impact of the observed COVID-19 vaccination programme, a counterfactual scenario of no vaccination was obtained and the number of cases and deaths directly prevented were computed.

In light of the definition of PPF given in Section 3.2.1, the number of events (in this case, cases or deaths) that occur in a population with a certain observed vaccination, $Events(OV)$, can be written considering the PPF and the number of events that would occur in a scenario of no vaccination, $Events(NV)$, as shown in Equation 4.1.

$$Events(OV) = Events(NV) - Events(NV) \times PPF \tag{4.1}$$

Which is equivalent to writing that the number of events in a no vaccination scenario would be calculated as in Equation 4.2.

$$Events(NV) = Events(OV) \times \frac{1}{1 - PPF} \tag{4.2}$$

The PPF can be dissected as the PPF that come from each of the 4 different possible vaccine doses (Equation 4.3). The four different doses d correspond to the most well-known first and second doses as well as the first additional dose (or first booster) and the second additional dose (or second booster). Those doses will be referred to as doses 1 to 4, respectively.

$$PPF = PPF_{d=1} + PPF_{d=2} + PPF_{d=3} + PPF_{d=4} \tag{4.3}$$

Considering a vaccine effectiveness VE against an event e (infection or death) and vaccine coverage VC, in a certain week w, the PPF from a certain dose d can be written as the sum of products of VE by VC for each of the past weeks and vaccine type/manufacturers v (Equation 4.4), considering the definition of PPF given in Section 3.2.1, Equation 3.3. In turn, VC can be written as the ratio between the number of individuals vaccinated and the number of individuals from that age group and country (N). It is also important to note that the number of events as well as the PPF are stratified by country and age group, so, such information is not displayed in the equations shown.

$$PPF_{d,w} = \sum_{i=1}^{w-1} \sum_{v} VE_{v,e,d}(i) \times \frac{N_{v,w-i,d}}{N} \tag{4.4}$$

$N_{v,w-i,d}$ corresponds to the number of individuals that took dose d from vaccine v in week $w - i$ and by the time PPF is being computed (week w) still haven't taken the next dose in the scheme, dose $d+1$.

Thus, the number of cases and deaths in a counterfactual scenario of no vaccination, can be calculated as in Equation 4.5 when considering functions of VE against infection and Equation 4.6 when considering functions of VE against death, respectively.

$$Cases(NV) = Cases(OV) \times \frac{1}{1 - \sum_{d=1}^{4} \sum_{i=1}^{w} \sum_{v} VE_{v,e=infection,d}(i) \times \frac{N_{v,w-i,d}}{N}} \tag{4.5}$$

$$Deaths(NV) = Deaths(OV) \times \frac{1}{1 - \sum_{d=1}^{4} \sum_{i=1}^{w} \sum_{v} VE_{v,e=death,d}(i) \times \frac{N_{v,w-i,d}}{N}} \tag{4.6}$$

The number of events directly averted by the observed COVID-19 vaccination programme, country and age-stratified, can then be obtained by calculating the difference between the observed events and the events estimated in the counterfactual no vaccination scenario. The number of cases and deaths averted are shown in Equations 4.7 and 4.8, respectively.

$$Cases(Averted) = Cases(NV) - Cases(OV) \tag{4.7}$$

$$Deaths(Averted) = Deaths(NV) - Deaths(OV) \tag{4.8}$$

4.4.2 Impact of Alternative Scenarios of Vaccination

The impact of each alternative scenario is evaluated by estimating the number of cases and deaths that would occur in each of the counterfactual scenarios. This calculation is done similarly to what was stated in Section 4.4.1 for the impact of observed vaccination. Instead of building upon the number of cases and deaths observed, it is built upon the number of cases and deaths obtained from in the scenario of no vaccination, computed previously. From the definition of PPF, Equation 4.9 is obtained, where AV refers to Alternative Vaccination and NV refers to No Vaccination.

$$Events(AV) = Events(NV) \times (1 - PPF) \tag{4.9}$$

Then, replacing the PPF as stated in Equations 4.3 and 4.4, the number of cases and deaths that would occur in a scenario of alternative vaccination is obtained. For each of the alternative scenarios, the number of cases, $Cases(AV)$, and deaths, $Deaths(AV)$, are computed as shown in Equations 4.10 and 4.11, respectively. To note that what differentiates the results obtained in each scenario is the fact that the matrix of vaccination given is different. Thus, $N_{v,w-i,d}$, the number of individuals that took dose d from vaccine v in week $w - i$ and by the time PPF is being computed (week w) still haven't taken the next dose, will vary while the other parameters remain the same.

$$Cases(AV) = Cases(NV) \times (1 - \sum_{d=1}^{4} \sum_{i=1}^{w} \sum_{v} VE_{v,e=infection,d}(i) \times \frac{N_{v,w-i,d}}{N}) \tag{4.10}$$

$$Deaths(AV) = Deaths(NV) \times (1 - \sum_{d=1}^{4} \sum_{i=1}^{w} \sum_{v} VE_{v,e=death,d}(i) \times \frac{N_{v,w-i,d}}{N}) \tag{4.11}$$

In turn, the number of events averted in each of the scenarios, in comparison to no vaccination, is calculated as in Equations 4.7 and 4.8, by replacing $Events(OV)$ by $Events(AV)$, for both cases and deaths, respectively.

4.5 Sensitivity Analysis

Taking into consideration the underlying uncertainty associated with vaccine effectiveness and the multiplicity of assumptions made regarding this variable, two uni-variate sensitivity analyses were performed by varying vaccine effectiveness by $+10$ and -10 percentage points, not going beyond the minimum and the maximum of 0% and 100% of vaccine effectiveness, respectively.

5

Results and Discussion

Contents

This chapter starts by individually presenting the impact results obtained for each of the strategies of vaccination, starting by the observed (Section 5.1) and then the alternative strategies (Section 5.2).

Then, a comparison and discussion of the key differences between strategies is done in Section 5.3. A summary of the results is first provided and then the impact over time (Section 5.3.1), by income group (Section 5.3.2) and by age group (Section 5.3.3) are further discussed.

Finally, a discussion of the limitations of the study is provided in Section 5.4 and a summary of the main contributions and recommendations towards the improvement of vaccine distribution strategies are presented in Section 5.5.

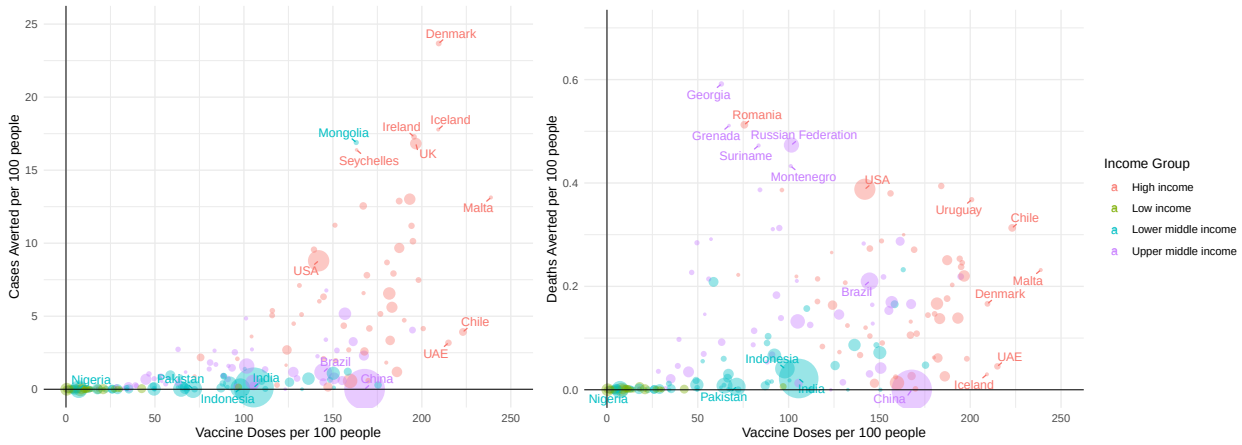
5.1 Impact of Observed Vaccination

Using the methodology described in Chapter 4, it was estimated that, approximately, 327.7 million infections and 9.2 million deaths of COVID-19 would have occurred worldwide in a scenario of no vaccination, since the beginning of vaccination (8 of December 2020) and until the end of 2021. Of these, it was estimated that the direct effect of observed vaccination prevented 105.3 million infections (32.1%) and 5.5 million deaths (59.8%). These results, also stratified by WHO Region, Income Group and Age Group, are shown in Table 5.1.

Table 5.1: Observed Vaccination: Observed events, estimated events averted and events averted per 100 people.

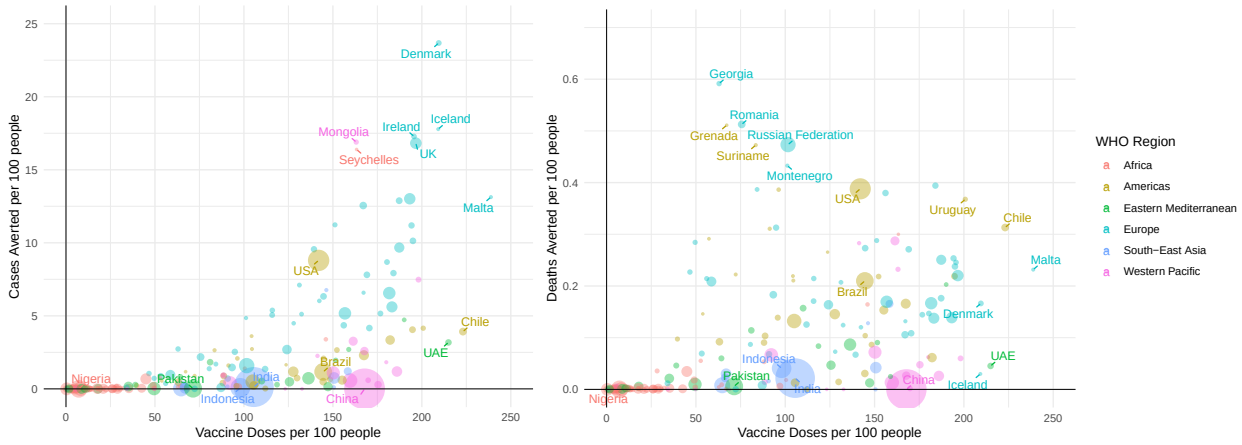
	Cases Observed	Deaths Observed	Cases Averted	Deaths Averted	Cases Averted per 10000	Deaths Averted per 10000
Worldwide	222 373 578	3 746 908	105 363 626	5 469 460	136.48	7.09
WHO Region						
Eastern Mediterranean	12 528 073	204 239	1 872 427	183 834	25.80	2.53
Africa	5 693 645	120 701	623 235	35 712	5.58	0.32
Europe	82 803 328	1 204 375	56 796 505	2 122 502	608.92	22.76
Americas	76 733 954	1 535 256	37 513 062	2 317 422	368.50	22.77
Western Pacific	10 673 688	136 860	5 724 334	296 383	29.64	1.53
South-East Asia	33 940 890	545 477	2 834 063	513 607	14.20	2.57
Income Group						
Low income	1 485 459	33 219	51 159	6 481	0.78	0.10
Lower middle income	50 156 280	891 386	6 148 587	908 414	18.56	2.74
Upper middle income	63 070 646	1 510 599	16 046 246	2 054 161	62.84	8.04
High income	107 661 193	1 311 704	83 117 634	2 500 404	692.53	20.83
Age Group						
0-24	59 477 821	50 844	6 183 057	2 408	19.51	0.01
25-49	100 584 684	415 037	50 398 758	166 927	187.24	0.62
50-59	29 134 963	482 204	19 195 964	386 061	233.11	4.69
60-69	18 426 339	788 040	13 887 791	898 256	237.69	15.37
70-79	9 352 458	900 985	9 367 846	1 531 629	303.75	49.66
80+	5 397 313	1 109 798	6 330 210	2 484 179	441.28	173.17

Furthermore, to estimate the impact of the number of vaccine doses administered in the number of events averted, graphs showing the interaction of these two variables, stratified by income group and WHO region can be seen in Figures 5.1 and 5.2, respectively.



((a)) Cases **((b))** Deaths

Figure 5.1: Observed Vaccination: Events averted against vaccine doses (per 100 people) stratified by income group. Point size is proportional to each country's population.



((a)) Cases **((b))** Deaths

Figure 5.2: Observed Vaccination: Events averted against vaccine doses (per 100 people) stratified by WHO region. Point size is proportional to each country's population.

Cases Averted per Vaccine Doses Administered

Regarding the number of cases averted, the vaccine doses administered appear roughly as a limiting factor, indicating that it is difficult to avert high proportions of cases without achieving high vaccination rates. However, it is possible to achieve high immunization rates and not show a considerable impact in the number of cases averted. In light of Equations 4.5 and 4.7, this can happen for two reasons: these countries use less effective vaccines or have a lower number of cases at the baseline.

Deaths Averted per Vaccine Doses Administered

However, the relationship discussed regarding cases is not so pronounced when considering the number of deaths averted. It is possible to have low vaccination rates but still experience a high impact in the number of deaths averted, and vice-versa. A possible explanation for this disparity between cases and deaths on the association of the number of events and vaccination rates may be the fact that vaccines' waning effectiveness is much more prominent against infection [62], requiring more vaccine doses for the effect of the vaccine to be felt.

Events Averted per Vaccine Doses Administered across Income Groups

As shown in Figure 5.1, HICs are the ones with both the highest vaccination rates and the highest impact on infections' prevention. Some UMICs are able to achieve comparable vaccination rates but don't see this immunization as reflected in the number of cases averted, mostly because these countries have limited access to more effective vaccines, such as mRNA vaccines, contrasting with HICs [98].

Contrarily, regarding deaths, some UMICs show the highest impact of vaccination in averting deaths even with low vaccination rates, whilst some HICs have high vaccination rates but do not have a matching impact in deaths' prevention. This can happen because the healthcare systems of most of HICs have more resources and are generally better equipped to deal with the pandemic, allowing these countries to have a smaller death toll, and thus seeing fewer effects from their vaccination campaigns on this dimension. Further, the difference in effectiveness between vaccine manufacturers/types aforementioned is less prominent against death.

It is also important to note that, while on Figure 5.1(b), the countries with the highest impact on the prevention of deaths appear to be mostly UMICs, other very populous UMICs like China, have pursued a zero-COVID approach, reporting very few deaths, which contributes to the overall impact on deaths shown in Table 5.1 to be higher in HICs.

LICs and LMICs, especially the first group, show both the lowest vaccination rates and the lowest impact in the number of events averted.

These results of impact are also confirmatory in the sense that they demonstrate not only inequalities in terms of vaccination, but also in the impact between different income groups.

Events Averted per Vaccine Doses Administered across WHO Regions

Figure 5.2 explores the impact of vaccination rates in cases and deaths by WHO region. The difference between regions is not as pronounced as between income groups.

As can be confirmed in Table 5.1, Europe appears as the WHO region with the highest impact of vaccination in infections, whereas in deaths, the biggest impact is seen in both Europe and the Americas.

A noteworthy region is the Western Pacific. Despite the achievement of high vaccination rates in several countries, the impact in infections and deaths is not very high since many countries in this region (such as New Zealand, Australia, Singapore, Japan, South Korea, Vietnam and China) aimed for zero-COVID policies [99]. Mongolia, on the other hand, had one of the highest rate of cases observed, and thus felt very strongly the impact of vaccination. Countries with zero-COVID policies set zero deaths as a goal and apply short-term lockdowns, followed by stringent find, test, trace and isolate methods to achieve this objective. Contrarily, most countries in Europe and some in America have followed a mitigation strategy, framed as ”flattening the curve”, which aims to reduce spread only until targets are met, to avoid overwhelming healthcare systems [99].

The African region stands out negatively by displaying both low vaccination rates and low impact in the number of events averted.

Overall Impact of the Observed Vaccination Strategy

Generally, the biggest impact of vaccination was seen in the nations that had administered the most vaccines by the end of 2021 while also easing off on NPIs, allowing SARS-CoV-2 transmission to rise, *i.e.,* showing high numbers of infections and/or deaths. By contrast, the nations with slower vaccine roll-outs as well as those pursuing zero-COVID policies which continued to implement harsher NPIs to stop transmission, saw fewer effects from their vaccination campaigns.

As shown in Table 5.1, Europe and the Americas were the WHO regions with the highest density of cases and deaths averted, respectively, while Africa had the lowest in both. Regarding income group, HICs were the ones with the highest density of cases and deaths averted and LICs had the lowest density. These results are in line with the ones obtained by Watson et al. [50]. However, the number of deaths averted by vaccination obtained by these authors (14.4 million) is significantly higher than the estimate provided by the present analysis. This was expected as Watson et al. [50] aims to model both the direct and indirect impact of vaccination.

In contrast, the estimates provided by this analysis are broadly comparable to others focused on the direct effect of vaccination [51–54]. For the same 33 European countries and time period, the analysis herein described estimated that 510 921 deaths were averted as a direct effect of vaccination in the population aged 60 years and older, approximately 8.9% more than the 469 186 deaths obtained by Meslé et al. [51]. Additionally, this analysis estimated that 496 935 cases and 33 365 deaths were averted in Italy from January to September 2021, compared to the 445 193 cases and 22 067 deaths obtained by Sacco et al. [52]. In South Korea, this analysis estimated that 72 658 cases and 1 699 deaths were averted, while Yi et al. [53] estimated that 46 508 infections and 718 deaths were averted in the same time period. Finally, in Japan, Kayano et al. [54] estimated that 564 596 cases and 18 622 deaths were averted, while the results provided by this analysis suggest that 710 004 cases and 16 640

were averted.

5.2 Impact of Alternative Strategies of Vaccination

5.2.1 Strategy 1 - Global Age-based Demographic Prioritization

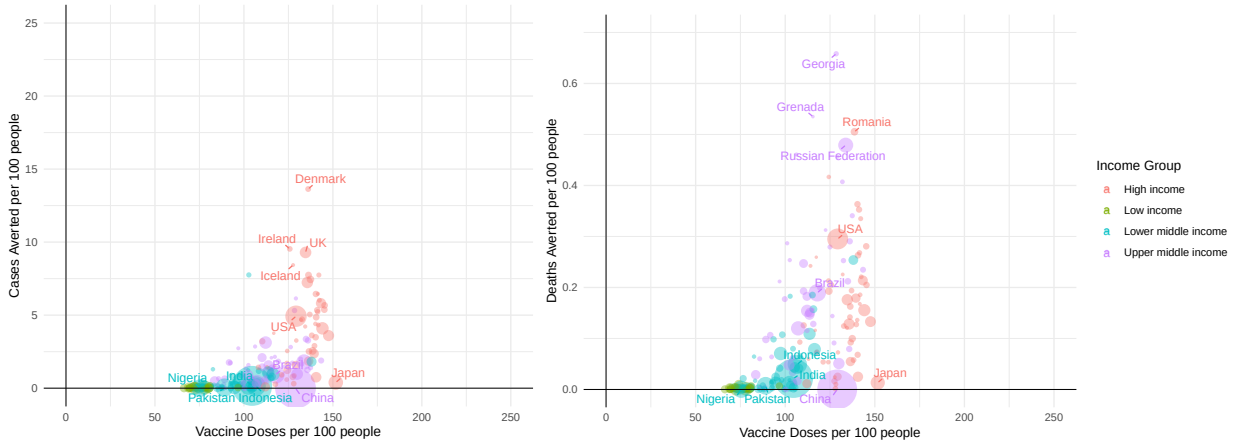
The alternative number of cases and deaths, cases and deaths averted and averted per 10000 people, using Strategy 1, are shown in Table 5.2. Using the methodology described in Chapter 4, it was estimated that, approximately, 257.7 million infections and 4.1 million deaths of COVID-19 would have occurred worldwide in this scenario of vaccines' allocation, since the beginning of vaccination (8 of December 2020) and until the end of 2021. As the number of cases and deaths without vaccination is the same as aforementioned (327.7 million infections and 9.2 million deaths), it was estimated that, in this scenario, the direct effect of vaccination prevented 70 million infections (21.4%) and 5.1 million deaths (55.4%). These results, stratified by WHO Region, Income Group and Age Group, are also shown in Table 5.2. In general, this strategy of vaccination produced worse results than the ones obtained according to the observed strategy of vaccination, even when considering the number of infections and deaths prevented in older populations.

Table 5.2: Scenario 1 Vaccination: Estimated events, estimated events averted and events averted per 10000 people.

	Cases Scenario 1	Deaths Scenario 1	Cases Averted	Deaths Averted	Cases Averted per 10000	Deaths Averted per 10000
Worldwide	257 709 262	4 108 173	70 027 942	5 108 195	90.71	6.62
WHO Region						
Eastern Mediterranean	12 413 862	179 417	1 986 638	208 656	27.38	2.88
Africa	5 275 017	103 593	1 041 863	52 820	9.33	0.47
Europe	102 806 315	1 252 927	36 793 518	2 073 950	394.47	22.24
Americas	91 822 837	1 924 096	22 424 179	1 928 582	220.28	18.94
Western Pacific	12 343 015	142 686	4 055 007	290 557	20.99	1.50
South-East Asia	33 048 216	505 454	3 726 737	553 630	18.68	2.77
Income Group						
Low income	1 321 604	25 266	215 014	14 434	3.29	0.22
Lower middle income	48 827 119	796 742	7 477 748	1 003 058	22.58	3.03
Upper middle income	65 167 100	1 541 836	13 949 792	2 022 924	54.62	7.92
High income	142 393 439	1 744 329	48 385 388	2 067 779	403.14	17.23
Age Group						
0-24	63 280 541	51 072	2 380 337	2 180	7.51	0.01
25-49	121 597 886	470 903	29 385 556	111 061	109.17	0.41
50-59	32 051 306	489 532	16 279 621	378 733	197.70	4.60
60-69	23 956 565	868 375	8 357 565	817 921	143.04	14.00
70-79	10 961 055	1 023 734	7 759 249	1 408 880	251.59	45.68
80+	5 861 909	1 204 557	5 865 614	2 389 420	408.89	166.57

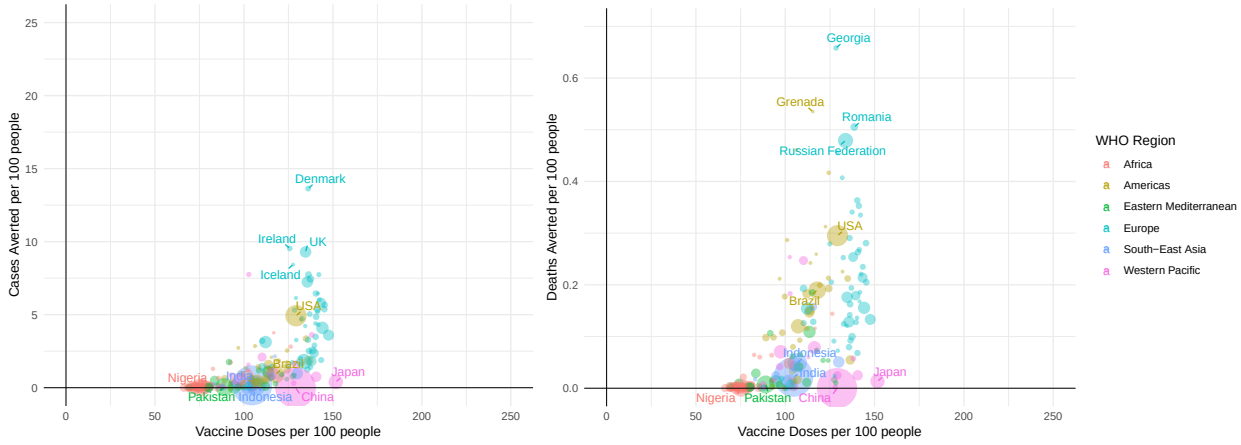
To evaluate the relation between vaccine doses administered and the number of events averted, graphs showing the interaction of these two variables stratified by income group and WHO region, and normalized to each country's population, can be seen in Figures 5.3 and 5.4, respectively. Both in cases and deaths averted, the outcomes between countries are much more alike than in the observed situation, seen in Figures 5.1 and 5.2, where the results were much more sparse. Furthermore, Figure

5.5 aims to show which countries benefit the most and which are the most negatively affected by this vaccination strategy. To do so, the horizontal axis shows the difference between the cases estimated in this scenario and the cases observed and the vertical axis does the same regarding deaths. Additionally, countries are stratified by income group [Figure 5.5(a)] and WHO region [Figure 5.5(b)].



((a)) Cases **((b))** Deaths

Figure 5.3: Scenario 1 Vaccination: Events averted against vaccine doses (per 100 people) for each country and stratified by income group.

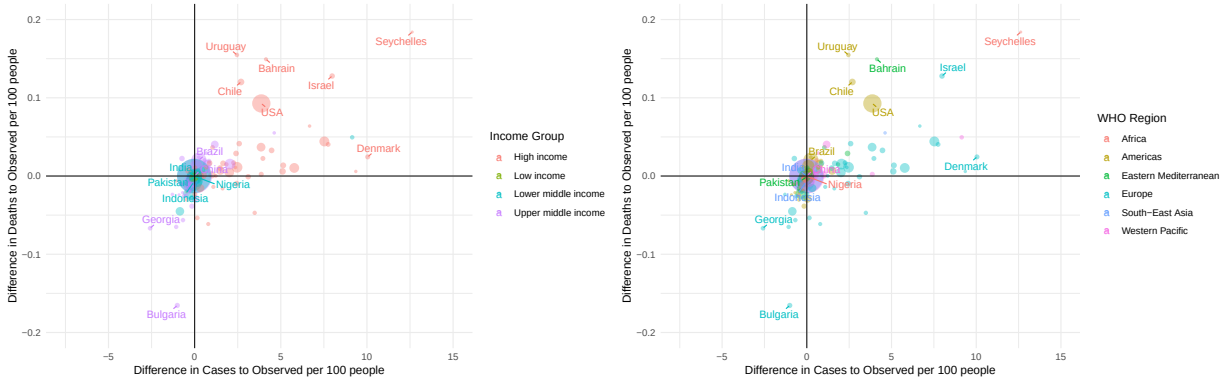


((a)) Cases **((b))** Deaths

Figure 5.4: Scenario 1 Vaccination: Events averted against vaccine doses (per 100 people) for each country and stratified by WHO Region.

Impact of Strategy 1 by Income Group

Regarding the differences among income groups (Figure 5.3), HICs are still the ones receiving more vaccine doses, as these are naturally also the countries with older populations. Consequently, these are the countries that benefit the most from vaccination both in terms of reducing infections and deaths.



((a)) Stratified by Income Group

((b)) Stratified by WHO Region

Figure 5.5: Scenario 1 Vaccination: Difference in deaths against difference in cases compared to observed (per 100 people) for each country.

However, compared to the observed situation, these are also the countries that are more negatively affected by this vaccination strategy. Figure 5.5(a) highlights this phenomenon very effectively. HICs are the most predominant among the first quadrant, showing that these countries where the ones with the biggest increase in cases and deaths in this scenario.

In contrast, the countries with the biggest negative differences both in cases and deaths are mostly UMICs but, as a whole, UMICs, still achieve better results regarding cases and fatalities using the observed vaccination strategy.

On the contrary, LICs and LMICs benefit from this vaccination strategy. In fact, in LICs, the number of cases averted has a four-fold increase from approximately 51.2 thousand to 215 thousand, and the number of deaths prevented more than doubles, from approximately 6.5 thousand to 14.4 thousand. This benefit is, however, out-scaled by the negative consequences for UMICs and especially HICs.

Impact of Strategy 1 by WHO Region

The difference between WHO regions is not as clear. Europe was the WHO region with the highest density of cases and deaths averted. As seen in Figure 5.5(b), European countries are both the ones who benefit and the ones that come at a disadvantage in this strategy. This happens as this WHO region is also the one with the biggest density of cases and deaths observed. In fact, as can be seen by the comparison of Table 5.1 and Table 5.2, all regions except Europe benefit from this strategy in terms of averted infections and half of the regions benefit from this strategy in terms of averted fatalities (Africa, Eastern Mediterranean and South-East Asia). In spite of that, just like in HICs, the negative impact in the European region is so prominent that it offsets the benefits for other nations.

5.2.2 Strategy 2 - Global Case-based Epidemiological Prioritization

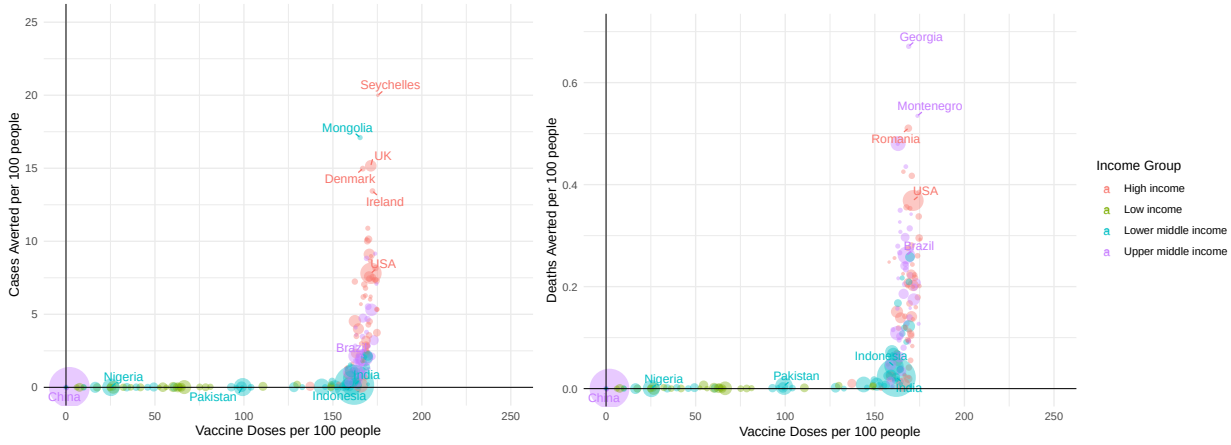
The alternative numbers of cases and deaths, cases and deaths averted and averted per 10000 people, using Strategy 2, are shown in Table 5.3. Using the methodology described in Chapter 4, it was estimated that, approximately, 226.6 million infections and 3.5 million deaths of COVID-19 would have occurred worldwide in this scenario of vaccines' allocation, since the beginning of vaccination (8 of December 2020) and until the end of 2021. As the number of cases and deaths without vaccination is the same as aforementioned (327.7 million infections and 9.2 million deaths), it was estimated that, in this scenario, the direct effect of vaccination prevented 101.1 million infections (30.8%) and 5.7 million deaths (62.6%). These results, stratified by WHO Region, Income Group and Age Group, are also shown in Table 5.3. Compared to the observed number of cases and deaths, this strategy would perform negatively in terms of infections but positively in terms of fatalities. In other words, using this strategy of allocation of vaccines, 4 262 486 additional cases would occur but 208 764 more deaths would be averted globally, as a result of vaccination. It would allow to decrease mortality by approximately 5.57%, compared to the observed distribution.

Table 5.3: Scenario 2 Vaccination: Estimated events, estimated events averted and events averted per 10000 people.

	Cases Scenario 2	Deaths Scenario 2	Cases Averted	Deaths Averted	Cases Averted per 10000	Deaths Averted per 10000
Worldwide	226 636 064	3 538 144	101 101 140	5 678 224	130.96	7.36
WHO Region						
Eastern Mediterranean	10 845 557	167 591	3 554 943	220 482	48.98	3.04
Africa	5 075 246	99 710	1 241 634	56 703	11.12	0.51
Europe	89 622 686	1 154 602	49 977 147	2 172 275	535.81	23.29
Americas	77 275 307	1 442 195	36 971 709	2 410 483	363.18	23.68
Western Pacific	10 870 123	144 902	5 527 899	288 341	28.62	1.49
South-East Asia	32 947 145	529 144	3 827 808	529 940	19.18	2.66
Income Group						
Low income	1 407 187	30 738	129 431	8 962	1.98	0.14
Lower middle income	47 199 476	827 020	9 105 391	972 780	27.49	2.94
Upper middle income	56 514 543	1 275 463	22 602 349	2 289 297	88.51	8.96
High income	121 514 858	1 404 923	69 263 969	2 407 185	577.10	20.06
Age Group						
0-24	52 634 279	45 064	13 026 599	8 188	41.11	0.03
25-49	105 122 615	366 217	45 860 827	215 747	170.38	0.80
50-59	31 262 024	437 172	17 068 903	431 093	207.28	5.24
60-69	20 437 943	737 829	11 876 187	948 467	203.26	16.23
70-79	10 995 480	883 766	7 724 824	1 548 848	250.48	50.22
80+	6 183 723	1 068 096	5 543 800	2 525 881	386.46	176.08

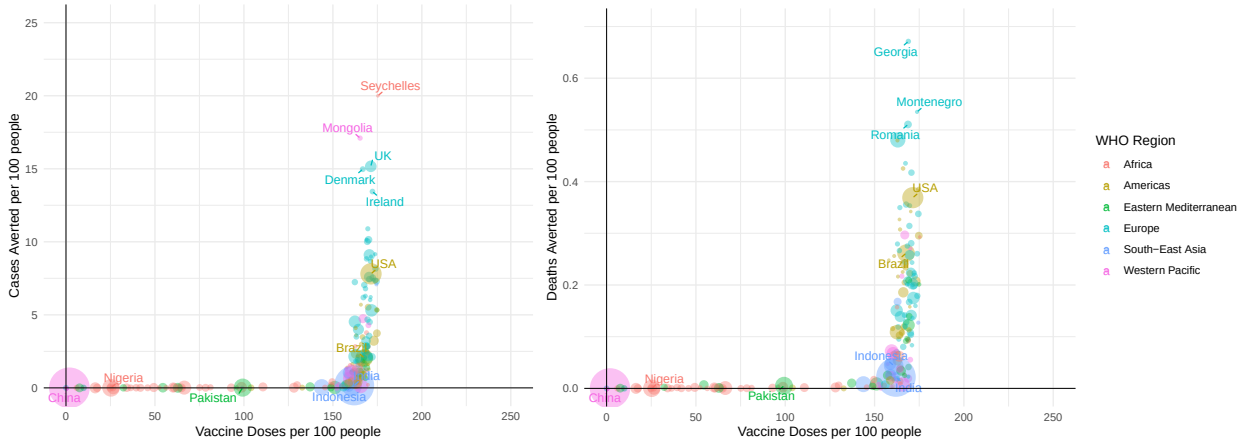
To evaluate the relation between vaccine doses administered and the number of events averted, graphs showing the interaction between these two variables stratified by income group and WHO region, and normalized to each country's population, can be seen in Figures 5.6 and 5.7, respectively. The use of this strategy of vaccination highlights the differences between countries which adopted zero-COVID policies or had high levels of under-reporting of cases or had naturally less COVID-19 infections opposed to countries that eased off on NPIs, allowing SARS-CoV-2 transmission to rise. The first group of countries had less cases reported and was then allocated less vaccines. These lower vaccination rates (less than 150 doses/100 people) coupled with the fact that these countries had already less

infections to prevent, led to an almost negligible impact of vaccination. Contrarily, most of the countries where vaccination rates were higher (more than 150 doses/100 people), felt a tremendous impact of the vaccination programme, both in terms of preventing infections and fatalities.



((a)) Cases **((b))** Deaths

Figure 5.6: Scenario 2 Vaccination: Events averted against vaccine doses (per 100 people) for each country and stratified by income group.



((a)) Cases **((b))** Deaths

Figure 5.7: Scenario 2 Vaccination: Events averted against vaccine doses (per 100 people) for each country and stratified by WHO Region.

Impact of Strategy 2 by Income Group

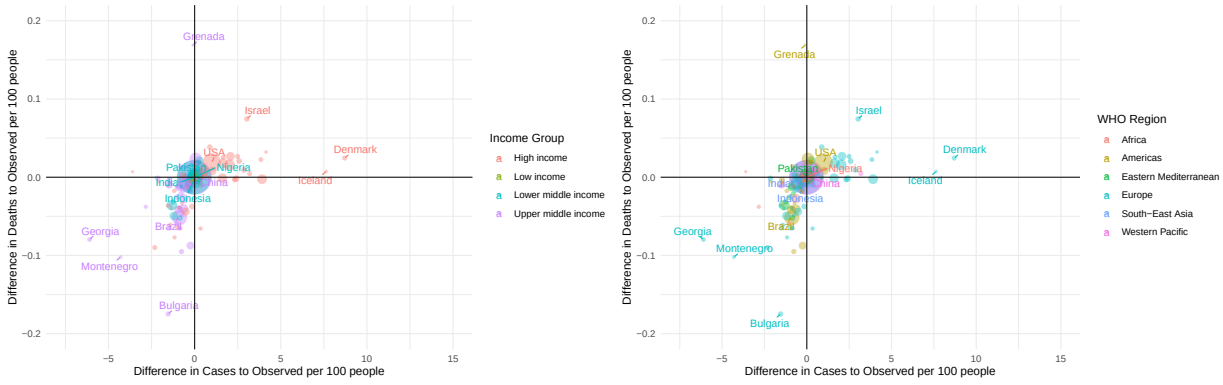
Regarding income group, as seen in Table 5.3 HICs were the ones with the highest density of cases and deaths averted and LICs were the ones with the lowest. The countries allocated with higher proportions of vaccine doses are mostly HICs or UMICs, as these are also the countries that report the most cases. Therefore, the impact will be more distinguished in these countries.

Impact of Strategy 2 by WHO Region

Again, the difference between WHO regions is not as clear between income groups. Europe and the Americas were the WHO regions with the highest density of cases and deaths averted, respectively, while Africa was the WHO region with the lowest. Once more, Mongolia and the Seychelles appear as outliers among their WHO region.

Differences between Strategy 2 and Observed Vaccination

As shown in Figure 5.8(a), the countries that felt negatively the impact of this vaccination strategy were mostly HICs, while the countries more benefited were UMICs. In fact, comparing Tables 5.1 and 5.3, one can see the all income groups benefit from this strategy of vaccination, as the number of cases and deaths averted per 10000 is higher, except for HICs. Again, the difference between WHO regions [Figure 5.8(b)] is not as noticeable. The countries that have a higher perception of the impact of this strategy of vaccination, both positively and negatively, are European, as these are also the countries that report more cases and deaths, in real-life. Overall, more countries are impacted positively than negatively by this allocation of vaccines.



((a)) Stratified by Income Group

((b)) Stratified by WHO Region

Figure 5.8: Scenario 2 Vaccination: Difference in deaths against difference in cases compared to observed (per 100 people) for each country.

5.2.3 Strategy 3 - Mixed Demographic and Epidemiological Prioritization

The number of cases and deaths, cases and deaths averted and averted per 10000 people are shown in Table 5.4. Using the methodology described in Chapter 4, it was estimated that, approximately, 241.9 million infections and 3.8 million deaths of COVID-19 would have occurred worldwide in this scenario of vaccines' allocation, since the beginning of vaccination (8 of December 2020) and until the end of 2021. As the number of cases and deaths without vaccination is the same as aforementioned (327.7 million

infections and 9.2 million deaths), it was estimated that, in this scenario, the direct effect of vaccination prevented 85.8 million infections (26.2%) and 5.4 million deaths (59.3%). These results, stratified by WHO Region, Income Group and Age Group, are also shown in Table 5.4.

Table 5.4: Scenario 3 Vaccination: Estimated events, estimated events averted and events averted per 10000 people.

	Cases Scenario 3	Deaths Scenario 3	Cases Averted	Deaths Averted	Cases Averted per 10000	Deaths Averted per 10000
Worldwide	241 902 419	3 823 903	85 834 785	5 392 465	111.18	6.98
WHO Region						
Eastern Mediterranean	11 617 379	173 381	2 783 121	214 692	38.35	2.96
Africa	5 168 484	101 730	1 148 396	54 683	10.29	0.49
Europe	96 095 960	1 204 475	43 503 873	2 122 402	466.41	22.75
Americas	84 473 871	1 684 744	29 773 145	2 167 934	292.47	21.30
Western Pacific	11 574 204	143 498	4 823 818	289 745	24.97	1.50
South-East Asia	32 972 521	516 075	3 802 432	543 009	19.05	2.72
Income Group						
Low income	1 363 455	28 082	173 163	11 618	2.65	0.18
Lower middle income	47 967 778	810 030	8 337 089	989 770	25.17	2.99
Upper middle income	60 763 988	1 408 308	18 352 904	2 156 452	71.87	8.44
High income	131 807 198	1 577 483	58 971 629	2 234 625	491.35	18.62
Age Group						
0-24	57 893 350	48 108	7 767 528	5 144	24.51	0.02
25-49	113 215 581	418 325	37 767 861	163 639	140.31	0.61
50-59	31 622 542	462 833	16 708 385	405 432	202.90	4.92
60-69	22 198 480	802 418	10 115 650	883 878	173.13	15.13
70-79	10 898 751	950 028	7 821 553	1 482 586	253.61	48.07
80+	6 073 715	1 142 191	5 653 808	2 451 786	394.13	170.92

Overall, Strategy 3 of vaccination performed better than Strategy 1 and worse than Strategy 2. In fact, as the distribution of vaccines was a combination of both Strategy 1 and Strategy 2, so were the outcomes. These were usually in-between the ones from the two strategies aforementioned. Concerning differences in the impact among WHO regions, Europe was the one with the highest density of cases and deaths averted, while Africa was the WHO region with the lowest. Regarding income group, similarly to the previous scenarios, HICs were the ones with the highest density of cases and deaths averted and LICs were the ones with the lowest.

5.3 Comparison of Allocation Strategies

A summary of the results obtained for each scenario of vaccination can be seen in Table 5.5. This table shows the number of events that would occur in each scenario, as well as the number of events observed, and the percentage of events that would be averted. This percentage is calculated based on the number of events that would occur in the counterfactual scenario of no vaccination. Additionally, this table shows the uncertainty intervals obtained from the sensitivity analyses, considering lower (-10%) and higher ($+10\%$) VE estimates.

In terms of directly averting infections, no alternative scenario of vaccination performed better than the observed. Contrarily, regarding directly averting fatalities, the strategy of case-based epidemiological prioritization (Strategy 2) out-performed the observed and was the best overall. The strategy of

Table 5.5: Summary of the results by vaccination scenario with sensitivity intervals.

	Cases $(-/+10\%$ VE)	**Deaths** $(-/+10\%$ VE)
No Vaccination		
Number of Events	327 737 204	9 216 368
	(295 315 489 − 382 658 201)	(7 096 037 − 16 982 890
Observed		
Number of Events	222 373 578	3 746 908
Percentage of Events Averted	32.15%	59.35%
	(24.7 − 41.89)	(47.2 − 77.94)
Scenario 1		
Number of Events	257 709 262	4 108 173
	(247 900 730 − 273 465 228)	(3 925 301 − 4 890 508)
Percentage of Events Averted	21.37%	55.43%
	(16.06 − 28.54)	(44.68 − 71.2)
Scenario 2		
Number of Events	226 636 064	3 538 144
	(225 301 366 − 231 151 225)	(3520734 − 4 114 725)
Percentage of Events Averted	30.85%	61.61%
	(23.71 − 39.59)	(50.38 − 75.77)
Scenario 3		
Number of Events	241 902 419	3 823 903
	(236 419 044 − 251 896 879)	(3 722 487 − 4 508 971)
Percentage of Events Averted	26.19%	58.51%
	(19.94 − 34.17)	(47.54 − 73.45)

allocation of vaccines based on the age pyramid of each country (Strategy 1) was the worst performing strategy both for the prevention of cases and deaths. The reason behind the poor performance of this strategy may be related to the arguments advocated by Castonguay et al. on their study about spatial allocation of a available supply of COVID-19 vaccines [71]. While equality of distribution is prioritized using Strategy 1, there are benefits in deviating from this rule, in a way that is more closely aligned with another crucial principle, the equity of outcomes, taken into account in Strategy 2. Overall, the results obtained in this study support results previously obtained by other authors which suggested that the pandemic has a degree of spatial heterogeneity which should be taken into account when allocating medical resources, such as vaccines [70–72]. However, the poor performance of Strategy 3 goes against the results obtained in some studies [70, 72]. It is important to note that those are regional studies, performed at a much smaller scale, where the degree of spatial heterogeneity of the severity of the pandemic is not as considerable. When dealing with worldwide data, this heterogeneity is much more prominent, affecting the results obtained by age-based prioritization strategies, where a considerable amount of vaccines are allocated to countries where the impact of vaccination is very low. This can also affect the results obtained by Strategy 3.

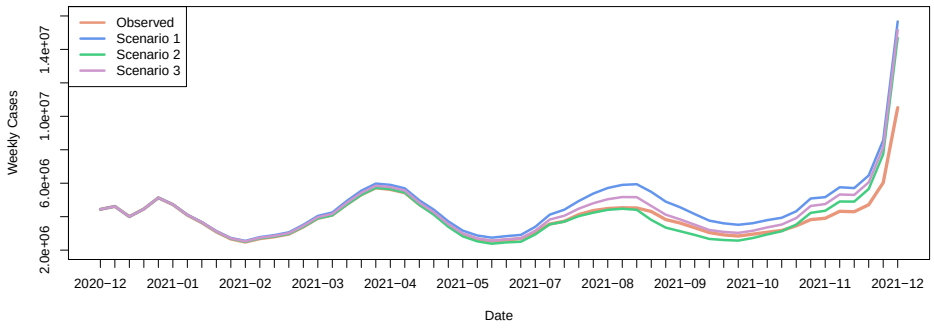
Uncertainty intervals show that the impact of these alternative strategies for vaccination is higher when considering a more pessimistic scenario of VE. In such case, both Strategy 2 and Strategy 3 allow to save more lives, compared to the observed situation. However, on the other hand, for very effective vaccines, the observed strategy performs better than all the others, both in terms of averting cases and averting deaths. A possible explanation for this result is that vaccine types are also re-distributed when considering alternative scenarios, therefore, the most effective vaccines are not concentrated

only in HICs. When augmenting VE, the difference in effectiveness from the most and least effective vaccines is not as prominent because VE cannot surpass 100%, which makes the observed strategy more desirable.

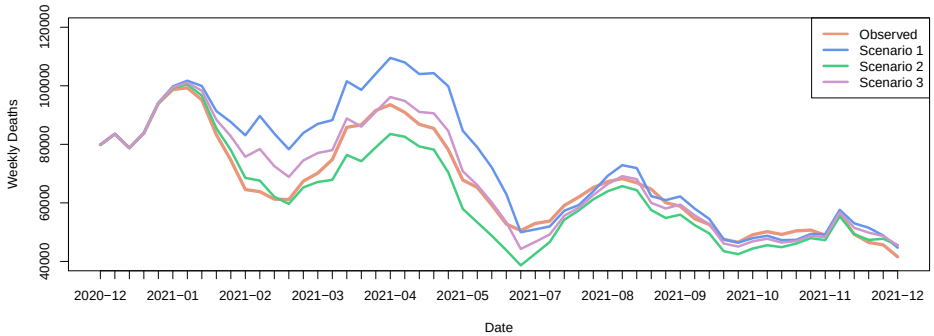
To further understand the differences between all the strategies considered, their comparative impact over time and across income and age groups will be discussed below. A comparison across WHO regions will not be carried out because this variable was not found to be as significant in the individual analyses of vaccination strategies presented above.

5.3.1 Impact Over Time

Figure 5.9 displays how each strategy of vaccination behaved over the time-period of the study. For the prevention of cases, the biggest differences across strategies occur at the end of the study period. In contrast, the first months of vaccination appear to be the most important time period for death prevention. This emphasizes the importance of selecting an appropriate prioritization mechanism, as soon as vaccination campaigns start, in order to save the most lives.



((a)) Cases



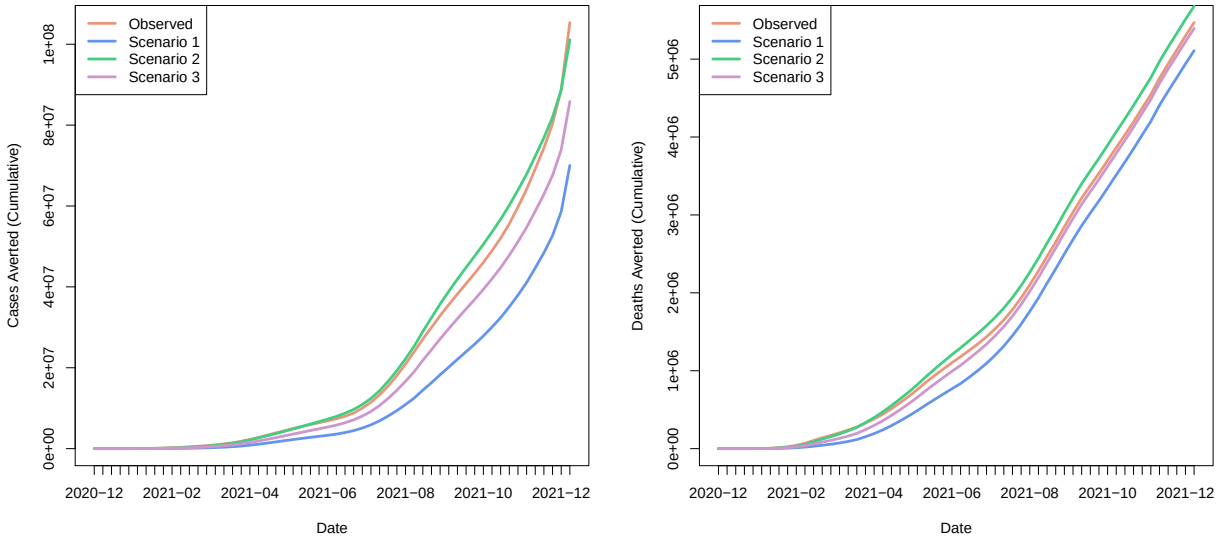
((b)) Deaths

Figure 5.9: Events averted worldwide over time in each vaccination strategy.

To further understand how each strategy performs over time, the cumulative number of events averted by each strategy for the time period of the study is shown in Figure 5.10.

Whilst regarding avoiding deaths, the relative position of each strategy in terms of performance was roughly the same across time, this is not veracious when it comes to avoided infections. Actually, Strategy 2 performs better than the observed until almost the end of the study period, having only worse results in the last two weeks, when the number of cumulative infections prevented in the observed situation surpasses the number of cumulative infections prevented using Strategy 2. As there were no boosters considered in this allocation of vaccines, at the end of the study period, the algorithm for the distribution is only either giving second doses and finishing vaccination schemes or giving first doses to countries that have low prevalence of COVID-19, as the countries with higher prevalence already have their populations almost completely vaccinated. As the waning of VE is more prominent against infection, this has an impact in the results obtained for cases, but not for deaths.

Graphs depicting the curves of cumulative events averted worldwide over time in each vaccination strategy for each of the sensitivity analysis scenarios can be found in Appendix B Section B.2.



((a)) Cases **((b))** Deaths

Figure 5.10: Cumulative events averted worldwide over time in each vaccination strategy.

5.3.2 Impact Across Income Groups

Bar graphs showing how each scenario performs in terms of cases and deaths averted across income groups can be seen in Figure 5.11.

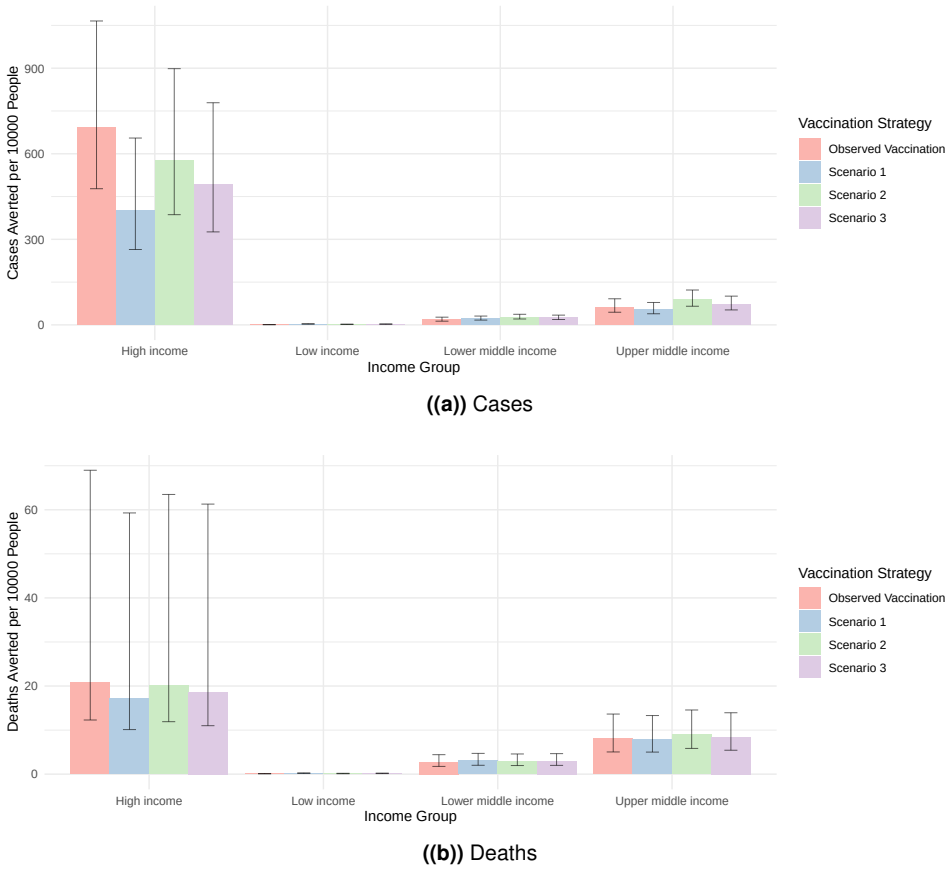


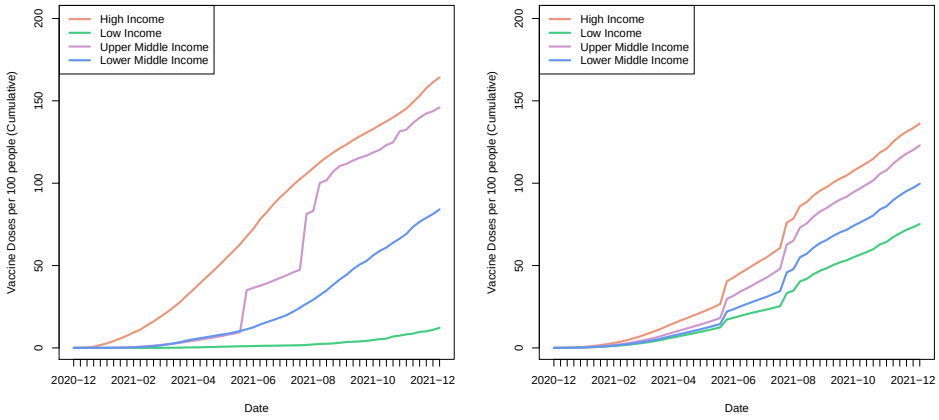
Figure 5.11: Comparison of events averted per 10000 people between vaccination scenarios and across income groups (with uncertainty error bars).

The comparison of the impact of vaccination across income groups is important as this distinctive factor among countries is what made the distribution of vaccines so unequal. HICs benefit most from the observed distribution of vaccines. However, as the other scenarios attempt to address disparities in vaccine access, LICs see more advantages in Strategy 1 and UMICs in Strategy 2. LMICs benefit most from Strategy 2 when it comes to infections averted, but from Strategy 1 regarding death prevention. While Strategy 1 is the best performing strategy in terms of addressing health inequalities, the marginal gain from lower income nations is not enough to pay-off the damage in wealthier nations.

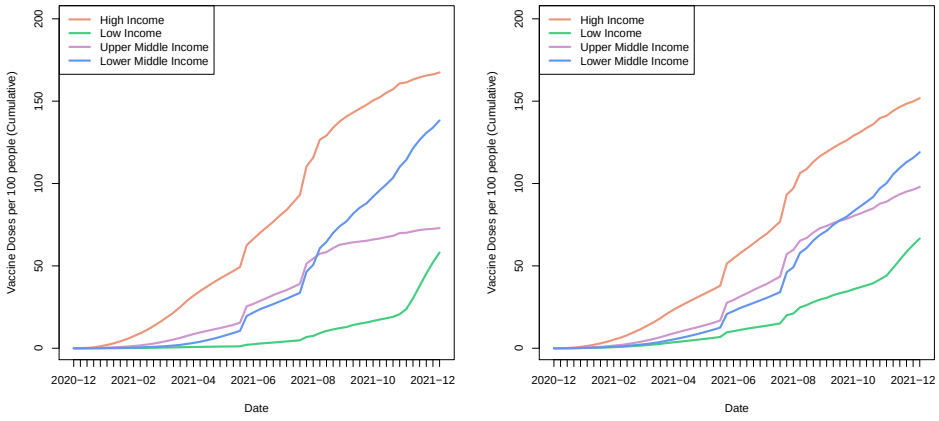
For all vaccination strategies tested, HICs were the ones that benefited most from vaccination, both in terms of preventing infections and deaths. The relative difference between HICs and other income groups is less prominent when concerning the prevention of deaths as these countries are naturally better equipped to deal with the pandemic, having smaller IFRs across ages [48], and thus feeling less the impact of vaccination for the prevention of those, when compared to the prevention of infections. Nonetheless, this group of countries is still the one that benefits most from vaccination in all scenarios of vaccination.

Distribution of Vaccines Over Time Across Income Groups

Figure 5.12 shows how the distribution of vaccines occurred over time across income groups.



((a)) Observed **((b))** Strategy 1



((c)) Strategy 2 **((d))** Strategy 3

Figure 5.12: Cumulative vaccine doses per 100 people across income groups in each strategy of vaccination.

In the observed situation, HICs were the ones that achieved higher vaccination rates, due to their economic condition. However, even in alternative scenarios of vaccination, where the financial power of countries was not taken into account, these countries ended up being the ones with the higher vaccination rates, even though the differences were not as striking. In Strategy 1, where prioritization was based on age, it was foreseeable that HICs would achieve higher vaccination rates, as these are also the countries with the eldest populations. Additionally, using Strategy 2, these were also the countries that received more vaccine doses, as they were the ones with the highest number of reported COVID-19 infections. Naturally, as Strategy 3 is a combination of both Strategy 1 and 2, also in this scenario, HICs

were allocated the most vaccine doses *per capita*. The reason behind HICs being the ones reporting more COVID-19 infections is not clear. Bayati [100] proposes some explanations for this phenomenon, some examples being:

- HICs have more resources and better healthcare infrastructures, allowing them to perform a larger number of COVID-19 diagnosis tests;
- HICs are more likely to disseminate the data more transparently and more accurately;
- There is much less air transport in poor countries, which naturally decreases transmission across distant geographic regions.

It should be noted that the first two proposed causes suggest that even though infections in these countries exist, they are under-reported. The aforesaid can also happen regarding the occurrence of fatalities. Even though just like regarding infections, the under-ascertainment of deaths varies globally, it is higher in low income and fragile settings [49, 98], based on estimates of excess mortality. The under-reporting of both infections and deaths biases the understanding of the pandemic's progression and the true burden of the disease, and has consequences when the allocation of resources, such as vaccines, is being discussed.

Furthermore, as mentioned in Section 5.1, the adoption of zero-COVID policies, which also entails that countries adopting these policies will have very low counts of infections and deaths, limits the understanding of the impact of vaccination in these countries. This is especially true for UMICs. China, being the most populated country in the world, corresponds to more than half of the population of UMICs. As China has adopted a zero-COVID strategy, the impact of vaccination in UMICs, when normalized for the population of this group, provides an extremely underestimated approximation for some countries in some strategies. Strategy 2 is an exception to this. As vaccines are distributed according to the proportion of new cases, China hardly receives any vaccines (Figures 5.6 and 5.7). In fact, this is the strategy in which UMICs achieve the lowest vaccination rates (Figure 5.12) as China accounts for almost half the population of this group. However, this is also the strategy in which UMICs obtained the best results, regarding outcomes.

In short, HICs show the greatest impact of vaccination in all scenarios, as these countries are dispensed more vaccine doses, but also because their counts of observed cases and deaths were initially also higher. Furthermore, it should be noted that the impact of vaccination programmes cannot be measured as only the number of infections and deaths averted. The lowest-income populations are the ones that benefit most from immunization, both in terms of health and economy, even though they are the groups with the least access to vaccines. If distributions of vaccines were equitable, the gains would be even greater for these populations [101].

5.3.3 Impact Across Age Groups

Bar graphs showing how each scenario performs in terms of cases and deaths averted across age groups can be seen in Figure 5.13.

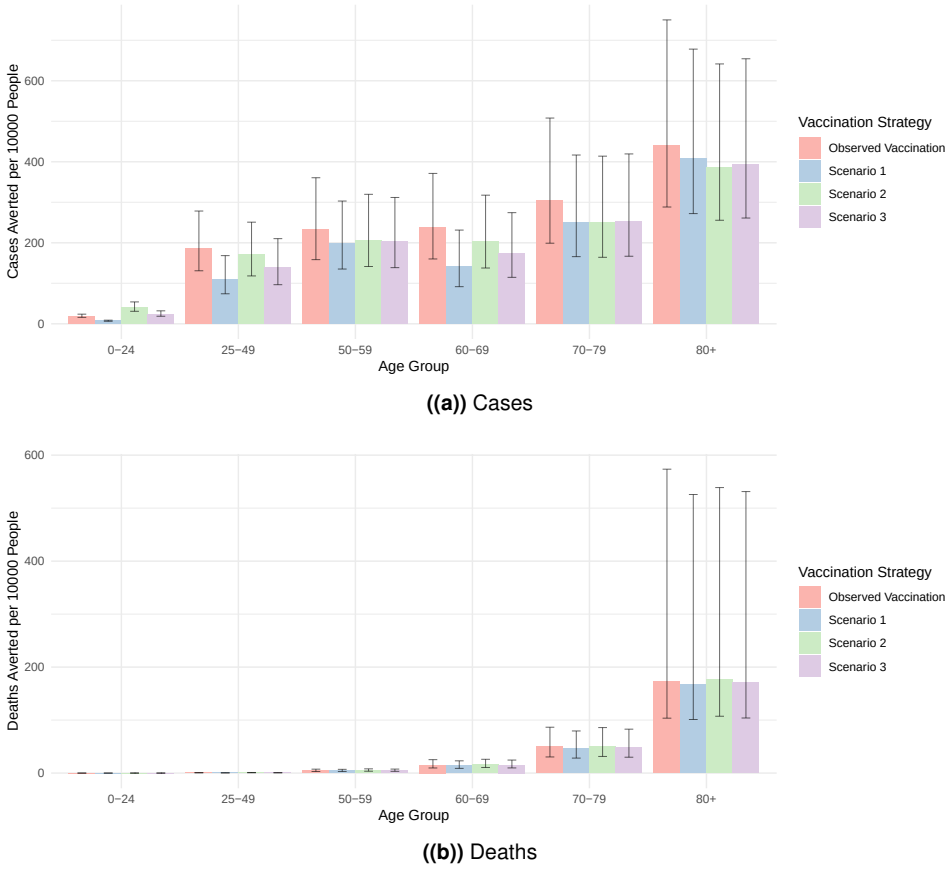
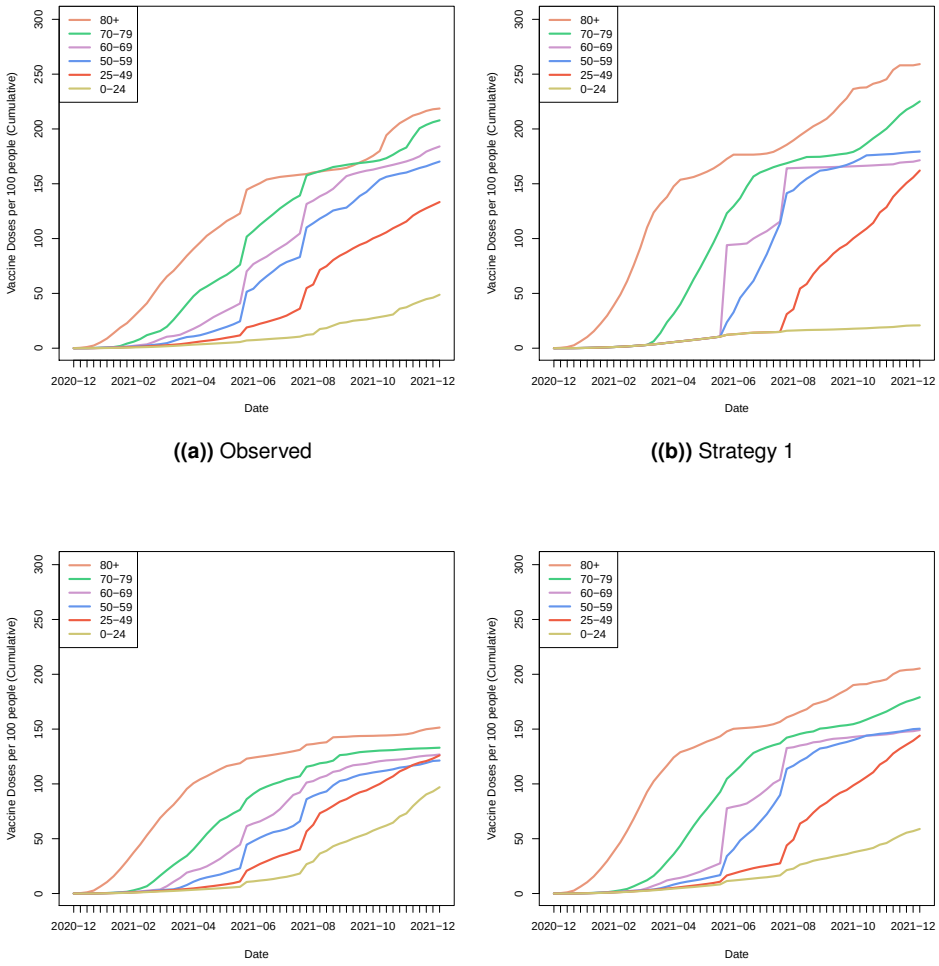


Figure 5.13: Comparison of events averted per 10000 people between vaccination scenarios and across age groups (with uncertainty error bars).

Of the alternative strategies studied, Strategy 1 prevents the most cases amongst older populations. However, as the age decreases, Strategy 1 performs progressively worse. This is natural, as this strategy of vaccination uses age as the main mechanism for prioritization. Regarding the prevention of fatalities, the impact of Strategy 1 is not so notorious, even for older populations, being Strategy 2 the best performing across all age groups. While Strategy 1 has the advantage of administering boosters to older populations, Strategy 2 has the advantage of delivering the base scheme of vaccination (2 doses, or 1 dose, for some vaccines) when it is most necessary, *i.e.* when cases are starting to rise. As was aforementioned, the waning of effectiveness of vaccines against death is not as prominent as against infection. Therefore, when it comes to preventing deaths, the marginal gain of the booster dose provided to older populations in Strategy 1 is not enough to account for the right timing of a 2-dose scheme of vaccination supplied in Strategy 2.

Distribution of Vaccines Over Time Across Age Groups

Figure 5.14 shows how the distribution of vaccines occurred over time across age groups. These distributions are very contrasting compared to the ones across income groups (Figure 5.12) regarding equity.



((a)) Observed

((b)) Strategy 1

((c)) Strategy 2

((d)) Strategy 3

Figure 5.14: Cumulative vaccine doses per 100 people across age groups in each strategy of vaccination.

For the distribution of vaccines across income groups, Strategy 1 [Figure 5.12(b)] appears to be the most equitable one. This happens as the aim of the strategy is to distribute vaccines equitably between countries according to age. In fact, the differences observed between income groups are derived from the inherent differences in the age pyramid of those populations, as low income populations tend to have a lower life expectancy and vice-versa.

On the other hand, regarding the distribution across age groups, Strategy 2 seems to be the most equitable. This happens as this strategy prioritizes countries in which the transmissibility is higher and

aims to cover as much population as possible before targeting older populations in countries where the prevalence of COVID-19 is lower.

Nevertheless, in all strategies, the vaccination of age groups follows an age-descent order, which was expected given their design. The only instance in which that does not happen is regarding the age groups ”50-59” and ”60-69” in Strategy 1. Even though the age group ”60-69” starts being vaccinated earlier, this age group ends the study period with lower vaccination rates. This can happen if the vaccines taken by these two groups differ in terms of manufacturers and consequently, the number of doses in the primary series (1 or 2) and the time between doses (in case of a 2-dose primary series).

Premature Deaths and Disability Years

Another dimension that should be taken into account when evaluating the occurrence and prevention of deaths across age groups is the presence of premature deaths. The total number of deaths alone assigns the same weight to a death at age 80 as it does for a deaths at age 20. However, in this study, the relative performance at preventing deaths between strategies shows to be the same across age groups. If this was not the case, another metric, such as the Years of Life Lost (YLLs) should be used, giving greater weight to deaths at a younger age and lower weight to deaths at an older age. Nevertheless, the impact of vaccination in averting infections across ages should be thoroughly discussed, as it varies greatly between strategies. The impact of averting infections in younger ages should not be underestimated or treated equally as averting infections in older ages. First, preventing infections at younger ages has an higher potential of decreased transmission of the disease, as the majority of infections occur in these age groups. Further, patients infected with COVID-19 can suffer from long-term effects [102] that can compromise quality of life. However, the impact of both these factors is hard to be exactly quantified.

5.4 Study Limitations

Since the counterfactual situation (*i.e.*, without immunizations) cannot be observed, it is impossible to directly measure the health impact of vaccination programs. Therefore, there are many factors that can influence the results obtain and limit the ability to draw conclusions.

As mentioned in previous sections, the algorithm used in this study to estimate the impact of alternative scenarios is highly sensitive to the observed number of cases and deaths. Therefore, it is extremely important that these numbers are accurate in order to assess the impact of each vaccination strategy and make comparisons between them. As is known, a high proportion of cases and deaths attributed to COVID-19 were unreported [48, 49]. This tremendously limits the ability to draw conclusions, as it biases the understanding of the true burden of COVID-19. To further exacerbate this limitation, this fac-

tor is not homogeneous among countries. Countries in low income settings and more fragile situations, such as those affected by conflict, are the most likely to have higher proportions of under-ascertained infections and deaths [49]. Therefore, it is possible that the impact of vaccination in these countries is under-estimated, especially in the alternative strategies, where these countries receive a higher proportion of vaccines, compared to the observed. However, this under-estimation could not be quantified. To prevent biases in reporting from further minimizing the perceived impact and requirement of vaccination in environments with lesser reporting, which are already unstable, it is imperative to invest in testing equipment, healthcare resources and vital registration systems in these settings.

Although the under-reporting of infections and deaths is expected to be the major limiting factor in this study concerning lack or incompleteness of data, there were other limitations in this study derived from the same problem. Some assumptions had to made regarding vaccination data, such as its distribution across age groups and vaccine manufacturers, as this stratification was not available for some countries. The distribution by age group also had to be done concerning cases and deaths counts in some countries. Moreover, even though vaccines were allocated to at-risk populations in all scenarios of vaccination tested, cases and deaths were not stratified considering this sub-population. Targeting this population first is expected to have an impact in the number of cases and deaths that could not be quantified. These populations are usually either more susceptible to infection (such as health and essential workers) or death (by the presence of co-morbidities) and that dimension was not captured as it was not available. Again, this factor is expected to have under-estimated the results of impact obtained. All these limitations, that arise from the poor quality of data available, show the importance of national governments in disseminating epidemiological data transparently and accurately.

Additionally, one of the most substantial limitations of the present study is only considering the direct impact of vaccination. It is expected that the number of averted events is even higher, when considering the impact of the observed vaccination strategy, as the vaccine also has other indirect effects, such as a reduction in transmission. However, one should be careful when interpreting the results from other vaccination strategies, as these are already obtained based on the scenario of no-vaccination that makes this assumption. Therefore, it is not necessarily expected that the number of averted events would be higher.

Furthermore, when considering alternative strategies of vaccination, it is expected that re-allocating vaccines alters the course of the pandemic and leads to other indirect effects, such as the appearance (or absence) of new VOCs and changes in policies and strategies of mitigation put in place by national governments, such as NPIs. Making assumptions regarding these dimensions in global studies is extremely complex as each country is an isolated case and those are difficult things to foreseen.

Lastly, the dimension of healthcare capacity was not taken into account. This is expected to have limited the results obtained in two manners. First, when confronted with an increase or decrease in

cases and deaths, it is expected that healthcare systems respond accordingly, given their capacity. However, it was assumed that healthcare systems responded in a way similar to the observed situation over time. Second, it is assumed that all countries have the necessary human resources and infrastructures required to administer the vaccines allocated to them. This is not always true, as especially LICs are very limited in this aspect. The delivery of vaccines is a complex process that requires not only human resources to administer them, but also means of transportation and storage. For example, mRNA vaccines, the more effective ones, require ultra-cold chain logistics, which may be challenging for some countries. However, this particular problem will be discussed further in subsequent sections.

5.5 Study Strengths and Implications

5.5.1 Synthesis of Study Contributions

This study is the first to explore the impact of worldwide alternative vaccination strategies against COVID-19 and leverages the knowledge available regarding the importance of globalization in an emergency situation like COVID-19, showing the direct influence it has on health outcomes. By showing that one global strategy out-performed the observed in terms of lives saved, this study calls attention to the need of having a global well-defined framework for the allocation of vaccines and reinforces the role of international health organizations. Such framework could not only be beneficial for the COVID-19 pandemic, still in course, but also have an extremely broad applicability for future pandemics.

Moreover, this analysis advances previous work regarding the comparison of strategies for the allocation of COVID-19 vaccines in terms of scale, by tremendously augmenting the number of regions considered, showing that some of the conclusions drawn from national studies can be expanded to the rest of the world. Fundamentally, this study highlights the need to allocate pharmaceutical interventions rationally when confronted with a constrained supply, showing that administering vaccines where those are the most needed allows to prevent more deaths. This study proposes an innovative strategy for the allocation of vaccines based on epidemiological prioritization, *i.e.,* based on the proportion of new cases. Distributing vaccines according to the ”hotspots” of the pandemic achieved the best results, allowing to decrease mortality by 5.57%, compared to the observed situation, showing that this strategy may be superior to the observed.

Finally, quantifying the direct effect of vaccination provides critical insights in the impact of vaccination programmes, and allows to compare them to other possible courses of action, *i.e.,* alternative allocations of vaccines. Compared to other studies using this method, this study additionally accounts for the dissimilarity of effectiveness from different types of vaccines, their waning immunity and the effect of booster vaccination. Similar methods can be applied to other settings and/or to assess further strategies of vaccination.

5.5.2 Recommendations for the Improvement of Vaccine Distribution Strategies

This study's findings have illustrated the importance of globalization in instances such as a pandemic, where global efforts are required to offer the best potential outcome for populations. Although COVAX was formed with the intention of bridging that gap, the trend of acquiring vaccines directly from manufacturers rather than via COVAX, which began with HICs, has greatly impacted its purpose, jeopardizing worldwide access to vaccines. In order to ensure global access and a fair distribution, an operational global allocation system, such as COVAX, is imperative and demands full funding in their role to provide adequate vaccination responses to different countries.

Moreover, these results demonstrated not only the importance of a global access to vaccines, but also of a rational allocation of those. At the beginning of vaccination programmes, when the supply is very restricted, fair distribution across nations must be thoroughly pondered. Thus, while a proportional allocation of vaccines according to priority groups seems equitable, it does not allow to obtain the best health outcomes, as it is not responsive to dynamic changes in the pandemic. Overall, limiting harm should be the priority when dealing with any public health crisis and while a plethora of factors play a role in limiting harm, preventing death is particularly urgent. Allocating vaccines to zones that are being the most severely hit by the pandemic, in terms of infections, while giving priority to the most at risk in those locations, has emerged in this study as the best strategy to reduce mortality. Thus, for the effective deployment of a global vaccination plan, it is important that a framework for the distribution of vaccines is well-defined and takes into account other important parameters, such as the aforementioned.

Notwithstanding, the allocation of vaccines is only one piece of the puzzle. In fact, Wouters et al. [103] states there are three additional dimensions of an effective global immunisation strategy against COVID-19, those being: development & production, affordability and deployment.

Regarding the production, a straightforward solution to supply constraints would be to simply increase supply. However, the protection of vaccines under Intellectual Property (IP) rights, along with production and supply chain barriers poses a challenge in this regard. The problem regarding IP rights has been partially solved as the World Trade Organization (WTO) has recently agreed on a IP waiver for COVID-19 tools, 20 months after its proposal. Despite being very limiting, as it does not cover all COVID-19 medical tools, nor all countries [104], an IP waiver is already a good step towards global vaccine equity and may serve as an example for future pandemics, even considering the delay. Additionally, a waiver also prevents businesses from setting unreasonable prices while shielding themselves from competition [105], which slightly attenuates the affordability issue.

The access to other COVID-19 medical tools aforementioned, that are not the vaccine, could also assist in vaccination endeavours. For example, the manufacture and deployment of tests in needing countries is useful in order to understand the true burden of COVID-19 in these countries and consequently the need for vaccination.

Nevertheless, while an IP waiver is a good first step towards ensuring global access to vaccines, especially when the supply is still very limited, which is especially true at the beginning of vaccination programmes, it does not solve the problem. Widespread knowledge and technology transfer would be necessary for the production bottleneck problem to be successfully solved, allowing for an increase in manufacturing capacity. However, the paucity of research and development facilities and staff in LICs and LMICs is a substantial barrier to vaccine technology transfer, reflecting the general necessity for international investment in research capacity enhancement for present and future public health threats [58]. Additionally, these countries also have very weak regulatory and surveillance capacities, hindering fully producing a vaccine. Facilitating "finish and fill" mechanisms through the export of vaccine components would be a short-term solution for both these problems [58].

Furthermore, additional pragmatic questions remain to be addressed. In order to administer vaccines, some countries need to overcome both logistical and administrative challenges [103]. As mentioned in previous sections, many of the top vaccination candidates need ultra-cold chains and have limited shelf lives after being taken out of storage. Additionally, local authorities require a robust data infrastructure in order to identify eligible individuals by priority group, recall them to take the second dose, *etc.* [103]. Although demanding, there are some strategies to tackle the differential capacity of countries to distribute vaccines in relation to dose and cold chain requirements. Examples include using one-dose vaccines, as well as vaccines that only require refrigeration during transport.

At the time of writing of this dissertation, the current challenge is the abovementioned. One and a half years after the beginning of COVID-19 vaccination, COVAX has secured enough doses to protect 70% of the population in 91 LICs [106]. To support vaccine delivery in these countries, the WHO, UNICEF and Gavi established the COVID-19 Vaccine Delivery Partnership (CoVDP) in January 2022, but there is still a long way to go in order to ensure reasonable protection in these countries. Notwithstanding, it is of utmost importance that these results and the lessons learned from the distribution of vaccines for the COVID-19 pandemic are taken into account in future public health threats.

6

Conclusions and Future Work

The current dissertation emphasizes and contributes to the topic of the need of securing worldwide access to COVID-19 vaccines. It tackles exclusively the direct health benefit, the number-one reason to consider global access, as enumerated in Section 3.3.1, and concludes that some global strategies may be superior to the observed. Secondary advantages of globally dispersing COVID-19 vaccinations, such as socioeconomic consequences, also mentioned in Section 3.3.1 were not taken into account in this analysis, although expected to contribute positively to the conclusions obtained. Future work regarding this secondary dimension is needed in order to fully understand the benefits of a global vaccination campaign.

Additionally, the choice of only measuring the direct impact of vaccination was made due to the complexity of modelling the worldwide situation. The development of mathematical models that also portray some of the indirect effects of vaccination, such as the reduction in transmission provided by vaccines, as well as capture the different VOCs and the impact of NPIs, is an example of future advancement in this field that may provide a better understanding of the benefits of a global vaccination campaign.

Regarding the strategies of vaccination explored in this study, the case-based epidemiological prioritization (Strategy 2) yielded the lowest mortality, whereas age-based demographic prioritization (Strategy 1) performed the poorest. Additionally, contrary to some national studies [70, 72], the strategy that combined both these dimensions (Strategy 3) was not the best performing. Although these results can be affected by the under-reporting of COVID-19 cases and deaths, discussed further below, this highlights that when dealing with a very limited supply of vaccines, the age and risk-based proportional allocation of vaccines is not necessarily the fairest, as the results obtained suggest that it is not the one which allows to save more lives.

Furthermore, the results obtained in Strategy 2, *i.e.*, poor performance regarding the prevention of cases but superior in terms of averting fatalities, where boosters were not used, highlight the importance of thoroughly assessing the impact of this additional dose in populations before starting its administration. As the waning of effectiveness of vaccines is much more prominent for preventing infections compared to deaths, the use of this dose may reveal superfluous and does not allow the administration of the primary series in populations where the benefit might be greater. The assessment of the benefit of this dose not only in terms of cases and deaths, but also regarding other important outcomes such as severe disease and/or hospitalization is further necessary.

Additionally, future work regarding the frameworks for prioritization can also be done:

1. For the demographic prioritization, the consideration of additional sub-priority groups can be a way to improve, as well as proportional allocation to countries considering their inherent differences in population size of these groups, which were not taken into account in this study.

2. For the epidemiological prioritization, as the rationale behind the use of this strategy is the allocation of vaccines to where they are the most needed, the previous week's infection counts may

not be the only appropriate measure. Hence, other factors such as the resilience of the healthcare systems to deal with the pandemic outbreaks may also be interesting to explore. Additionally, the consideration of regional instead of national ”hotspots” can also be a possible source of additional analysis. Further, there are also some issues with the consideration of the number of cases alone as the prioritizing factor. As the nations that are ”rewarded” with an allocation of more vaccines are the ones with highest number of cases, this may trigger national governments into not implementing enough NPIs, which can augment the death toll of the pandemic. This issue needs to be taken into account in future work.

Finally, as discussed in Section 5.4, one of the main limitations of the present work was the lack of complete and reliable data, which illustrates the need for an investment in testing campaigns as well as reporting and surveillance systems, especially in LICs and LMICs. It is particularly challenging to estimate the impact of a vaccination programme against a certain disease when the burden of the same disease is not clearly perceived in some countries. There are certain strategies that may be employed in future work to lessen the effects of this constraint. Consideration of excess mortality estimates while calculating the number of deaths prevented by vaccination is one example. However, even using estimates from excess mortality requires access to reliable mortality data, which is not always the case as many nations lack functional vital registry systems. It is essential to additionally invest in these systems to stop biases in infections and mortality reporting from further undermining the perceived impact and need of vaccination in circumstances with reduced reporting, which are already unstable.

As a conclusion, while there are many ways in which this work can be improved, the present dissertation provides important results and conclusions on the topic of global allocation of vaccines. It is the first study of this kind and it proposes an innovative strategy for vaccine allocation that may be superior to the observed distribution: the epidemiological prioritization. It is also important to mention that the two main limitations of this study (disregarding the indirect effect of vaccines and the underreporting of cases and deaths) are both expected to underestimate the impact of this strategy. Therefore, the positive health impact of this strategy is likely even higher.

Additionally, this study reinforces the role and articulation of national and international health organizations. The conclusions drawn here have the broadest applicability in situations where the supply of vaccines is extremely low, such as in the beginning of vaccination programmes. While for this vaccination programme this is no longer the case, as 18 months after the beginning of immunization efforts, COVAX has finally secured a fair amount of vaccine doses to deliver to countries in fragile settings, these results highlight the retrospective impact of alternative strategies of vaccination, which are of major importance for the future. Particularly, these findings have the potential to lead to new international strategies which will be of utmost importance not only for future pandemics, but also for the distribution of new vaccines for the control of SARS-CoV-2 and other global infectious agents' genetic variants.

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A

Additional Information on Input Data

A.1 Countries Considered

The list of the 180 countries considered in this study, and their respective ISO 3166-1 alpha-3 code, WHO region and income group classification, are shown in Table A.1.

Table A.1: Countries considered and respective Codes, Names, WHO Region and Income Group classification.

Code	Name	WHO Region	Income Group
AFG	Afghanistan	Eastern Mediterranean	Low income
AGO	Angola	Africa	Lower middle income
ALB	Albania	Europe	Upper middle income
ARE	United Arab Emirates	Eastern Mediterranean	High income
ARG	Argentina	Americas	Upper middle income
ARM	Armenia	Europe	Upper middle income
ATG	Antigua and Barbuda	Americas	High income
AUS	Australia	Western Pacific	High income
AUT	Austria	Europe	High income
AZE	Azerbaijan	Europe	Upper middle income

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Table A.1 – continued from previous page

Code	Name	WHO Region	Income Group
BDI	Burundi	Africa	Low income
BEL	Belgium	Europe	High income
BEN	Benin	Africa	Lower middle income
BFA	Burkina Faso	Africa	Low income
BGD	Bangladesh	South-East Asia	Lower middle income
BGR	Bulgaria	Europe	Upper middle income
BHR	Bahrain	Eastern Mediterranean	High income
BHS	Bahamas	Americas	High income
BIH	Bosnia and Herzegovina	Europe	Upper middle income
BLR	Belarus	Europe	Upper middle income
BLZ	Belize	Americas	Upper middle income
BOL	Bolivia (Plurinational State of)	Americas	Lower middle income
BRA	Brazil	Americas	Upper middle income
BRB	Barbados	Americas	High income
BRN	Brunei Darussalam	Western Pacific	High income
BTN	Bhutan	South-East Asia	Lower middle income
BWA	Botswana	Africa	Upper middle income
CAF	Central African Republic	Africa	Low income
CAN	Canada	Americas	High income
CHE	Switzerland	Europe	High income
CHL	Chile	Americas	High income
CHN	China	Western Pacific	Upper middle income
CIV	Côte d'Ivoire	Africa	Lower middle income
CMR	Cameroon	Africa	Lower middle income
COD	Congo, Democratic Republic of the	Africa	Low income
COG	Congo	Africa	Lower middle income
COL	Colombia	Americas	Upper middle income
COM	Comoros	Africa	Lower middle income
CPV	Cabo Verde	Africa	Lower middle income
CRI	Costa Rica	Americas	Upper middle income
CUB	Cuba	Americas	Upper middle income
CYP	Cyprus	Europe	High income
CZE	Czechia	Europe	High income
DEU	Germany	Europe	High income
DJI	Djibouti	Eastern Mediterranean	Lower middle income
DNK	Denmark	Europe	High income
DOM	Dominican Republic	Americas	Upper middle income
DZA	Algeria	Africa	Lower middle income
ECU	Ecuador	Americas	Upper middle income
EGY	Egypt	Eastern Mediterranean	Lower middle income
ESP	Spain	Europe	High income
EST	Estonia	Europe	High income
ETH	Ethiopia	Africa	Low income
FIN	Finland	Europe	High income
FJI	Fiji	Western Pacific	Upper middle income
FRA	France	Europe	High income

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Table A.1 – continued from previous page

Code	Name	WHO Region	Income Group
GAB	Gabon	Africa	Upper middle income
GBR	United Kingdom	Europe	High income
GEO	Georgia	Europe	Upper middle income
GHA	Ghana	Africa	Lower middle income
GIN	Guinea	Africa	Low income
GMB	Gambia	Africa	Low income
GNB	Guinea-Bissau	Africa	Low income
GNQ	Equatorial Guinea	Africa	Upper middle income
GRC	Greece	Europe	High income
GRD	Grenada	Americas	Upper middle income
GTM	Guatemala	Americas	Upper middle income
GUY	Guyana	Americas	Upper middle income
HND	Honduras	Americas	Lower middle income
HRV	Croatia	Europe	High income
HTI	Haiti	Americas	Lower middle income
HUN	Hungary	Europe	High income
IDN	Indonesia	South-East Asia	Lower middle income
IND	India	South-East Asia	Lower middle income
IRL	Ireland	Europe	High income
IRN	Iran (Islamic Republic of)	Eastern Mediterranean	Lower middle income
IRQ	Iraq	Eastern Mediterranean	Upper middle income
ISL	Iceland	Europe	High income
ISR	Israel	Europe	High income
ITA	Italy	Europe	High income
JAM	Jamaica	Americas	Upper middle income
JOR	Jordan	Eastern Mediterranean	Upper middle income
JPN	Japan	Western Pacific	High income
KAZ	Kazakhstan	Europe	Upper middle income
KEN	Kenya	Africa	Lower middle income
KGZ	Kyrgyzstan	Europe	Lower middle income
KHM	Cambodia	Western Pacific	Lower middle income
KIR	Kiribati	Western Pacific	Lower middle income
KOR	Korea, Republic of	Western Pacific	High income
KWT	Kuwait	Eastern Mediterranean	High income
LAO	Lao People's Democratic Republic	Western Pacific	Lower middle income
LBN	Lebanon	Eastern Mediterranean	Lower middle income
LBR	Liberia	Africa	Low income
LBY	Libya	Eastern Mediterranean	Upper middle income
LCA	Saint Lucia	Americas	Upper middle income
LKA	Sri Lanka	South-East Asia	Lower middle income
LSO	Lesotho	Africa	Lower middle income
LTU	Lithuania	Europe	High income
LUX	Luxembourg	Europe	High income
LVA	Latvia	Europe	High income
MAR	Morocco	Eastern Mediterranean	Lower middle income
MDA	Moldova, Republic of	Europe	Upper middle income

Continued on next page

Table A.1 – continued from previous page

Code	Name	WHO Region	Income Group
MDG	Madagascar	Africa	Low income
MDV	Maldives	South-East Asia	Upper middle income
MEX	Mexico	Americas	Upper middle income
MKD	North Macedonia	Europe	Upper middle income
MLI	Mali	Africa	Low income
MLT	Malta	Europe	High income
MMR	Myanmar	South-East Asia	Lower middle income
MNE	Montenegro	Europe	Upper middle income
MNG	Mongolia	Western Pacific	Lower middle income
MOZ	Mozambique	Africa	Low income
MRT	Mauritania	Africa	Lower middle income
MUS	Mauritius	Africa	Upper middle income
MWI	Malawi	Africa	Low income
MYS	Malaysia	Western Pacific	Upper middle income
NAM	Namibia	Africa	Upper middle income
NER	Niger	Africa	Low income
NGA	Nigeria	Africa	Lower middle income
NIC	Nicaragua	Americas	Lower middle income
NLD	Netherlands	Europe	High income
NOR	Norway	Europe	High income
NPL	Nepal	South-East Asia	Lower middle income
NZL	New Zealand	Western Pacific	High income
OMN	Oman	Eastern Mediterranean	High income
PAK	Pakistan	Eastern Mediterranean	Lower middle income
PAN	Panama	Americas	High income
PER	Peru	Americas	Upper middle income
PHL	Philippines	Western Pacific	Lower middle income
PNG	Papua New Guinea	Western Pacific	Lower middle income
POL	Poland	Europe	High income
PRT	Portugal	Europe	High income
PRY	Paraguay	Americas	Upper middle income
QAT	Qatar	Eastern Mediterranean	High income
ROU	Romania	Europe	High income
RUS	Russian Federation	Europe	Upper middle income
RWA	Rwanda	Africa	Low income
SAU	Saudi Arabia	Eastern Mediterranean	High income
SDN	Sudan	Eastern Mediterranean	Low income
SEN	Senegal	Africa	Lower middle income
SGP	Singapore	Western Pacific	High income
SLB	Solomon Islands	Western Pacific	Lower middle income
SLE	Sierra Leone	Africa	Low income
SLV	El Salvador	Americas	Lower middle income
SOM	Somalia	Eastern Mediterranean	Low income
SRB	Serbia	Europe	Upper middle income
SSD	South Sudan	Africa	Low income
STP	Sao Tome and Principe	Africa	Lower middle income

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Table A.1 – continued from previous page

Code	Name	WHO Region	Income Group
SUR	Suriname	Americas	Upper middle income
SVK	Slovakia	Europe	High income
SVN	Slovenia	Europe	High income
SWE	Sweden	Europe	High income
SWZ	Eswatini	Africa	Lower middle income
SYC	Seychelles	Africa	High income
SYR	Syrian Arab Republic	Eastern Mediterranean	Low income
TCD	Chad	Africa	Low income
TGO	Togo	Africa	Low income
THA	Thailand	South-East Asia	Upper middle income
TJK	Tajikistan	Europe	Lower middle income
TKM	Turkmenistan	Europe	Upper middle income
TLS	Timor-Leste	South-East Asia	Lower middle income
TON	Tonga	Western Pacific	Upper middle income
TTO	Trinidad and Tobago	Americas	High income
TUN	Tunisia	Eastern Mediterranean	Lower middle income
TUR	Turkey	Europe	Upper middle income
TZA	Tanzania, United Republic of	Africa	Lower middle income
UGA	Uganda	Africa	Low income
UKR	Ukraine	Europe	Lower middle income
URY	Uruguay	Americas	High income
USA	United States of America	Americas	High income
UZB	Uzbekistan	Europe	Lower middle income
VCT	Saint Vincent and the Grenadines	Americas	Upper middle income
VEN	Venezuela (Bolivarian Republic of)	Americas	Upper middle income [1]
VNM	Viet Nam	Western Pacific	Lower middle income
VUT	Vanuatu	Western Pacific	Lower middle income
WSM	Samoa	Western Pacific	Lower middle income
YEM	Yemen	Eastern Mediterranean	Low income
ZAF	South Africa	Africa	Upper middle income
ZMB	Zambia	Africa	Low income
ZWE	Zimbabwe	Africa	Lower middle income

A.2 Vaccine Effectiveness

The vaccines used until the end of 2021, divided by vaccine type, can be found in Table A.2. For mRNA and NRVV vaccines, the most widely used and with more available literature, a function of VE was made for each of the vaccine manufacturers included in the data: Pfizer/BioNTech (BNT162b2), Moderna (mRNA-1273), Oxford/AstraZeneca (ChAdOx1), Johnson & Johnson (Ad26.COV2.S), Sputnik V/Sputnik Light (Ad26-Ad5) and CanSino (Ad5-nCoV-S). Due to the absence of studies, for Inactivated

[1] Venezuela was temporarily unclassified for the fiscal year of 2023, therefore the last available classification was used

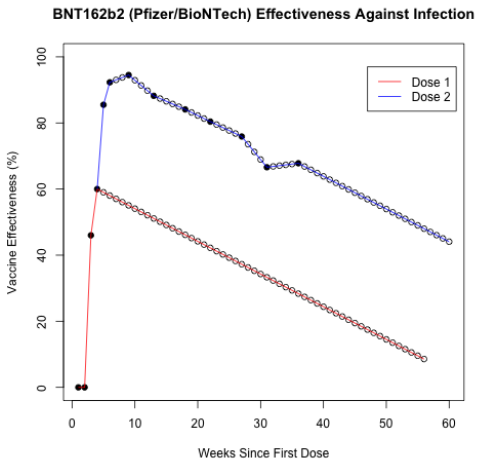
and Protein Subunit vaccines, only one function of VE was made for each, based on one or more vaccines of that vaccine type.

Table A.2: Vaccines used until the end of 2021, divided by vaccine type.

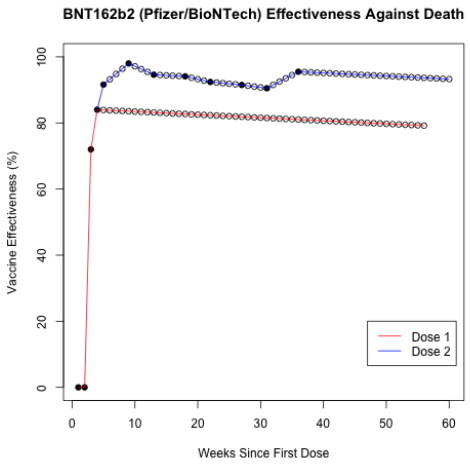
mRNA	Non Replicating Viral Vector	Inactivated	Protein Subunit
• Pfizer/BioNTech • Moderna	• Oxford/Astrazeneca • Johnson&Johnson • Sputnik V/Sputnik Light • CanSino	• Sinopharm/Beijing • Sinopharm/Wuhan • Sinovac (CoronaVac) • Covaxin • QazVac • KCONVAC • COVIran Barekat • IMBCAMS	• Novavax • Soberana02 • Abdala • ZF2001 (Zifivax) • EpiVacCorona

The respective VE functions considered in this study are shown in Figures A.1 - A.8. Full black dots represent data points retrieved from literature and empty black dots represent data points estimated from those. The following estimations were made:

- Where there were missing data points between two weeks with known VE from literature, VE in those missing weeks was linearly interpolated.
- When the effectiveness waning after the second dose wasn't available for the whole period of the study, the rest of the VE data points were linearly estimated given the slope of existing data between maximum VE and VE from the last known week from literature. For the Protein Subunit function, for which only the peak VE was available, the slope of the waning was estimated as an average of the slope of the other two-dose vaccines for the same weeks.
- The weekly decay slope after the first dose was considered the same as after the second dose for all vaccines except Sputnik V. In this case, some waning after the first dose was available in literature, so the waning slope was calculated as aforementioned for the second doses.
- Booster shots were considered to have the same waning and replenish effectiveness as a second dose.
- Johnson & Johnson and CanSino were considered one-dose vaccines, while the rest were considered two-dose vaccines. For the two-dose vaccines, the time-interval between doses was considered to be 4 weeks for all vaccines except for the Oxford/AstraZeneca, for which it was considered to be 12 weeks.

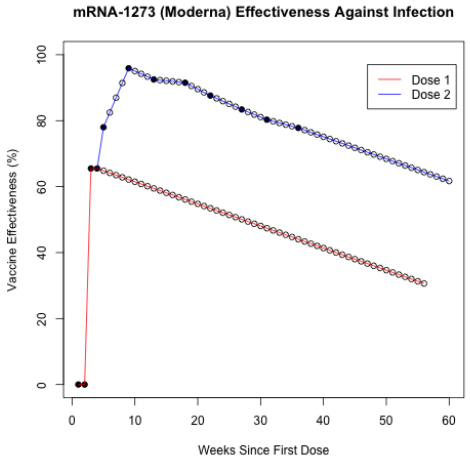


(a) Against Infection

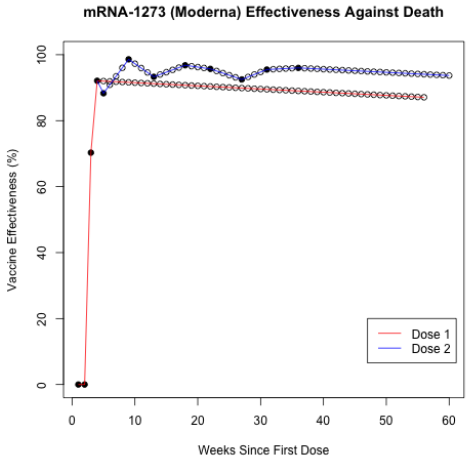


(b) Against Death

Figure A.1: Vaccine Effectiveness Functions: Pfizer/BioNTech (BNT162b2) [79, 80, 86].

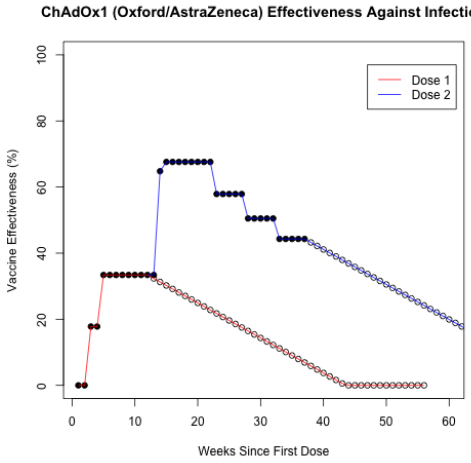


(a) Against Infection

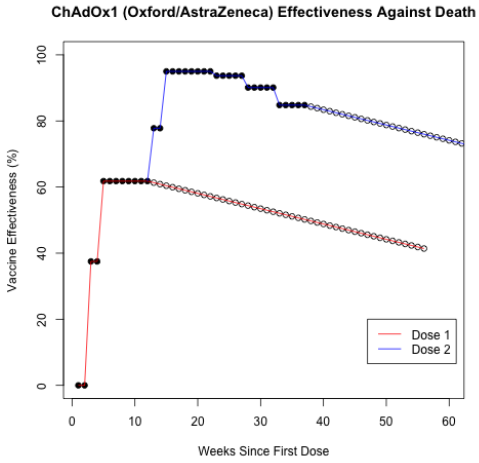


(b) Against Death

Figure A.2: Vaccine Effectiveness Functions: Moderna (mRNA-1273) [79, 85, 92].

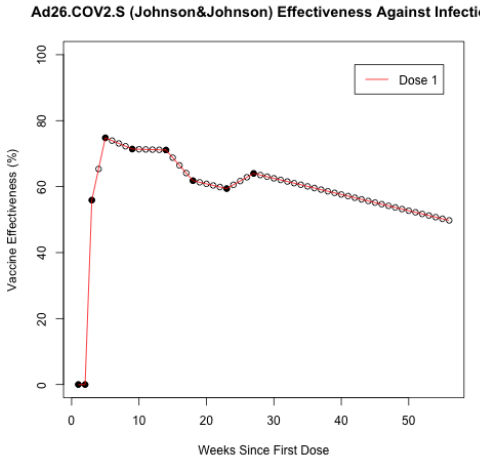


(a) Against Infection

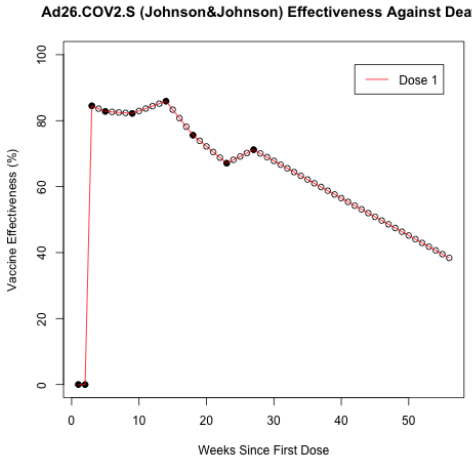


(b) Against Death

Figure A.3: Vaccine Effectiveness Functions: Oxford/AstraZeneca (ChAdOx1) [80, 88].

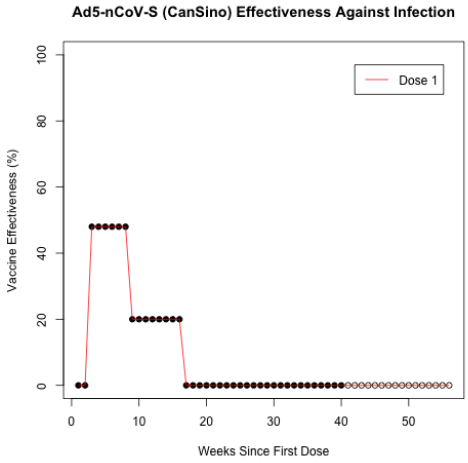


(a) Against Infection

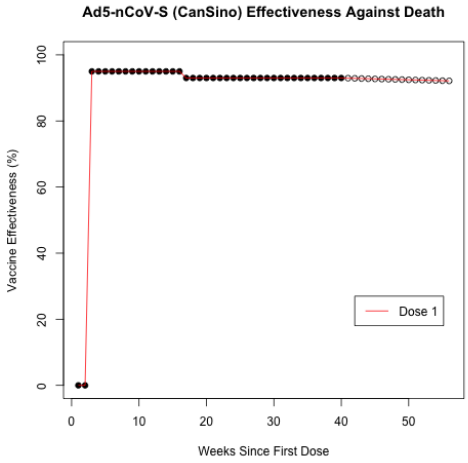


(b) Against Death

Figure A.4: Vaccine Effectiveness Functions: Johnson & Johnson (Ad26.COV2.S) [79, 91].

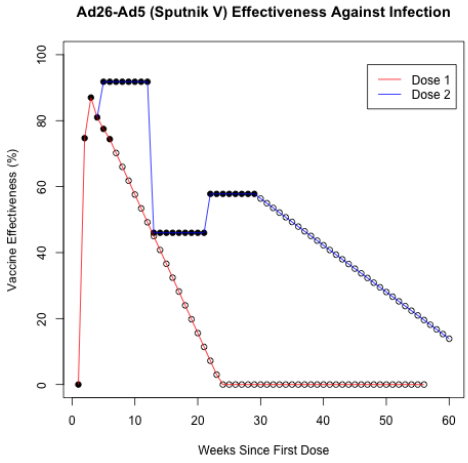


(a) Against Infection

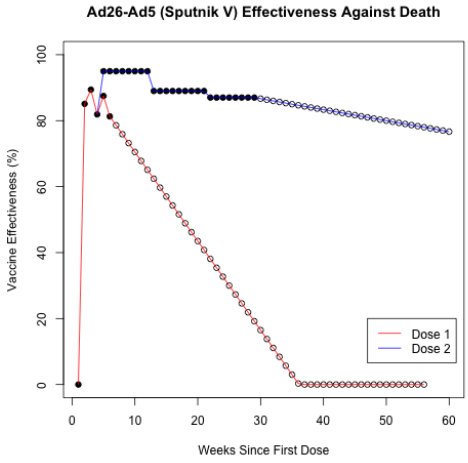


(b) Against Death

Figure A.5: Vaccine Effectiveness Functions: CanSino (Ad5-nCoV-S) [84].

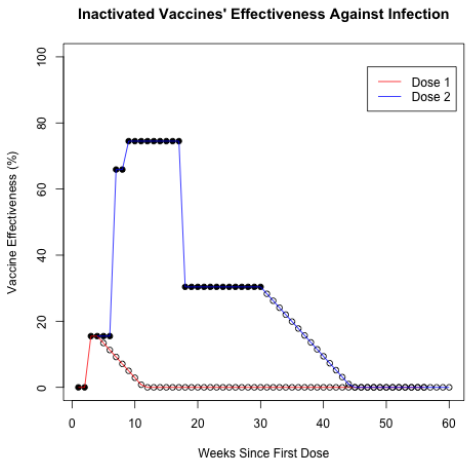


(a) Against Infection

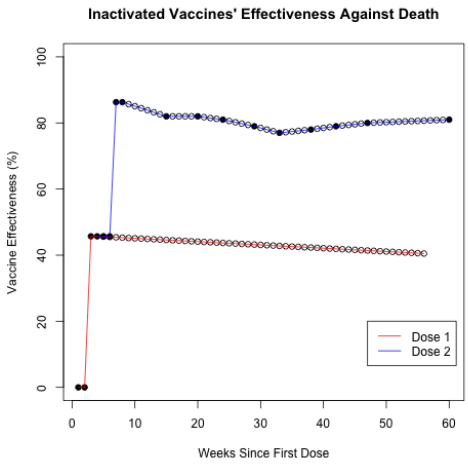


(b) Against Death

Figure A.6: Vaccine Effectiveness Functions: Sputnik V / Sputnik Light (Ad26-Ad5) [81, 89].

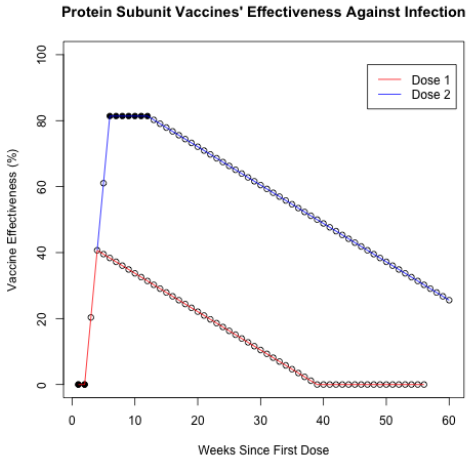


(a) Against Infection

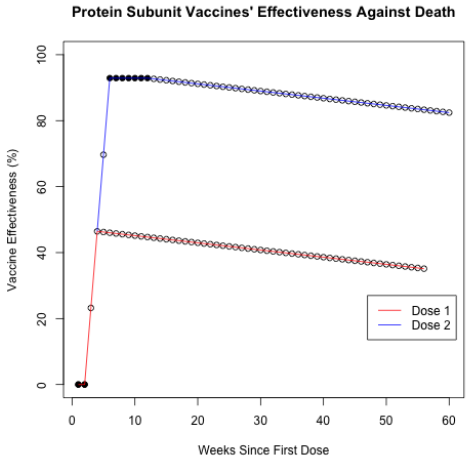


(b) Against Death

Figure A.7: Vaccine Effectiveness Functions: Inactivated Vaccines [82, 83, 87].



(a) Against Infection



(b) Against Death

Figure A.8: Vaccine Effectiveness Functions: Protein Subunit Vaccines [90].

B

Supplementary Results

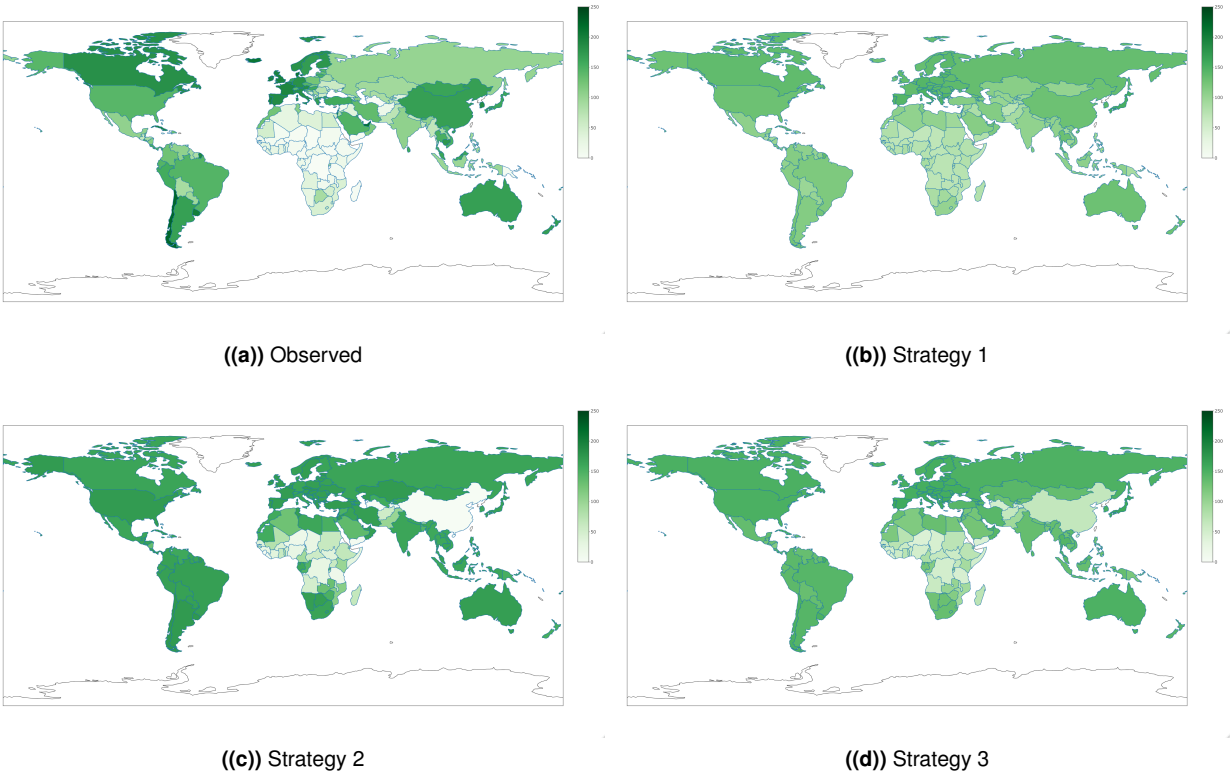
B.1 Results by Country

This section provides the general results obtained for each country over the full time-period of the study.

First, the distribution of vaccines by country, expressed as doses administered per 100 people, at the end of 2021, for each of the vaccination strategies is illustrated in Figure B.1, to understand how this distribution as varied globally.

Then, the number of cases estimated as well as the percentage of cases averted for each country according to each of the strategies of vaccination is shown in Table B.1.

Similarly, and finally, the number of deaths estimated as well as the percentage of deaths averted for each country according to each of the strategies of vaccination is shown in Table B.2.



((a)) Observed

((b)) Strategy 1

((c)) Strategy 2

((d)) Strategy 3

Figure B.1: Map of doses per 100 people at the end of 2021 in each strategy of vaccination.

Table B.1: Number of cases and percentage of cases averted in each scenario, including observed, by country.

Country	Number of Cases					Percentage of Cases Averted			
Code	No Vacc	Obs.	Sc. 1	Sc. 2	Sc. 3	Obs.	Sc. 1	Sc. 2	Sc. 3
AFG	112894	110540	102692	108919	105772	2.09%	9.04%	3.52%	6.31%
AGO	73684	67328	57990	65588	61703	8.63%	21.3%	10.99%	16.26%
ALB	207661	167899	158254	156152	157134	19.15%	23.79%	24.8%	24.33%
ARE	904913	590664	828374	626380	726548	34.73%	8.46%	30.78%	19.71%
ARG	5265515	4224106	4556496	3806783	4178818	19.78%	13.47%	27.7%	20.64%
ARM	213993	203059	171259	159757	165315	5.11%	19.97%	25.34%	22.75%
ATG	5738	4125	4221	4367	4289	28.11%	26.44%	23.89%	25.25%
AUS	1124845	464595	720594	538839	626288	58.7%	35.94%	52.1%	44.32%
AUT	1693059	979308	1212203	1058748	1132003	42.16%	28.4%	37.47%	33.14%
AZE	608407	470994	466580	445694	455654	22.59%	23.31%	26.74%	25.11%
BDI	26672	26671	21077	23848	22435	0%	20.98%	10.59%	15.89%
BEL	2871577	1378426	1974220	1711240	1839557	52%	31.25%	40.41%	35.94%
BEN	21935	21868	18670	21474	20068	0.31%	14.88%	2.1%	8.51%
BFA	14515	14415	13144	14266	13712	0.69%	9.45%	1.72%	5.53%
BGD	1165184	1108918	1006707	1083678	1044529	4.83%	13.6%	7%	10.36%
BGR	649497	588122	518068	480763	498576	9.45%	20.24%	25.98%	23.24%
BHR	269297	188904	259333	178652	218708	29.85%	3.7%	33.66%	18.79%
BHS	21728	18224	16435	15307	15813	16.13%	24.36%	29.55%	27.22%

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Table B.1 – continued from previous page

Country	Number of Cases					Percentage of Cases Averted			
Code	No Vacc	Obs.	Sc. 1	Sc. 2	Sc. 3	Obs.	Sc. 1	Sc. 2	Sc. 3
BIH	221199	197534	175265	169939	172420	10.7%	20.77%	23.17%	22.05%
BLR	620605	554030	502658	466744	483907	10.73%	19.01%	24.79%	22.03%
BLZ	35913	25068	25056	21619	23324	30.2%	30.23%	39.8%	35.05%
BOL	568209	465469	460313	429888	444722	18.08%	18.99%	24.34%	21.73%
BRA	18045543	15565601	16081402	13685233	14865018	13.74%	10.88%	24.16%	17.62%
BRB	39051	28672	25608	22684	23950	26.58%	34.42%	41.91%	38.67%
BRN	23306	15328	16992	17582	17203	34.23%	27.09%	24.56%	26.19%
BTN	3005	2218	2773	2970	2874	26.19%	7.72%	1.16%	4.36%
BWA	230006	207972	189292	141276	164936	9.58%	17.7%	38.58%	28.29%
CAF	7321	7229	6411	7146	6778	1.26%	12.43%	2.39%	7.42%
CAN	3077484	1815410	2378704	2202148	2287596	41.01%	22.71%	28.44%	25.67%
CHE	1845856	1018560	1287630	1219227	1251376	44.82%	30.24%	33.95%	32.21%
CHL	2310335	1560857	2074762	1595445	1832621	32.44%	10.2%	30.94%	20.68%
CHN	30645	22487	24159	30619	27373	26.62%	21.16%	0.08%	10.68%
CIV	52740	50910	45311	50121	47689	3.47%	14.09%	4.97%	9.58%
CMR	85040	84625	75925	82181	78989	0.49%	10.72%	3.36%	7.12%
COD	61291	61267	52108	60410	56243	0.04%	14.98%	1.44%	8.24%
COG	14846	14319	12343	13593	12963	3.55%	16.86%	8.44%	12.68%
COL	4477920	3879268	3928790	3559885	3742879	13.37%	12.26%	20.5%	16.41%
COM	7119	6218	5675	5583	5618	12.66%	20.28%	21.58%	21.08%
CPV	39504	31750	32664	29619	31131	19.63%	17.31%	25.02%	21.2%
CRI	453760	318274	360629	276693	317979	29.86%	20.52%	39.02%	29.92%
CUB	1417073	958163	1036582	791611	911492	32.38%	26.85%	44.14%	35.68%
CYP	210925	156698	171540	138199	154671	25.71%	18.67%	34.48%	26.67%
CZE	2615199	1937223	2094952	1834455	1964710	25.92%	19.89%	29.85%	24.87%
DEU	11487597	5993526	8055530	7694241	7863097	47.83%	29.88%	33.02%	31.55%
DJI	8045	7976	7347	7767	7552	0.86%	8.68%	3.46%	6.13%
DNK	2114176	742629	1324354	1246882	1284892	64.87%	37.36%	41.02%	39.22%
DOM	354395	274165	294500	270898	282395	22.64%	16.9%	23.56%	20.32%
DZA	133312	130898	117693	128154	122863	1.81%	11.72%	3.87%	7.84%
ECU	550895	463546	478573	448790	463274	15.86%	13.13%	18.53%	15.91%
EGY	289145	268723	243899	267283	255274	7.06%	15.65%	7.56%	11.71%
ESP	9633715	5111261	6913382	6081036	6488499	46.94%	28.24%	36.88%	32.65%
EST	287719	207817	229342	189925	209447	27.77%	20.29%	33.99%	27.2%
ETH	315085	313375	271400	295133	283123	0.54%	13.86%	6.33%	10.14%
FIN	540699	254721	380140	346874	361802	52.89%	29.69%	35.85%	33.09%
FJI	74338	54088	60187	49063	54467	27.24%	19.04%	34%	26.73%
FRA	16382732	7886410	11659928	10438558	11027263	51.86%	28.83%	36.28%	32.69%
GAB	33575	32549	27927	27368	27592	3.06%	16.82%	18.49%	17.82%
GBR	23176682	11758029	16868169	12880031	14866431	49.27%	27.22%	44.43%	35.86%
GEO	884104	775162	671986	531771	601546	12.32%	23.99%	39.85%	31.96%
GHA	95381	92782	82864	89799	86282	2.72%	13.12%	5.85%	9.54%
GIN	20628	19435	18161	19988	19062	5.78%	11.96%	3.1%	7.59%
GMB	6521	6402	5888	6335	6116	1.82%	9.71%	2.85%	6.21%
GNB	4051	4033	3614	3945	3785	0.44%	10.79%	2.62%	6.57%

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Table B.1 – continued from previous page

Country	Number of Cases					Percentage of Cases Averted			
Code	No Vacc	Obs.	Sc. 1	Sc. 2	Sc. 3	Obs.	Sc. 1	Sc. 2	Sc. 3
GNQ	9180	8554	7647	8199	7918	6.82%	16.7%	10.69%	13.75%
GRC	1979582	1165733	1419428	1204148	1309258	41.11%	28.3%	39.17%	33.86%
GRD	7577	6255	5235	6148	5679	17.45%	30.91%	18.86%	25.05%
GTM	584537	503147	474635	426550	449968	13.92%	18.8%	27.03%	23.02%
GUY	46969	34392	36274	30084	33122	26.78%	22.77%	35.95%	29.48%
HND	307871	268385	265654	242635	253897	12.83%	13.71%	21.19%	17.53%
HRV	791401	570605	576858	512509	543794	27.9%	27.11%	35.24%	31.29%
HTI	16651	16612	14219	16208	15209	0.23%	14.61%	2.66%	8.66%
HUN	1428803	1008384	1092196	993146	1040624	29.42%	23.56%	30.49%	27.17%
IDN	3878801	3687371	3495146	3597587	3544759	4.94%	9.89%	7.25%	8.61%
IND	26943492	25245674	24776534	24625290	24688041	6.3%	8.04%	8.6%	8.37%
IRL	1551138	697694	1080292	887465	983238	55.02%	30.35%	42.79%	36.61%
IRN	5766259	5156367	4863345	4039775	4446651	10.58%	15.66%	29.94%	22.88%
IRQ	1594525	1529895	1399185	1170011	1282677	4.05%	12.25%	26.62%	19.56%
ISL	86076	25390	57311	51435	54277	70.5%	33.42%	40.24%	36.94%
ISR	2019914	1051410	1742172	1313391	1526465	47.95%	13.75%	34.98%	24.43%
ITA	8153217	4759094	5976300	5730546	5846179	41.63%	26.7%	29.71%	28.3%
JAM	90950	84064	74825	73955	74312	7.57%	17.73%	18.69%	18.29%
JOR	1011773	825479	832279	720668	775858	18.41%	17.74%	28.77%	23.32%
JPN	2292630	1570426	1799310	2118640	1957739	31.5%	21.52%	7.59%	14.61%
KAZ	1227777	952282	958419	829916	891924	22.44%	21.94%	32.4%	27.35%
KEN	219376	210125	186349	197814	191935	4.22%	15.05%	9.83%	12.51%
KGZ	115637	109385	97777	96083	96864	5.41%	15.44%	16.91%	16.23%
KHM	168429	120161	140663	144704	142533	28.66%	16.49%	14.09%	15.38%
KIR	1	1	1	1	1	0%	0%	0%	0%
KOR	1213590	604041	829627	761835	791802	50.23%	31.64%	37.22%	34.76%
KWT	357265	273959	318267	249249	283531	23.32%	10.92%	30.23%	20.64%
LAO	179680	112722	118047	93679	105327	37.27%	34.3%	47.86%	41.38%
LBN	650954	595624	570691	510602	540324	8.5%	12.33%	21.56%	17%
LBR	4845	4714	4265	4793	4536	2.7%	11.97%	1.07%	6.38%
LBY	322109	303068	272938	248474	260234	5.91%	15.27%	22.86%	19.21%
LCA	14889	13472	12187	10898	11536	9.52%	18.15%	26.81%	22.52%
LKA	818360	560047	649308	582265	614489	31.56%	20.66%	28.85%	24.91%
LSO	31433	27603	24356	23592	23866	12.18%	22.51%	24.95%	24.07%
LTU	796775	491033	585893	500247	542503	38.37%	26.47%	37.22%	31.91%
LUX	112676	71463	86258	73775	79951	36.58%	23.45%	34.52%	29.04%
LVA	352204	255685	270579	233664	251973	27.4%	23.18%	33.66%	28.46%
MAR	765360	587123	631235	686796	658002	23.29%	17.52%	10.26%	14.03%
MDA	302578	260231	235531	224806	229929	14%	22.16%	25.7%	24.01%
MDG	32988	32805	29644	32430	31035	0.55%	10.14%	1.69%	5.92%
MDV	109486	72914	97882	71156	84278	33.4%	10.6%	35.01%	23.02%
MEX	3396137	2764001	2871804	2847520	2854882	18.61%	15.44%	16.15%	15.94%
MKD	192973	157626	151339	141910	146404	18.32%	21.58%	26.46%	24.13%
MLI	16615	16413	14076	15759	14919	1.22%	15.28%	5.15%	10.21%
MLT	102165	44193	73646	62476	67950	56.74%	27.91%	38.85%	33.49%

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Table B.1 – continued from previous page

Country	Number of Cases					Percentage of Cases Averted			
Code	No Vacc	Obs.	Sc. 1	Sc. 2	Sc. 3	Obs.	Sc. 1	Sc. 2	Sc. 3
MMR	456373	431876	372464	403130	387362	5.37%	18.39%	11.67%	15.12%
MNE	168958	138487	130364	111476	120883	18.03%	22.84%	34.02%	28.45%
MNG	1246622	692700	992452	685995	837936	44.43%	20.39%	44.97%	32.78%
MOZ	189225	176221	158772	168558	163382	6.87%	16.09%	10.92%	13.66%
MRT	34443	32664	29385	29920	29619	5.17%	14.69%	13.13%	14.01%
MUS	111395	68247	75622	75224	75178	38.73%	32.11%	32.47%	32.51%
MWI	71465	70019	62358	68307	65287	2.02%	12.74%	4.42%	8.64%
MYS	3629318	2573605	2951673	2095895	2519332	29.09%	18.67%	42.25%	30.58%
NAM	138993	134402	122354	107592	114848	3.3%	11.97%	22.59%	17.37%
NER	5620	5580	5040	5580	5319	0.71%	10.32%	0.71%	5.36%
NGA	175827	173619	155318	172731	163984	1.26%	11.66%	1.76%	6.74%
NIC	13106	11644	9956	12105	11021	11.16%	24.03%	7.64%	15.91%
NLD	4759668	2609003	3483492	3021854	3251162	45.19%	26.81%	36.51%	31.69%
NOR	836159	365467	580205	500733	539724	56.29%	30.61%	40.12%	35.45%
NPL	631558	586600	557373	537531	546887	7.12%	11.75%	14.89%	13.41%
NZL	40669	12228	25729	30789	28100	69.93%	36.74%	24.29%	30.91%
OMN	195739	180942	181980	162111	171893	7.56%	7.03%	17.18%	12.18%
PAK	924202	876937	828836	886239	857133	5.11%	10.32%	4.11%	7.26%
PAN	411301	321064	349786	306856	328175	21.94%	14.96%	25.39%	20.21%
PER	1526997	1329992	1343566	1249094	1295398	12.9%	12.01%	18.2%	15.17%
PHL	2852629	2412100	2282847	2148305	2209889	15.44%	19.97%	24.69%	22.53%
PNG	36037	35517	29970	33454	31672	1.44%	16.84%	7.17%	12.11%
POL	4082160	3063984	3186583	2865730	3017996	24.94%	21.94%	29.8%	26.07%
PRT	2141131	1107741	1563156	1371676	1466906	48.26%	26.99%	35.94%	31.49%
PRY	392184	378186	366772	323516	344904	3.57%	6.48%	17.51%	12.06%
QAT	190184	112454	165521	137410	151294	40.87%	12.97%	27.75%	20.45%
ROU	1695988	1276633	1204929	1140869	1170542	24.73%	28.95%	32.73%	30.98%
RUS	10241273	7918936	7627367	7102952	7361217	22.68%	25.52%	30.64%	28.12%
RWA	126488	107453	102828	103566	103112	15.05%	18.71%	18.12%	18.48%
SAU	253044	199395	220366	228660	224396	21.2%	12.91%	9.64%	11.32%
SDN	27368	26781	23167	26500	24822	2.14%	15.35%	3.17%	9.3%
SEN	60374	59192	55331	58769	57031	1.96%	8.35%	2.66%	5.54%
SGP	659551	222018	448136	408692	424077	66.34%	32.05%	38.03%	35.7%
SLB	3	3	3	3	3	0%	0%	0%	0%
SLE	4828	4739	4318	4802	4570	1.84%	10.56%	0.54%	5.34%
SLV	123643	81809	96272	96708	96174	33.83%	22.14%	21.78%	22.22%
SOM	19190	19005	16865	18764	17809	0.96%	12.12%	2.22%	7.2%
SRB	1304665	1083210	1018831	895887	955853	16.97%	21.91%	31.33%	26.74%
SSD	12130	12063	10687	11891	11280	0.55%	11.9%	1.97%	7.01%
STP	3179	2902	2693	2724	2701	8.71%	15.29%	14.31%	15.04%
SUR	63083	47567	46356	39055	42510	24.6%	26.52%	38.09%	32.61%
SVK	1382849	1106949	1107572	980655	1044096	19.95%	19.91%	29.08%	24.5%
SVN	528628	380909	403470	348472	375834	27.94%	23.68%	34.08%	28.9%
SWE	1471818	1051286	1217694	1112698	1164284	28.57%	17.27%	24.4%	20.89%
SWZ	68617	59780	53588	50629	52054	12.88%	21.9%	26.22%	24.14%

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Table B.1 – continued from previous page

Country	Number of Cases					Percentage of Cases Averted			
Code	No Vacc	Obs.	Sc. 1	Sc. 2	Sc. 3	Obs.	Sc. 1	Sc. 2	Sc. 3
SYC	40720	24602	37021	21057	28986	39.58%	9.08%	48.29%	28.82%
SYR	42745	41937	34988	40358	37623	1.89%	18.15%	5.58%	11.98%
TCD	4465	4455	4033	4386	4220	0.22%	9.68%	1.77%	5.49%
TGO	29524	28065	24893	26605	25724	4.94%	15.69%	9.89%	12.87%
THA	2746925	2225473	2071283	2025434	2040906	18.98%	24.6%	26.27%	25.7%
TJK	5352	5095	4597	5313	4952	4.8%	14.11%	0.73%	7.47%
TKM	0	0	0	0	0	-	-	-	-
TLS	21769	19799	18746	18104	18396	9.05%	13.89%	16.84%	15.49%
TON	0	0	0	0	0	-	-	-	-
TTO	115067	85899	79410	73082	76150	25.35%	30.99%	36.49%	33.82%
TUN	687428	624256	605350	522898	563644	9.19%	11.94%	23.93%	18.01%
TUR	12049963	7689389	9415486	7574418	8483285	36.19%	21.86%	37.14%	29.6%
TZA	29366	28796	21782	28998	25356	1.94%	25.83%	1.25%	13.66%
UGA	125783	122040	108518	115778	112021	2.98%	13.73%	7.95%	10.94%
UKR	3297880	2879551	2505192	2351888	2424632	12.68%	24.04%	28.68%	26.48%
URY	552205	407941	493135	366787	428981	26.13%	10.7%	33.58%	22.31%
USA	69547877	40432181	53240704	43703381	48438554	41.86%	23.45%	37.16%	30.35%
UZB	155023	125072	117918	132312	124961	19.32%	23.94%	14.65%	19.39%
VCT	6458	5857	5001	4678	4834	9.31%	22.56%	27.56%	25.15%
VEN	405955	340538	314975	314696	314395	16.11%	22.41%	22.48%	22.55%
VNM	2825727	1761666	1902623	1712026	1800460	37.66%	32.67%	39.41%	36.28%
VUT	2	2	2	2	2	0%	0%	0%	0%
WSM	0	0	0	0	0	-	-	-	-
YEM	8061	8044	7204	8041	7634	0.21%	10.63%	0.25%	5.3%
ZAF	3044221	2639290	2519607	2263673	2387625	13.3%	17.23%	25.64%	21.57%
ZMB	246300	241758	215453	211079	213136	1.84%	12.52%	14.3%	13.46%
ZWE	236254	203498	180922	174963	177754	13.86%	23.42%	25.94%	24.76%

Table B.2: Number of deaths and percentage of deaths averted in each scenario, including observed, by country.

Country	Number of Deaths					Percentage of Deaths Averted			
Code	No Vacc	Obs.	Sc. 1	Sc. 2	Sc. 3	Obs.	Sc. 1	Sc. 2	Sc. 3
AFG	7719	5492	3970	5119	4547	28.85%	48.57%	33.68%	41.09%
AGO	2128	1418	1134	1496	1320	33.36%	46.71%	29.7%	37.97%
ALB	4816	2312	2193	2080	2138	51.99%	54.46%	56.81%	55.61%
ARE	6045	1563	4418	1963	3179	74.14%	26.91%	67.53%	47.41%
ARG	146644	71720	78555	53063	65629	51.09%	46.43%	63.82%	55.25%
ARM	12007	5657	3730	3728	3715	52.89%	68.93%	68.95%	69.06%
ATG	350	90	96	107	105	74.29%	72.57%	69.43%	70%
AUS	8137	1352	1750	3221	2486	83.38%	78.49%	60.42%	69.45%
AUT	47452	11954	15683	15430	15509	74.81%	66.95%	67.48%	67.32%
AZE	19452	6735	6428	6468	6438	65.38%	66.95%	66.75%	66.9%
BDI	31	31	22	30	26	0%	29.03%	3.23%	16.13%

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Table B.2 – continued from previous page

Country	Number of Deaths					Percentage of Deaths Averted			
Code	No Vacc	Obs.	Sc. 1	Sc. 2	Sc. 3	Obs.	Sc. 1	Sc. 2	Sc. 3
BEL	30970	10533	12112	11622	11772	65.99%	60.89%	62.47%	61.99%
BEN	97	96	72	94	88	1.03%	25.77%	3.09%	9.28%
BFA	297	228	150	229	200	23.23%	49.49%	22.9%	32.66%
BGD	34305	21230	15584	20909	18230	38.11%	54.57%	39.05%	46.86%
BGR	31046	26228	14735	14082	14351	15.52%	52.54%	54.64%	53.78%
BHR	4493	1041	3581	1070	2320	76.83%	20.3%	76.19%	48.36%
BHS	1456	582	503	449	471	60.03%	65.45%	69.16%	67.65%
BIH	19115	9785	7937	7642	7758	48.81%	58.48%	60.02%	59.41%
BLR	10823	4396	3322	3235	3279	59.38%	69.31%	70.11%	69.7%
BLZ	1248	411	406	388	404	67.07%	67.47%	68.91%	67.63%
BOL	22793	10717	10254	8905	9558	52.98%	55.01%	60.93%	58.07%
BRA	888380	442355	485429	332601	408260	50.21%	45.36%	62.56%	54.04%
BRB	860	230	212	213	216	73.26%	75.35%	75.23%	74.88%
BRN	366	93	104	160	132	74.59%	71.58%	56.28%	63.93%
BTN	0	0	0	0	0	-	-	-	-
BWA	3666	2407	2165	1519	1847	34.34%	40.94%	58.57%	49.62%
CAF	29	29	27	29	29	0%	6.9%	0%	0%
CAN	38929	15729	18271	18683	18477	59.6%	53.07%	52.01%	52.54%
CHE	12364	6555	6477	6286	6388	46.98%	47.61%	49.16%	48.33%
CHL	84245	24388	47366	27777	37475	71.05%	43.78%	67.03%	55.52%
CHN	11	3	2	11	6	72.73%	81.82%	0%	45.45%
CIV	700	570	406	561	484	18.57%	42%	19.86%	30.86%
CMR	1514	1407	1083	1270	1179	7.07%	28.47%	16.12%	22.13%
COD	849	848	701	822	771	0.12%	17.43%	3.18%	9.19%
COG	344	246	157	221	193	28.49%	54.36%	35.76%	43.9%
COL	163287	89234	88682	68735	78622	45.35%	45.69%	57.91%	51.85%
COM	155	146	144	143	145	5.81%	7.1%	7.74%	6.45%
CPV	321	220	219	167	196	31.46%	31.78%	47.98%	38.94%
CRI	16421	5301	6267	5987	6124	67.72%	61.84%	63.54%	62.71%
CUB	32962	8173	8933	7771	8361	75.2%	72.9%	76.42%	74.63%
CYP	1551	671	674	543	617	56.74%	56.54%	64.99%	60.22%
CZE	56392	27137	28221	20241	24565	51.88%	49.96%	64.11%	56.44%
DEU	231070	91414	100767	104666	102449	60.44%	56.39%	54.7%	55.66%
DJI	132	116	88	100	94	12.12%	33.33%	24.24%	28.79%
DNK	11967	2336	3751	3753	3757	80.48%	68.66%	68.64%	68.61%
DOM	3285	1718	1900	1795	1860	47.7%	42.16%	45.36%	43.38%
DZA	4346	3763	2778	3565	3171	13.41%	36.08%	17.97%	27.04%
ECU	16146	10725	10286	9237	9750	33.57%	36.29%	42.79%	39.61%
EGY	24918	15021	12249	16062	14130	39.72%	50.84%	35.54%	43.29%
ESP	157615	40412	57649	52926	55596	74.36%	63.42%	66.42%	64.73%
EST	3240	1646	1434	1122	1288	49.2%	55.74%	65.37%	60.25%
ETH	5439	5210	3757	4690	4225	4.21%	30.92%	13.77%	22.32%
FIN	9778	1776	2714	3195	2932	81.84%	72.24%	67.32%	70.01%
FJI	3227	691	953	805	886	78.59%	70.47%	75.05%	72.54%
FRA	148624	58120	64873	56500	60486	60.89%	56.35%	61.98%	59.3%

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Table B.2 – continued from previous page

Country	Number of Deaths					Percentage of Deaths Averted			
Code	No Vacc	Obs.	Sc. 1	Sc. 2	Sc. 3	Obs.	Sc. 1	Sc. 2	Sc. 3
GAB	241	198	136	144	144	17.84%	43.57%	40.25%	40.25%
GBR	249430	99967	129971	112078	121585	59.92%	47.89%	55.07%	51.25%
GEO	35978	12380	9719	9202	9582	65.59%	72.99%	74.42%	73.37%
GHA	1198	957	781	910	845	20.12%	34.81%	24.04%	29.47%
GIN	428	296	247	343	301	30.84%	42.29%	19.86%	29.67%
GMB	219	185	143	181	164	15.53%	34.7%	17.35%	25.11%
GNB	85	82	55	78	64	3.53%	35.29%	8.24%	24.71%
GNQ	105	65	49	63	57	38.1%	53.33%	40%	45.71%
GRC	46087	17843	16826	16829	16696	61.28%	63.49%	63.48%	63.77%
GRD	769	194	167	384	280	74.77%	78.28%	50.07%	63.59%
GTM	28350	11854	10793	9961	10377	58.19%	61.93%	64.86%	63.4%
GUY	3321	877	1066	903	979	73.59%	67.9%	72.81%	70.52%
HND	16452	7492	6709	5764	6237	54.46%	59.22%	64.96%	62.09%
HRV	19229	10425	8228	7921	8034	45.79%	57.21%	58.81%	58.22%
HTI	524	508	226	405	317	3.05%	56.87%	22.71%	39.5%
HUN	68977	32280	33875	28663	31077	53.2%	50.89%	58.45%	54.95%
IDN	237989	126357	103283	116663	109936	46.91%	56.6%	50.98%	53.81%
IND	634151	333945	334503	330364	331361	47.34%	47.25%	47.9%	47.75%
IRL	15830	3703	5697	4816	5323	76.61%	64.01%	69.58%	66.37%
IRN	154196	81370	62627	51400	57004	47.23%	59.38%	66.67%	63.03%
IRQ	20219	11732	8623	6625	7606	41.98%	57.35%	67.23%	62.38%
ISL	113	11	31	36	31	90.27%	72.57%	68.14%	72.57%
ISR	27273	5326	16388	11776	14096	80.47%	39.91%	56.82%	48.32%
ITA	157497	74252	77046	73507	75059	52.85%	51.08%	53.33%	52.34%
JAM	5091	2207	1672	1667	1662	56.65%	67.16%	67.26%	67.35%
JOR	21308	9662	10431	7059	8745	54.66%	51.05%	66.87%	58.96%
JPN	32864	16046	15956	23293	19613	51.17%	51.45%	29.12%	40.32%
KAZ	50314	15938	14110	13011	13549	68.32%	71.96%	74.14%	73.07%
KEN	4874	3850	3202	3609	3405	21.01%	34.3%	25.95%	30.14%
KGZ	2270	1503	1048	1063	1054	33.79%	53.83%	53.17%	53.57%
KHM	10974	3013	4006	4750	4371	72.54%	63.5%	56.72%	60.17%
KIR	0	0	0	0	0	-	-	-	-
KOR	18515	5174	5737	6401	6047	72.06%	69.01%	65.43%	67.34%
KWT	5430	1565	3127	1417	2262	71.18%	42.41%	73.9%	58.34%
LAO	1416	369	339	308	326	73.94%	76.06%	78.25%	76.98%
LBN	12149	8054	7704	5904	6818	33.71%	36.59%	51.4%	43.88%
LBR	215	194	134	190	165	9.77%	37.67%	11.63%	23.26%
LBY	7655	4486	3401	3024	3205	41.4%	55.57%	60.5%	58.13%
LCA	818	283	244	218	238	65.4%	70.17%	73.35%	70.9%
LKA	50297	14870	16577	14395	15462	70.44%	67.04%	71.38%	69.26%
LSO	799	606	488	611	554	24.16%	38.92%	23.53%	30.66%
LTU	14651	6814	5533	5029	5310	53.49%	62.23%	65.67%	63.76%
LUX	1469	644	713	614	666	56.16%	51.46%	58.2%	54.66%
LVA	6277	3933	2776	2482	2645	37.34%	55.78%	60.46%	57.86%
MAR	25892	8606	10525	16595	13549	66.76%	59.35%	35.91%	47.67%

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Table B.2 – continued from previous page

Country	Number of Deaths					Percentage of Deaths Averted			
Code	No Vacc	Obs.	Sc. 1	Sc. 2	Sc. 3	Obs.	Sc. 1	Sc. 2	Sc. 3
MDA	16442	7286	6249	5693	5976	55.69%	61.99%	65.38%	63.65%
MDG	777	752	657	738	711	3.22%	15.44%	5.02%	8.49%
MDV	890	198	496	203	347	77.75%	44.27%	77.19%	61.01%
MEX	309612	139108	155157	169330	162236	55.07%	49.89%	45.31%	47.6%
MKD	13836	5779	5353	4766	5061	58.23%	61.31%	65.55%	63.42%
MLI	530	487	405	474	446	8.11%	23.58%	10.57%	15.85%
MLT	1379	356	638	498	573	74.18%	53.73%	63.89%	58.45%
MMR	33644	17156	10109	18671	14360	49.01%	69.95%	44.5%	57.32%
MNE	4613	1895	1747	1254	1517	58.92%	62.13%	72.82%	67.11%
MNG	9666	2052	3674	2552	3102	78.77%	61.99%	73.6%	67.91%
MOZ	2279	1908	1572	1796	1681	16.28%	31.02%	21.19%	26.24%
MRT	854	664	547	582	563	22.25%	35.95%	31.85%	34.07%
MUS	2853	763	1022	856	934	73.26%	64.18%	70%	67.26%
MWI	2541	2176	1818	2116	1965	14.36%	28.45%	16.73%	22.67%
MYS	123851	30880	43910	27797	35817	75.07%	64.55%	77.56%	71.08%
NAM	4410	3504	2881	2005	2436	20.54%	34.67%	54.54%	44.76%
NER	205	176	135	183	166	14.15%	34.15%	10.73%	19.02%
NGA	2212	1830	1476	1874	1679	17.27%	33.27%	15.28%	24.1%
NIC	0	0	0	0	0	-	-	-	-
NLD	29169	11059	12075	10765	11522	62.09%	58.6%	63.09%	60.5%
NOR	9125	1168	2386	2609	2475	87.2%	73.85%	71.41%	72.88%
NPL	16505	9958	9311	9830	9556	39.67%	43.59%	40.44%	42.1%
NZL	102	16	24	51	37	84.31%	76.47%	50%	63.73%
OMN	6931	2659	3197	2017	2603	61.64%	53.87%	70.9%	62.44%
PAK	33754	20537	17708	22554	20107	39.16%	47.54%	33.18%	40.43%
PAN	8712	4226	4705	3836	4274	51.49%	45.99%	55.97%	50.94%
PER	164028	113445	103841	84625	94037	30.84%	36.69%	48.41%	42.67%
PHL	115966	43019	38724	36862	37656	62.9%	66.61%	68.21%	67.53%
PNG	1032	569	327	439	376	44.86%	68.31%	57.46%	63.57%
POL	139449	77490	71648	60841	65820	44.43%	48.62%	56.37%	52.8%
PRT	38188	13947	17288	16046	16824	63.48%	54.73%	57.98%	55.94%
PRY	24645	14751	12005	7974	9968	40.15%	51.29%	67.64%	59.55%
QAT	1072	354	783	352	566	66.98%	26.96%	67.16%	47.2%
ROU	141930	43311	44713	43715	44143	69.48%	68.5%	69.2%	68.9%
RUS	952486	261601	253341	251181	253054	72.53%	73.4%	73.63%	73.43%
RWA	2093	1294	1117	1231	1183	38.17%	46.63%	41.18%	43.48%
SAU	7298	2906	3353	3751	3552	60.18%	54.06%	48.6%	51.33%
SDN	2461	2033	1515	2071	1795	17.39%	38.44%	15.85%	27.06%
SEN	1829	1555	1341	1525	1436	14.98%	26.68%	16.62%	21.49%
SGP	4297	789	920	1054	982	81.64%	78.59%	75.47%	77.15%
SLB	0	0	0	0	0	NaN%	NaN%	NaN%	NaN%
SLE	42	38	33	41	39	9.52%	21.43%	2.38%	7.14%
SLV	8261	2652	3080	3921	3494	67.9%	62.72%	52.54%	57.7%
SOM	1445	1204	833	1107	971	16.68%	42.35%	23.39%	32.8%
SRB	38142	10804	12759	10684	11803	71.67%	66.55%	71.99%	69.06%

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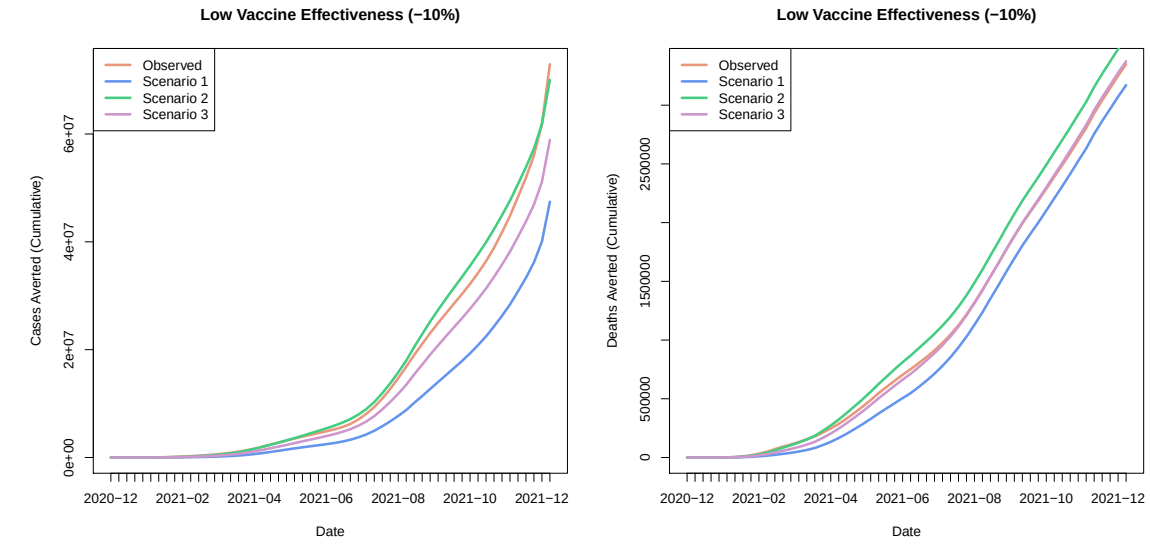
Table B.2 – continued from previous page

Country	Number of Deaths					Percentage of Deaths Averted			
Code	No Vacc	Obs.	Sc. 1	Sc. 2	Sc. 3	Obs.	Sc. 1	Sc. 2	Sc. 3
SSD	59	59	52	58	58	0%	11.86%	1.69%	1.69%
STP	40	30	25	29	28	25%	37.5%	27.5%	30%
SUR	3819	1047	1116	1005	1061	72.58%	70.78%	73.68%	72.22%
SVK	24388	15068	13802	10164	12087	38.22%	43.41%	58.32%	50.44%
SVN	8477	4172	3884	3416	3694	50.78%	54.18%	59.7%	56.42%
SWE	18675	7709	9347	8193	8810	58.72%	49.95%	56.13%	52.82%
SWZ	1811	1170	1063	1034	1045	35.39%	41.3%	42.9%	42.3%
SYC	396	101	282	108	189	74.49%	28.79%	72.73%	52.27%
SYR	2881	2455	1708	2186	1944	14.79%	40.72%	24.12%	32.52%
TCD	65	65	60	64	63	0%	7.69%	1.54%	3.08%
TGO	224	156	118	151	137	30.36%	47.32%	32.59%	38.84%
THA	50987	21658	15500	18029	16735	57.52%	69.6%	64.64%	67.18%
TJK	68	38	18	68	44	44.12%	73.53%	0%	35.29%
TKM	0	0	0	0	0	-	-	-	-
TLS	316	105	91	80	88	66.77%	71.2%	74.68%	72.15%
TON	0	0	0	0	0	-	-	-	-
TTO	8172	2765	2340	2219	2281	66.16%	71.37%	72.85%	72.09%
TUN	40592	22026	18700	15860	17264	45.74%	53.93%	60.93%	57.47%
TUR	209579	66655	79491	62115	70906	68.2%	62.07%	70.36%	66.17%
TZA	836	708	360	824	596	15.31%	56.94%	1.44%	28.71%
UGA	3570	3089	2360	2800	2583	13.47%	33.89%	21.57%	27.65%
UKR	173730	82468	62736	60858	61431	52.53%	63.89%	64.97%	64.64%
URY	18863	6089	11465	5487	8430	67.72%	39.22%	70.91%	55.31%
USA	1825939	541914	848919	605012	729957	70.32%	53.51%	66.87%	60.02%
UZB	3524	883	791	1190	990	74.94%	77.55%	66.23%	71.91%
VCT	221	59	47	46	47	73.3%	78.73%	79.19%	78.73%
VEN	8075	4412	3384	3727	3557	45.36%	58.09%	53.85%	55.95%
VNM	102819	32794	26260	37198	31661	68.11%	74.46%	63.82%	69.21%
VUT	0	0	0	0	0	-	-	-	-
WSM	0	0	0	0	0	-	-	-	-
YEM	1483	1357	876	1355	1120	8.5%	40.93%	8.63%	24.48%
ZAF	89566	69027	61203	52765	56964	22.93%	31.67%	41.09%	36.4%
ZMB	3734	3375	2801	2656	2728	9.61%	24.99%	28.87%	26.94%
ZWE	7407	4722	4215	4835	4527	36.25%	43.09%	34.72%	38.88%

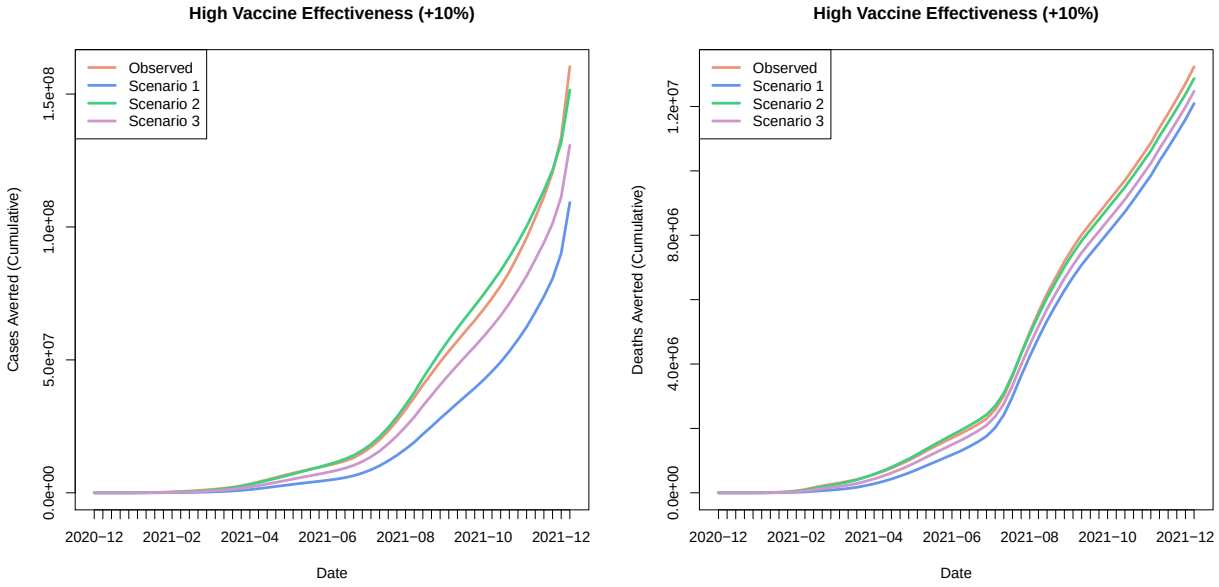
B.2 Sensitivity Analysis Results

This section presents additional results from the sensitivity analyses performed. Figure B.2 shows the cumulative events (cases and deaths) averted over time in a low VE setting. Alternatively, Figure B.3 shows the cumulative events (cases and deaths) averted over time in a high VE setting.



((a)) Cases **((b))** Deaths

Figure B.2: Cumulative events averted worldwide over time in each vaccination strategy (-10% VE).



((a)) Cases **((b))** Deaths

Figure B.3: Cumulative events averted worldwide over time in each vaccination strategy ($+10\%$ VE).