Advance Market Commitments (AMC) model application for Colombian purchase strategy of COVID-19 vaccines

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ABSTRACT

This research estimated the optimal size and composition of the portfolio, and its benefit–cost ratio, of COVID-19 vaccines that Colombia should negotiate as a price-taking country. The Advance Market Commitments (AMC) mathematical model was applied using the parameters from the Colombian context and from a literature review. The findings indicate that the optimal portfolio of Colombia should include 13 vaccines, mainly from two platforms: i) RNA and ii) inactivated virus. The benefit–cost ratio was always greater than one in the baseline scenario and after performing many sensitivity analyses on parameters such as the percentage of the population at risk, the price per treatment, and the herd immunity threshold, among others. In a context of high uncertainty, the best decision – with high benefit – is to anticipate the negotiation processes with the providers of COVID-19 vaccines, which will generate positive economic and health impacts.

Introduction

Fundamental issues in implementing public health programs against COVID-19 are a good understanding of the disease and its transmission, developing an adequate vaccine, rigorous epidemiological surveillance mechanisms, and political commitment to equity of access and funding (which are the result of history, culture, and laws), among other factors of social relevance [3,29].

Vaccination has become a central axis to combat the pandemic. Accessing vaccines as early as possible reduces the population's morbidity and mortality, while allowing economic recovery [5,13]. However, vaccine development is a scientific challenge which may take several years and requires investments of millions in the production process, without guaranteeing 100 % success [15,25].

According to Michael Kremer, a winner of the Nobel Memorial Prize in Economic Sciences, and his collaborators, society will benefit significantly if the pharmaceutical industry can be encouraged to increase its manufacturing capacity while simultaneously advancing linical trials that establish the safety and efficacy of vaccines in development [2].

Different models on the spread dynamics of the COVID-19 disease outbreak have been estimated, showing its devastating effects on humans and society [10,18,28], and therefore governments play a leading role as facilitators of these types of options and promoters of possible initiatives to accelerate the manufacturing development of COVID-19 vaccines.

The economic impacts of a lack of access to vaccination or any health technology that allows the nation to combat COVID-19 may mean the materialization of bigger risks for the economy of a country like Colombia. This country has a high rate of informal labor, limited health system funding, and more than 50 % of its population under the subsidized health insurance regime – with participation increasing given the double-digit unemployment

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rate, a pronounced fall in the Gross Domestic Product (GDP), and the devaluation of the Colombian peso (COP) against the dollar, among other conjunctural factors [9].

Given this scenario, Colombia has joined COVAX, a multilateral mechanism that offers equitable access to safe and effective vaccines, as a way to access vaccines to immunize 20 % of the population [6]. Nevertheless, despite its valuable advantages, it has certain limitations, such as: i) the possibility that doses acquired in this way will be delivered after manufacturers have attended direct negotiations with countries, and ii) the fact that no additional doses will be delivered beyond the stated 20 % until all countries participating in the mechanism have met their needs.

For this reason, and given the uncertainty about effectiveness and safety in the development of health technologies that allow the problem of COVID-19 to be addressed [5,13], it was necessary to analyze options for bilateral anticipation (agreement) in vaccination, with the aim of obtaining gains in health and economic outcomes for the population of the Colombian territory.

In a risk management framework, studying possible scenarios of an investment strategy in manufacturing capacity for the production of this health technology is vital for decision-making in an environment with little evidence and high uncertainty about the probabilities of success of the various COVID-19 vaccines [19].

From a holistic perspective, this kind of approach that evaluates the return on investment of early access to vaccines against COVID-19, along with effective communication processes and societal participation, in addition to adequate financing by the state, can contribute to the construction of positive scenarios regarding people's quality of life [22].

Thus, this research paper's main objective was to estimate the model AcceleratingHT for the Colombian context, making use of different sources of information available from the Colombian General System of Social Security in Health (SGSSS, by its Spanish acronym). This mathematical model allows the authors, even with some limitations, to estimate the relationship between the benefit and cost of investing in a portfolio of vaccines through acquisition via bilateral purchases, which supports the advancement of the vaccination process.

The application of the mathematical model for Colombia presented here was developed at the beginning of the year 2021, in a scenario with high uncertainty and little information on progress in negotiations, vaccine prices, and their clinical effectiveness. This mathematical application was a key input for the construction and updating of the National Vaccination Plan (against COVID-19) of the country of Colombia, with more than 50 million inhabitants.

Method and data

From the perspective of economic theory, circumstances may arise that motivate strategic market players (such as the pharmaceutical industry) to accelerate COVID-19 vaccine development and increase manufacturing production capacity so that vaccines will be available in the shortest possible time for the largest number of people (restricted to certain conditions and scenarios) [17].

Understanding the complexity involved in vaccine development and the challenges of socio-economic development that it implies, from the beginning of the twenty-first century a prominent group of economists, led by Professor Kremer, began to devise incentive systems, on the part of the funders (governments or blocks of them, i.e. the European Union), to motivate investment in research and development (R&D) by the pharmaceutical industry.

This initiative led to the construction of the mathematical model *'Advance Market Commitment'* (AMC), an initiative built and applied by professors from Harvard, Pennsylvania, and Stanford, among other research centers, due to the need to tackle the COVID-19 pandemic. It is considered a unique and innovative approach and is a novel vision that has no antecedents in the related international literature, since optimization of the vaccine portfolio had never before been studied from such a perspective.

This quantitative approach addresses different types of features such as the capacity to manufacture vaccines, portfolio effective capacity, benefits as a function of capacity, the vaccines' success, and the costs and benefits of vaccination, in order to estimate the optimal portfolio for a price-taking country [2]. Although it involves a large number of parameters, the authors indicate that, according to various robustness controls performed on the model, the main findings of the AMC mathematical model are consistent [2].[1] A summary of the AMC model is described below.

Advance Market commitment mathematical model[2]

The objective is to find for a country i the optimal portfolio of vaccines $v_i = (v_{i1}, v_{i2}, ..., v_{ij})$, where v_{ij} denotes how much production capacity country i buys from candidate j. By mathematical construction, the AMC model does not specifically return the names of the pharmaceutical companies from which the vaccine should be purchased. The approach that is developed is more closely related to the selection of the "best platforms"[3] used for vaccine production.

The benefits for country i of buying v_i are measured through economic and health benefits, for which the total effective capacity distribution V of portfolio v_i is modeled, where the total effective capacity is the number of safe and effective treatments offered by the portfolio, once these treatments have completed clinical trials; therefore, the country's effective capacity will depend on the success of individual candidates (denoted by the dummy variable y_j). Each candidate vaccine belongs to a platform l and subcategory s. A candidate will be listed as successful in vaccine development if any of the following events occur:

- No overall problem prevents the feasibility of developing a vaccine candidate (denoted by $x_0 = 1$, with probability q_0).
- No problem shows up at the platform level ($x_p = 1$, with probability q_p).
- No problem shows up at the subcategory level ($x_s = 1$, with probability q_s).
- No problem shows up at the individual vaccine level ($x_j = 1$, with probability q_j).

The dummy variable for candidate j is then given by $y_j = x_0 x_p x_s x_j$ and the probability of success for this candidate is $\Pr(y_j = 1) = q_0 q_p q_s q_j$. This model implicitly introduces correlations between different candidates through x_0, x_p, and x_s. If country i chooses some portfolio v_i, the total effective capacity it obtains is the sum of the installed capacities over all successful candidates:

$$V_i = \sum_j y_i v_{ij}, \tag{1}$$

which is a random variable whose value depends on the success or failure of candidates with non-zero capacity investment. The distribution of effective capacity depends on the probabilities q_0,

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[1] Despite the limitations and criticisms of this type of quantitative application (understanding the high uncertainty that is handled in this regard), this model is considered a useful approximation for decision-making, by understanding the scope explicitly addressed in the document.

[2] This section accurately follows the mathematical development in the study of Ahuja et al. [2], including transcribed excerpts.

[3] A platform is defined as any underlying technology (a mechanism, delivery method, or cell line) that can be used to develop multiple vaccines [26],[23].

q_l, q_s, and q_j. The authors assume that q_s is the same for all candidates, while the probabilities for platforms q_l are set according to the track record of past vaccines and recent scientific developments. The probabilities for individual candidates q_j are assigned depending on the current phase of trials of the candidate; phase 3 candidates have a higher probability of success.

The larger the effective capacity, the larger the total benefits, which are split into economic and health benefits, considering the specific characteristics of country i: i) GDP losses, ii) monthly mortality due to COVID-19, and iii) the fraction of high-risk population. Moreover, estimated benefits take into account that an effective treatment may be developed, that non-pharmaceutical interventions may stop the pandemic, or that herd immunity might be achieved before any capacity becomes available.

Benefits vary as a function of the number of people who are vaccinated at any point in time. Let $\lambda_i(t)$ be the fraction of the population of country i that has been vaccinated at time t. If country i does not obtain any vaccine, no person will be able to be vaccinated before $t = t_0$, the time when vaccine production starts if there is no early capacity investment. At time T, country i starts receiving V_{NP} vaccines per month, whereby the fraction of its population (P), that is vaccinated is:

$$\lambda_{NP}(t) = \begin{cases} 0 & if \quad t \le t_0 \\ \frac{V_{NP}}{P}(t - t_0) & if \quad t > t_0 \end{cases}, \quad (2)$$

If, instead, country i achieves an effective capacity of V, it starts vaccinating V people per month at time $t = t_0 - T$, where T measures how much earlier capacity is available with early capacity investment. At time t_0, capacity ramps up to V_{NP}, whereby the fraction of the population vaccinated is:

$$\lambda(t; V) = \begin{cases} 0 & if & t \le t_0 - T \\ \frac{V}{P}(t - t_0 + T) & if & t_0 - T < t \le t_0 \\ \frac{V}{P}T + \frac{V_{NP}}{P}(t - t_0) & if & t > t_0 \end{cases}.$$

The fraction of the population vaccinated $\lambda(t)$ translates into benefits per unit of time. Let H_i be the monthly health and economic harm due to COVID-19 for country i. The authors assume that the health and economic benefits of vaccination at time t, relative to no vaccination, are given by:

$$\delta H_i f_i(\lambda_i(t)) \qquad with \qquad \delta \in [0, 1], \quad (4)$$

where δ is a factor by which benefits are discounted because of the possibility that effective alternatives to vaccination are developed and $f_i(.)$ is a function that measures the fraction of harm that is avoided. For simplicity, the authors assume that it is a continuous, piecewise linear function with three change points: i) the first kink is at λ_i^{HR}, the fraction of high-risk population; up to that point, vaccinating every additional person brings a large benefit, so f_i increases more quickly than after that point; ii) the second kink is at $\lambda(t) = \lambda_i^{herd\,low}$, a lower estimate for the point at which herd immunity is reached; and iii) the third kink is at $\lambda(t) = \lambda_i^{herd\,high}$, at which point herd immunity is reached for sure and there is no more harm from COVID-19.

Then, the net benefit from effective capacity V is given by:

$$b_i(V) = \delta H_i \int f_i(\lambda(t; V))dt - \delta H_i \int f_i(\lambda_{NP}(t))dt. \quad (5)$$

The left integral is the sum over time of the monthly benefits when effective capacity is V. The right integral makes the same computation when there is no early investment. Besides, the expected benefit, B_i, given some portfolio v_i, is the expectation of $b_i(V)$, given the optimal portfolio; namely:

$$B_i(v_i) = E[b_i(V) | v_i]. \quad (6)$$

The above implicitly assumes that country i will vaccinate the same fraction of the population with and without early capacity and that the costs of each individual vaccine are the same in both cases; therefore, benefits from the optimal portfolio are provided not only by the ability to obtain vaccines but also by early vaccination. Then, the problem for a price-taking country is $\max_{v_i} B_i(v_i) - p_* \sum v_{ij}$, where p_* is, for simplicity, the single price per unit of capacity across all candidates.

It is important to comment that this mathematical model has the following limitations: i) adverse effects of vaccination are not considered; ii) storage, distribution, and logistics costs are not considered; iii) investments are made at risk: the cost of the vaccine must be paid, even if the vaccine is not approved; iv) legal considerations are not included; and v) it is assumed that as the vaccines arrive, they are administered.

Parameters in the context of the SGSSS

Using different official databases, expert criteria, and real world evidence, Table 1 presents, for the different parameters of the model, the methodology used and the value calculated according to the context of Colombia (adjusting for the economic and socio-demographic reality).

The remaining parameters of the AMC mathematical model for COVID-19 are taken by default from experts' descriptions in a study by Ahuja et al. [2]. For the fraction of harm avoided due to lockdown restrictions or other non-pharmaceutical interventions, the value of 0.50 is taken, considering studies such as plasma from recovered patients [1], isolation, the contact tracing and testing program [20], and better social distancing measures [28], among others.

Regarding the vaccine development process, vaccines that belong to platforms such as inactivated virus, RNA, and DNA which have been approved [24] are assumed to have a 0.9 probability of being successful, while viral vector and live attenuated virus platforms are assigned a probability of success of 0.8 [2]. Likewise, this model also considers as inputs the probabilities of vaccine success from preclinical trials (0.14), to phase 1 (0.23), phase 2 (0.32), and phase 3 (0.50), obtaining greater probabilities with a greater degree of advance of clinical trials.

Besides, it is assumed that the first COVID-19 vaccines that arrive in the country are the result of direct negotiations with pharmaceutical companies, which accelerates access to these vaccines by two (2) months compared to the period in which they are received by COVAX. Due to the uncertainty in the model parameters, whose values may also vary over time, various sensitivity analyses are carried out to establish the robustness of the model and to identify possible scenarios in which significant changes may occur.

Results

This model estimates the benefits expected in Columbia through accelerating access to COVID-19 vaccines through early investments. The results presented here are based on advances in vaccine development available to date.[4] The optimal portfolio is made up of 13 vaccines, which are grouped into four platforms: i) ribonucleic acid (RNA); ii) inactive virus; iii) viral vector; and iv) protein subunits (see Fig. 1). More than 98 % of vaccines use the first two options.

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[4] Information from the World Health Organization (WHO) on advances in vaccines against COVID-19 with a cutoff date of January 29, 2021. The following website can be consulted: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines.

Table 1

Model parameters for Colombia.[9]

Variable	Estimation	Definition	Source
Population (number of people)	51,049,498	It corresponds to population projections for 2021, made from the 2018 National Population and Housing Census.	Departamento Administrativo Nacional de Estadística (DANE) [8].
GDP per capita	6.432 thousand USD	Taken from a multilateral entity.	World Bank (Mundial, 2020) [31].
High risk population	21.61 %	Percentage of the total Colombian population aged 60 or over, or who have been diagnosed with comorbidities, or who are health professionals.	Ministerio de Salud y Protección Social et al. (Ministerio de Salud y Protección Social Ministerio de Hacienda y Crédito Público, Instituto de Evaluación Tecnológica en Salud, 2020).
Treatment cost	15 USD	Does not apply.	Assumption
Value of a statistical life	1.343 million USD	Data extracted from literature and updated with USA CPI.	Viscusi & Masterman [30] based on meta-analysis techniques.
Life expectancy	76.32 years	Weighted average life expectancy for women and men, by sex ratio according to the 2018 Census.	DANE [8].
Monthly mortality	8,305	Monthly average of the number of confirmed deaths from COVID-19 between December 2020 and January 2021.	Instituto Nacional de Salud (INS) [16].
Fraction of one life that is lost on average due to COVID-19 deaths	6.45	Difference between 'Life expectancy' and average age of people who have died from COVID-19 in Colombia with information up to January 31, 2021.	INS (Salud, 2020) y DANE (Estadística, 2020).
Cumulative economic loss	16.02	Average of the estimated cumulative loss forecasts for 2020–2021 of: i) the Colombian central bank (25 %); ii) a center for economic thought (25 %); iii) private sector (25 %) and iv) public sector (25 %).	Banco de la República [4], Fedesarrollo [11], Grupo Bancolombia [14] y Corficolombiana [7]. The public sector corresponds to Ministerio de Hacienda y Crédito Público (MinHacienda) and Departamento Nacional de Planeación (DNP).
Percentage of people needed to achieve herd immunity	67.00 %	Data extracted from the most recent literature on the subject (from a conservative scenario) and from consulting thematic experts in the field.	Fontanet & Cauchemez [12], Randolph & Barreiro [27] y Reuters (Reuters, 2020).
Treatments per month to apply	3.3 million	Division between the number of Colombians who must be vaccinated to achieve herd immunity and the number of days, in 2021, during which the vaccine will be applied.	Ministerio de Salud y Protección Social et al. (Ministerio de Salud y Protección Social Ministerio de Hacienda y Crédito Público, Instituto de Evaluación Tecnológica en Salud, 2020).

[9] By mid-2020, a first application of this model was developed for the National Vaccination Plan (Ministerio de Salud y Protección Social Ministerio de Hacienda y Crédito Público, Instituto de Evaluación Tecnológica en Salud, 2020). This research, as of January 2021, updates and refines the parameters.
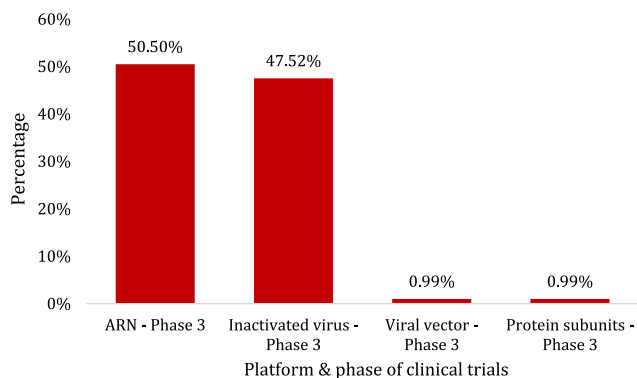

Fig. 1. Composition of the optimal portfolio.

If all vaccines in the portfolio became successful, Colombia would expect to receive 10.1 million treatments per month; however, allowing for the high probability that not all the vaccines that make up the optimal portfolio will generate satisfactory results, effective capacity would be approximately 3.3 million treatments per month on average (which represents about 32 % of the production). The benefits of this portfolio would be $2.51 billion USD, while the costs would be $1.67 billion USD, which implies a benefit–cost ratio of 1.51.

Table 2 shows the results of various sensitivity analyses carried out from the central scenario, where one parameter is varied at a time.

In all cases, except when the price per dose is US $25 or the expected harm that is avoided is 70 %, the ratio between benefit and cost remains above 1. This value is greater if there is an increase in the number of months in advance when the purchase of the optimal portfolio is made (this is the most sensitive parameter), the price per treatment decreases, or there is a higher monthly mortality rate. On the other hand, the higher the percentage of the population at risk, the greater the benefit of purchasing the vaccines in advance. Furthermore, the more treatments are administered per month, the more the benefit–cost ratio decreases, however, it is still greater than 1; the reason for this behavior is that vaccinating the people at highest risk first generates a greater benefit for society.

The size of the optimal portfolio changes with modification of parameters in several of the sensitivity analyses, in most cases being a value close to the 13 candidates of the central scenario. Only in the advance-purchase time analysis of the vaccines and in the average number of treatments is there a significant increase in the number of candidates that would be part of the optimal portfolio.

Discussion and conclusions

From the contextualized application of the mathematical model to the intrinsic conditions of Colombia, understanding the uncertainty in the parameters, and the limitations and scope of this quantitative approach, it can be concluded that the benefit of ensuring early access to vaccines against COVID-19 exceeds the cost.

The analyses presented here suggest that it is a consistent model that can be used as a public policy decision tool. The results found in this study are consistent with the document by Ahuja

Table 2
Results of benefit-cost ratio according to sensitivity analysis.*

Variable object of sensitivity	Central scenario	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Months the purchase is in advance	2	4	6	8	10
	1.51 [13]	2.87 [21]	4.20 [21]	5.51 [21]	6.80 [21]
Price per treatment	US $15	US $5	US $10	US $20	US $25
	1.51 [13]	4.52 [13]	2.26 [14]	1.13 [15]	0.90 [14]
Herd immunity percentage	67 %	60 %	80 %	90 %	100 %
	1.51 [13]	1.50 [20]	1.52 [11]	1.52 [11]	1.52 [11]
Monthly mortality	8,305	5,000	7,000	9,000	11,000
	1.51 [13]	1.39 [14]	1.46 [14]	1.53 [14]	1.60 [14]
Expected harm avoided	50 %	30 %	40 %	60 %	70 %
	1.51 [13]	2.11 [14]	1.81 [14]	1.20 [14]	0.90 [14]
Fraction of high-risk population	21.6 %	10 %	20 %	40 %	50 %
	1.51 [13]	1.50 [16]	1.50 [16]	1.53 [11]	1.54 [11]
Average number of treatments	3.3	2.3	2.8	3.8	4.3
	1.51 [13]	1.61 [11]	1.56 [11]	1.45 [21]	1.39 [21]

* Number of industries that should that Colombia should negotiate with under that specific scenario in square brackets.

et al. [2], where the advance purchase of vaccines achieves an increase in benefits over costs.

The results of this work suggest that it is valuable to invest in acquiring vaccines for a greater proportion of the population through bilateral contracts with producers that allow for advance arrangement of vaccination with respect to the expected arrival date of the doses assigned by COVAX.

The results of this research allow appropriate decisions to be made –although with opportunities for improvement[5] – regarding the immunization of the population of Colombia, and proof of this is that at the beginning of 2022, more than 28 million people were already fully vaccinated. Likewise, the arrival of vaccines by bilateral negotiation has been relatively constant (also, donations from countries like the United States have helped). In retrospect, the diversification of the vaccine portfolio has worked as a good strategy to bring continuous deliveries by different pharmaceutical industries.

As a final message of great relevance to Colombian public policy, and bearing in mind the possible future booster doses of vaccines against COVID-19 for the population, it is considered prudent to continue negotiating both with multilateral organizations, for example COVAX, and through bilateral agreements.[6]

Declaration of Competing Interest

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[5] Unfortunately, in the year 2021 it was not possible to comply with the total number of vaccines calculated (and applied) in the central scenario of our model to arrive at the so-called herd immunity. This was due to different problems including the high global demand for biologicals, the lack of raw materials, and failures in the manufacturing production of some industries, among others.

[6] Between 2020 and 2021 (*as of January 31, 2021*), the Colombian Government was in more than eleven processes of rapprochement with vaccine-producing industries, having purchased 25.25 million treatments from five pharmaceutical companies in addition to the ten million purchased from COVAX.