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Impact on affordability and profit of non-cooperative procuring entities on a hypothetically coordinated global vaccine market

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This study considers a hypothetical global vaccine market where multiple coordinating entities make optimal procurement decisions on behalf of countries with different purchasing power. Each entity aims to improve affordability for the countries it supports while maintaining a profitable market for vaccine producers. This study analyzes the effect of several factors on affordability and profitability: the number of non-cooperative coordinating entities making procuring decisions, the number of market segments in which countries are grouped for tiered pricing purposes, how producers recover fixed production costs, and the procuring order of the coordinating entities. The study relies on a framework where entities negotiate sequentially with vaccine producers following a three-stage optimization process that solves a MIP and two LP problems to determine the optimal procurement plans and prices per dose that maximize savings for the entities' market segments and profit for the vaccine producers. Key results show that the order in which the coordinating entities negotiate with vaccine producers and how the latter recuperate their fixed cost investments, can significantly affect profitability and affordability. Furthermore, low-income countries can procure vaccines more affordably while satisfying their demand by negotiating through entities handling a higher number of market segments, each with a smaller group of countries. In contrast, upper-middle and high-income countries increase their affordability by procuring through entities with fewer and more extensive market segments. A procurement order that follows entities based on the ascending income level of their countries offers higher opportunities to increase affordability and profit.

Key words: vaccines, welfare, affordability, Operations Research, market design

1. Introduction

Pediatric vaccines are credited for saving more than 2 million lives every year [11], and they are among the most cost-effective public healthcare interventions of all times, as treating ill patients is

Classification	Abbreviation	Lower Country GNI Limit (US$)	Upper Country GNI Limit (US$)
High income	HIC	12,055	-
Upper middle income	UMIC	3,896	12,055
Lower middle income	LMIC	996	3,896
Low income	LIC	-	995

Table 1 World Bank classification for countries based on income [33].

many times more expensive than preventing diseases through immunization [39]. Whitney et al. [38] estimates that in the US alone, pediatric vaccines saved over $1.38 trillion dollars in total societal costs between 1994 and 2013.

The global pediatric vaccine market consists of countries that procure vaccines to satisfy their immunization needs from a limited set of producers. High- and upper-middle-income countries typically buy vaccines on their own via public and private purchases. In contrast, lower-income countries rely on pool procurement and tiered pricing [35] to take advantage of economies of scale and secure better prices. For example, over thirty Latin American countries procure vaccines as a group through the Pan American Health Organization (PAHO) Revolving Fund. Similarly, the United Nations Children's Fund (UNICEF) procures vaccines for nearly 70 low- and lower-middle-income countries eligible to receive financial support from donors such as Gavi. All countries buying vaccines through either PAHO Revolving Fund or UNICEF pay the same price per dose for a given vaccine. Although, Gavi has different co-financing levels with different countries.

Pooled procurement also benefits vaccine producers. By securing more affordable vaccines for low-income countries, PAHO, UNICEF, and Gavi also help develop a more stable and predictable demand for pediatric vaccine producers [18], facilitating their manufacturing and fostering their ability to use tiered pricing to push vaccines inventories[36]. Furthermore, PAHO and UNICEF act as coordinators between buyers and producers that aim to benefit both groups simultaneously. These coordinators negotiate vaccine prices at the most affordable levels for their countries, while trying to ensure that at such prices, the pediatric vaccine market remains financially attractive for the producers, and do not jeopardize future supply. Although PAHO and UNICEF collaborate, they independently administer their vaccine tenders to secure supply for the countries they serve; consequently, PAHO and UNICEF can have different price levels.

Through the use of tiered pricing, producers set different price levels for a vaccine depending on the buyers' income [36]. Traditionally, vaccine producers have grouped buying countries in four tiers, as high-, upper-middle-, lower-middle-, or low-income countries based on The World Bank country classification (see Table 1); but some producers have their own tier structures for different vaccines. Reselling low-priced vaccines to higher-income countries is usually not feasible due to market regulations, cold-chain logistics, and differences in immunization schedules.

Despite the positive effect of tiered pricing and pooled procurement, pediatric vaccines are not always available and affordable for low-income countries. The World Health Organization (WHO [40]) claimed that 19.5 million infants did not have access to essential vaccines in 2018, with 60% of them concentrated in ten low- and middle- income countries [28, 40, 41]. Interruptions to national routine immunizations programs due to Covid could result in nearly 700,000 children deaths in [1], unless immunization programs are soon restored and access to affordable vaccines is strengthen. This lack of access results from multiple reasons including (1) the vaccine supply by volume is highly concentrated in a limited number of producers [39]; (2) the monetary value of the vaccine market is concentrated on sales to high-income countries; (3) logistics factors affect vaccine distribution and increase costs; (4) weak local immunization programs; (5) political turmoil disrupting immunization campaigns; and (6) low national health investments.

This study considers a hypothetical globally-coordinated vaccine market where demand for multiple antigens is met via a single tender. In this global market, multiple coordinating entities procure vaccines on behalf of countries grouped into market segments based on their income level. In contrast to UNICEF's and PAHO's single markets, each coordinating entity can have multiple price levels for each vaccine. The entities make vaccine procurement decisions that foster an affordable and profitable vaccine market by determining the optimal amount of vaccines to buy for each market segment in their cohort of countries, and the range of affordable prices that secure a desired profitability for the producers. We consider a vaccine to be affordable to a market segment if its price per dose is lower than the average willingness-to-pay for the vaccine among the countries in the market segment. Furthermore, it is assumed that the coordinating entities are trusted intermediaries that seek no financial benefit for themselves and do not cooperate with each other in making their procuring recommendations.

Considering that vaccine purchases must clear antigen demand for each market segment during a procuring cycle (e.g., a year) and that entities do not cooperate, producers generate their profit from a sequence of negotiations with the coordinating entities. This procuring sequence is important as a successful negotiation reduces the available supply for other entities in subsequent negotiations. Furthermore, producers can offer discounts to push inventory, also affecting subsequent procurement decisions. In this study, the coordinating entities' procuring order is based on the income level of their represented countries. We explore procuring orders based on the ascending and descending average income per capita for the countries represented by each entity.

We consider that the investment costs to manufacture vaccines are annualized and charged for vaccines that are effectively sold. These costs incorporate a desired return on investment, high enough to cover the research and fixed costs of the commercialized vaccine products in their portfolio.

Under a market with non-cooperative coordinating entities, it is assumed that producers can follow two policies to recover their annualized fixed costs: (1) offering discounts on vaccines whose supply has been partially sold to other entities, and (2) offering no discounts.

We consider a global vaccine market that buys vaccines to clear its demand once a year and investigate the effects on the global affordability and profit of three relevant factors: (1) the number of coordinating entities in the global vaccine market, (2) the order those coordinating entities follow to buy vaccines, and (3) whether producers push their products by offering discounts on vaccines.

To address the effect of those factors, we extend the mathematical framework proposed by Proano et al. [25] to compare scenarios in which a varying number of coordinating entities interact, not only to represent non-cooperative entities but also when entities work together.

This paper is organized as follows. Section 2 reviews relevant literature on vaccine pricing and group buying. Section 3 describes the mathematical model and the three-stage optimization process, the experimental framework, and the performance metrics used in this study. Section 4 describes the experimental data used and the results obtained in the study. Finally, Section 5 offers a discussion and relevant extensions.

2. Literature Review

In this section, we review the literature on group buying and mathematical modeling on vaccine pricing. Although there is abundant literature on general group buying and its effects on tiered pricing [2, 7, 14, 42], we are unaware of studies considering group buying for vaccines. Vaccine pricing studies that rely on mathematical programming models have focused on the pricing of a new vaccine into a single competitive market [4, 5, 27]. Proano et al. [25] proposes a mathematical programming model and a three-stage optimization-based process to explore a hypothetically coordinated vaccine market where the number of vaccines to buy and their prices maximize affordability and profit. From an economic perspective, several studies question the mechanisms through which pediatric vaccines are sold, and how they affect their affordability [9, 12, 22, 24]. Studies on vaccine pricing based on cost-benefit analysis vary broadly and without consensus, highlighting the difficulty of valuing preventive care and saving lives over multiple regions [3, 8, 19, 20, 21, 32].

The group buying literature relies on pool procurement to affect affordability and profit considering unlimited supplies, a single product, a producer, and an online mediator that charges membership fees to allow customers access to price discounts [2, 7, 14, 42]. These assumptions are used in modeling frameworks that capture the relationship between order quantities, price, and the benefit of joining a group. Those assumptions may not adequately fit the characteristics of the vaccine market, which has no membership fees to access discounted prices. In a global vaccine market, countries need to meet other criteria to be eligible in a group, such as being part of a geographical region or having specific income levels.

Hu et al. [14] assumes that a set of customers can be coordinated into group buying entities negotiating online deals with a single seller. The study deals specifically with the issue of sequencing buyers, as the negotiating order can affect whether or not there is enough demand to justify the deal. Hu et al. [14] relies on game theory to model the interaction between customers and the seller, considering a sequence of discrete interaction periods, in which several customers may choose independently. Buyers from Hu et al. [14] have the option of not satisfying their demand or choosing outside sources not represented in the model.

Under a general coordinated group-buying framework, Yang et al. [42] studies the conditions that might make it more advantageous for sellers to serve each participating buyer in a given market. The study assumes that the seller can obtain other business if the entities refuse to negotiate and that there is a single seller whose decisions affect the market.

Chen and Roma [7] models group-buying through a three-step process involving producers, retailers, and buyers. Retailers can choose whether to cooperate with a group-buying entity or not. Assuming a linear demand, Chen and Roma [7] suggests that group-buying might be more advantageous to smaller, less powerful retailers than to bigger ones. It is assumed that retailers operate for profit, and would never cooperate.

Anand and Aron [2] considers group-buying mechanisms for a monopoly on web-based transactions under uncertain demand. There is uncertainty in the valuations customers make on products, and prices are assumed to be unknown. However, these uncertainties may not hold for the vaccine market [34]. Any variations on purchased quantities are more likely to come from changes in available budgets, existing stockpile levels, reaction to outbreaks, logistical issues, and political instabilities, than in birth rate changes.

Game theory models have been the core of several studies on vaccine pricing decision problems [4, 5, 27]. These approaches have focused on the impact of new vaccines in a single market, ignoring the implications of potential buyer coordination. These studies aim to find solutions that balance the interests of multiple market agents when multiple vaccines are alternatives to satisfy vaccine demand for a single national buyer.

Robbins et al. [27] uses a game theory model to frame the US vaccine market as an oligopoly of asymmetric producers in a Bertrand competition where each producer can supply the entire market. Consumers attempt to purchase enough doses of all the antigens for which there is demand in the country. The framework is offered as a mathematical approach to capture oligopolistic market interactions that in the US market suggests a different pricing strategy for combination vaccines.

Other studies approach vaccine pricing through mathematical programming models [13, 16, 30, 37], assuming a central planner for the US market without considering supply limitations. Additional studies have focused on determining how combination vaccines fit the overall schedule for the US market under a central planner [6, 15, 17, 26].

Proano et al. [25] proposes an optimization-based methodology to model pricing coordination between different market segments and producers when a single coordinating entity acts as a decision-maker to improve affordability and profit simultaneously. Countries are grouped in market segments to procure vaccines from multiple producers via a trusted intermediary who determines procuring quantities and prices that are affordable and profitable. The procurement is done via a synchronized multi-antigen tender. The feasible prices satisfy tiered pricing restrictions, ensure a desired profitability to the producers, and are lower than the market's reservation prices. Proano et al. [25] shows that it is possible to price vaccines more affordably for all coordinated market segments (including high-income markets) when the supply of combination vaccines is available to all market segments. Additionally, Proano et al. [25] shows that the total social surplus (total welfare) is a consequence of the choice and volume of vaccines procured.

Considering a hypothetically coordinated vaccine market with a single entity, Mosquera [23] extends Proano et al. [25] to evaluate the effect on profits and affordability when grouping countries into a varying number of market segments (2, 4, 8, 12), and considering uncertainty on the vaccines' reservation prices and different rates on the producers return of investment. Mosquera [23] concludes that grouping countries into more market segments improves the affordability of low-income countries while decreasing the profits of vaccine producers. However, by increasing the number of market segments in which low- and low-middle-income countries are grouped while decreasing the number of market segments for upper-middle- and high-income countries, one could increase savings without affecting producers' profit; and not making vaccines increasingly expensive for high-income countries (vaccines remain priced below each market's reservation price). Mosquera [23] also shows that uncertainty in reservation prices and the return on investment rates do not have a significant effect on affordability.

Several studies have focused on Gavi, an existing coordinating entity for the vaccine market, and its impact on countries when they are no longer eligible for its financial support[18, 29, 31]. Saxenian et al. [29] evaluates the readiness of 16 countries if they stop receiving financial assistance from Gavi as they graduate, concluding that the incremental financial load on graduating countries may provoke these countries to cancel or scale down immunization programs and face issues with their vaccine supply [29], potentially decreasing their coverage levels.

Frontieres [9] discusses how the GNI-based tiered pricing does not guarantee higher affordability on its own, and might instead limit access to vaccines that become prohibitively expensive when jumping from low-income prices to lower-middle-income prices. This criticism is supported by Moon et al. [22], claiming that tiered pricing may overburden middle-income countries in an unsustainable manner while incentivizing producers to focus on the higher profits obtained from high-income markets.

3. Methodology

This study proposes the Group Vaccine Allocation (GVA) model, a three-stage mathematical programming framework, to optimize the procurement decisions of a coordinating entity. We apply GVA to an ordered set of coordinating entities as part a multi-stage experimental approach to test the influence on affordability and profit of four factors: (F1) the number of market segments in which 194 countries can be grouped; (F2) the number of coordinating entities facilitating procurement in the global market; (F3) the order followed by the entities in negotiating their procurement plans; and (F4) the producers' decision of adjusting or not their minimum prices to recover their return on investment. Each experimental factor has multiple levels. For each experimental instance we create multiple replications by randomizing vaccines' reservation prices in each market segment. For each of these experimental instances, the GVA problem is sequentially solved for each entity, while following a particular procuring order. After solving the GVA for an entity, the overall antigen demand and vaccine supply are adjusted to account for the entity's purchases.

The GVA iteratively solves a sequence of three optimization problems. The first stage determines the vaccine quantities to buy for each of its market segments. The second stage determines a lower bound on the prices for the procured vaccines, and the third stage determines their upper bounds. Prices per dose between these bounds maximize total social surplus. The lower-bound prices correspond to the most affordable and least profitable vaccine prices per dose, while the upper-bound prices correspond to the least affordable and most profitable prices. GVA ensures that these prices are lower than the reservation prices for each vaccine at each entity's market segments. Without loss of generality, the GVA is solved for a single-year procurement cycle, assuming that all countries in a global market are served by coordinating entities that make procurement decisions on their behalf.

3.1. GVA: Group Vaccine Allocation Model

For each coordinating entity, the GVA's first stage determines which vaccines and in which quantities should be bought for each of the entity's market segments. The second stage uses the recommended procurement quantities to determine prices that maximize affordability for vaccine buyers. In contrast, the third stage uses these procurement quantities to determine prices that maximize the producers' profits. As a result, GVA determines a vaccine procurement plan and the feasible range of prices per dose that maximizes savings for the entity's market segments and profits for the vaccine producers (i.e., the total social surplus). The following notation and formulation describe the GVA:

Sets:

B: set of vaccines

A: set of antigens offered through immunization

E: set of coordinating entities

M_e: set of market segments that procure through coordinating entity $einE$

P: set of vaccine producers

B_a^1: set of vaccines offering antigen $a \in A$

Q_b: sets of vaccines that together offer the same antigen protection as vaccine $b \in B$, and are fabricated by the same producer.

N_q: vaccines in each subset $q \in Q_b$.

L_t: set of all countres that qualify as $t \in$ { low-income (LIC) , lower-middle-income (LMIC), upper-middle-income (UMIC), high-income (HIC) }

Parameters:

R_{bm}: Reservation price of vaccine $b \in B$ in market segment $m \in M$. The maximum price per dose that the market $m \in M$ is willing to pay for vaccine $b \in B$. R_{bm} corresponds to the average reservation price of countries in market m.

l_m: Average birth cohort per year in market $m \in M$

C_b: Annualized production, research and development fixed costs necessary to manufacture vaccine $b \in B$, considering a desired rate of return

d_{am}: Number of doses of antigen $a \in A$ needed to immunize a child in market $m \in M$ according to the market's immunization schedule.

D_{bm}: Maximum number of doses of vaccine $b \in B$ allowed per child in market segment $m \in M$ to avoid over-immunization

S_b: Total supply of vaccine $b \in B$ per year

gni_m: Average gross national income (GNI) per capita among the countries in market segment $m \in M$

α: Scaling factor that allows vaccine prices to increase when purchases for the vaccine are smaller than the available supply

θ: Scaling factor that indicates the level of prices above the reservation price after which vaccine demand is null. No vaccine b will be bought if vaccine price is above θR_{bm}

u_b: Minimum price paid for a dose of vaccine $b \in B$

γ: Relative importance of maximizing the profit for producers.

ψ: Relative importance of ensuring the antigen demand is met.

η: Scaling factor that ensures unnecessary vaccines are not produced.

Variables:

X_{bm}: Quantity of vaccine $b \in B$ to be purchased by market segment $m \in M$

Y_{bm}: Price paid for vaccine $b \in B$ in market segment $m \in M$

g_b: Binary variable indicating whether $b \in B$ is being produced (i.e., $g_b = 1$) or not (i.e., $g_b = 0$)

3.1.1. Stage 1 For each entity $e \in E$:

$$\underset{X,Y,g}{\text{Max}} \;\; \gamma\left(\sum_{b\in B}\sum_{m\in M_e} R_{bm}X_{bm} - \sum_{b\in B} C_b \frac{\sum_{m\in M_e} X_{bm}}{S_b}\right) - \psi \sum_{a\in A}\sum_{m\in M_e}\left(d_{am}l_m - \sum_{b\in B1_a} X_{bm}\right) - \eta \sum_{b\in B} g_b \tag{1}$$

$$\text{s.t.} \quad Y_{bm} + (1-g_b)\sum_{t\in N_q} R_{tm} \geq \sum_{t\in N_q} Y_{tm} \qquad \forall \;\; b\in B,\; q\in Q_b:\; ||Q_b|| \geq 1 \tag{2}$$

$$\sum_{m\in M_e} X_{bm} \leq S_b g_b \qquad \forall \;\; b\in B \tag{3}$$

$$Y_{bm} \geq \left(\frac{(S_b g_b - X_{bm})\alpha + S_b g_b}{S_b}\right)\frac{C_b}{S_b} \qquad \forall \;\; b\in B,\; m\in M_e:\; S_b > 0 \tag{4}$$

$$Y_{bm} \leq \theta R_{bm} g_b \qquad \forall \;\; b\in B,\; m\in M_e \tag{5}$$

$$Y_{bm} \geq g_b u_b \qquad \forall \;\; b\in B,\; m\in M_e \tag{6}$$

$$\sum_{b\in B1_a} X_{bm} \leq d_{am} l_m \qquad \forall \;\; a\in A, m\in M_e \tag{7}$$

$$X_{bm} \leq D_{bm} l_m \qquad \forall \;\; b\in B,\; m\in M_e \tag{8}$$

$$X_{bm} \geq 0 \qquad \forall\, b\in B,\; m\in M_e \tag{9}$$

$$g_b = \{0,1\} \qquad \forall\, b\in B \tag{10}$$

In Stage 1, the mixed integer programming model described above determines all procurement quantities, X_{bm}, of vaccine b in market $m\in M_e$ that maximize total social surplus, penalizes not meeting demand, and result in the lowest number of vaccine choices. The total social surplus aggregates profits for manufacturers and savings for the market segments.

In the non-cooperative scenario, revenue results from a subsequent negotiation between the producers and the coordinating entities. Therefore, it is assumed that the fraction of the annualized fixed cost met from vaccine sales can only be determined after all the negotiations have been completed. Additionally, GVA's Stage 1 model considers that the price per dose decreases linearly as procurement quantities increase, and that failing to meet demand is possible but intensively penalized.

Since we aim to increase affordability for target low-income countries, the objective function in (1) simultaneously maximizes total social surplus for an entity's negotiation, and through penalty multipliers, minimizes gaps in meeting its vaccine demands. The total social contribution from each entity considers the fraction of the annualized fixed costs corresponding to the number of vaccines bought in the current iteration $\left(\frac{\sum_{m\in M} X_{bm}}{S_b}\right)$. The closer the purchase order for a vaccine is to its total supply, the higher the proportion of the fixed costs covered by the entity. The objective also minimizes the gap between the vaccine purchases and the entity's market segments' demands. The penalty function $\left(\psi \sum_{a\in A, m\in M}\left(d_{am}l_m - \sum_{b\in B1_a} X_{bm}\right)\right)$ in objective (1) allows for small gaps in meeting demands that otherwise would render the problem infeasible. Together, the penalty function and constraint (7) help meet the expected antigen demand for the entity's markets. The last term in (1) minimizes the number of vaccine types used in the entity's procurement plan.

Restriction (2) guarantees that the price negotiated for a combination vaccine is higher than the aggregated price of combining other vaccines from the same producer that offer similar antigen protection (e.g., the price of a vaccine containing antigens for diphtheria-tetanus-pertussis (DTP) and hepatitis B is higher than buying separate vaccines against hepatitis B and DTP from the same producer.)

Constraint (3) ensures that purchases do not exceed the available vaccine supply. In a scenario where coordinating entities do not cooperate, vaccine producers cannot guarantee that the annualized R&D and production fixed costs are fully recovered until the vaccine quantities sold to all markets are known. Thus under a non-cooperative scenario, decisions are unveiled iteratively for each coordinating entity without having a full picture of the purchases made, or to be made, by other coordinating entities. Under a non-cooperative scenario, no market agent knows the orders placed by all entities until the end of the last iteration. Through the price-elasticity constraint (4), producers can incentivize the coordinating entities to buy their remaining vaccine supply by following an adjusted fixed-cost recovery policy, where the portion of the annuity C_b is reduced after part of vaccine b' supply has been sold. If the entire supply of a vaccine is bought, the price should cover the annualized fixed costs (that is, $Y_{bm} \geq \frac{C_b}{S_b}$). When producers sell less than their total supply, this constraint adjusts vaccine prices based on the remaining supply increasing their price to cover fixed costs. The difference between the total vaccine supply and the amount that has been purchase before an entity makes its decisions is adjusted by a factor α, so that $\frac{(S_b g_b - X_{bm})\alpha + S_b g_b}{S_b} \geq 1$.

Restriction (5) guarantees that the negotiated prices do not exceed a threshold over the reservation prices for each vaccine in each market segment. Restriction (6) forces prices per dose to be above a pre-established minimum price. Restriction (7) guarantees that the coordinating entities do not buy more vaccines than their demand. Restriction (8) prevents that the optimal purchases of each vaccine in a market cause over-immunization.

3.1.2. Stage 2 For each entity $e \in E$:

$$\begin{aligned} \underset{Y}{\text{Max}} \qquad & \text{TCS:} \ \sum_{b \in B} \sum_{m \in M_e} (R_{bm} - Y_{bm}) X^*_{bm} \qquad (11) \\ \text{subject to} \qquad & \text{Restrictions (2)} - (6) \end{aligned}$$

In Stage 2, for the market segments of entity $e \in E$, a linear programming model maximizes the savings that countries can obtain by procuring vaccines at prices lower than the average reservation prices in their market segments, considering as inputs the vaccine quantities resulting from the solution of the Stage 1 problem. The Stage 2 problem establishes a lower bound on vaccine prices that can ensure that producers achieve the optimal total social surplus from Stage 1. Given that profits can only be calculated once all coordinating entities complete their negotiations and all prices are already known, the model in this stage determines vaccine prices that facilitate securing the desired return on investment for entity e's procuring quantities resulting from Stage 1 (e).

3.1.3. Stage 3 For entity $e \in E$:

$$\begin{aligned} \underset{Y}{\text{Max}} \qquad & \text{TPF: } \sum_{b\in B}\sum_{m\in M_e} Y_{bm}X^*_{bm} - \sum_{b\in B} C_b g^*_b \frac{\sum_{m\in M_e} X^*_{bm}}{S_b} \qquad (12) \\ \text{subject to} \qquad & \text{Restrictions } (2)-(6) \end{aligned}$$

In Stage 3, a similar linear programming model maximizes profits for the vaccine allocations resulting from Stage 1 for e. This LP formulation establishes an upper bound on the vaccine prices that maintain the optimized total social surplus resulting from Stage 1, without exceeding the reservation prices beyond θR.

It is assumed that all market segments can purchase any vaccine. Table 2 summarizes the constraints enforced at each stage of the GVA for an entity and a problem instance.

Without loss of generality, restriction (6) sets a minimum vaccine price per dose at each market [10, 18].

While in a coordinated market, it is possible to estimate profit, this approach is not feasible in a non-cooperative framework. It is not trivial to determine how much of the annuity should be attributed to each coordinating entity. For this reason, the objective function (12) is similar to (4) but considers that the annualized fixed costs are proportional to the fraction of the supply sold to the entity. Notice that during the procurement exercise, total profits cannot be estimated until all entities have completed their procurement; hence, we also report on the actual revenue per vaccine during the experimentation. Finally, any remaining supply available after a negotiation with an entity remains available for the subsequent entity negotiations.

After GVA has been applied to all entities, the overall profit corresponds to the revenue from the sales to all entities minus the the annualized fixed costs for all vaccines procured. When a vaccine yields a negative profit even at the highest acceptable prices in the optimal procurement plan, producing the vaccine is not financially sustainable. Similarly, if the profit is positive even at the lowest prices in the optimal procurement plan, the vaccine is guaranteed to do financially well.

3.2. Experimental framework

We design experimental scenarios by controlling four key factors: (F1) the number of market segments in which 194 countries can be grouped; (F2) the number of coordinating entities facilitating

Stage	Variables	Objective Function	Constraints
1	X_{bm}, Y_{bm}, g_b	(1)	(2), (7), (3), (4), (5), (6), (8)
2	Y_{bm}	(11)	(7), (3), (4), (5), (6)
3	Y_{bm}	(12)	(7), (3), (4), (5), (6)

Table 2 Expressions and constraints used in each problem associated with stages of the model.

Factors	Levels						
F1: Number of market segments	2		4		8		12
F2: Number of coordinating entities	1	2	3	4	6	8	12
F3: Coordinating entities procurement order	Ascending income				Descending income		
F4: Fixed cost recovering policies	Adjusted				Invariant		

Table 3 Experimental factors and levels

procurement in the global market; (F3) the order followed by the entities in negotiating their procurement plans; and (F4) the producers' decision of adjusting or not their minimum prices to recover their return on investment. Table 3 summarizes the experimental scenarios tested to answer the research questions.

For factor (F1), 194 countries are grouped into 2, 4, 8, or 12 different market segments based on the similarity of their gni_p. The market segments are then ranked based on their average income per capita and assigned to coordinating entities so that all entities make decisions for an equal number of market segments. For example, in a scenario with 2 coordinating entities and 12 market segments, coordinating entity 1 would be responsible for the 6 market segments with the highest gni_p. In contrast, the second coordinating entity would be assigned the 6 market segments with the lowest gni_p.

Factor (F2), allows the number of non-cooperative coordinating entities to vary in six levels (1, 2, 3, 4, 6, 12). Under an equal distribution of market segments per entity, if the number of market segments is 12, the numbers of markets per entity decreases (12, 6, 4, 3, 2, and 1), as the number of entities increases (1, 2, 3, 4, 6, and 12), respectively. The maximum number of entities that can be used per experimental scenario is equal to the number of market segments.

The case when a single coordinating entity represents all market segments serves as a benchmark scenario.

For factor (F3), the coordinating entities' procurement order can be ascending or descending based on the gni_p of the market segments served by the coordinating entity. In practice, high-income market countries are the first ones to make purchases and secure vaccine access. Descending procuring order may be favored by producers, given their need to secure profit rapidly, while the ascending order incentives large volume purchases to be secured first.

For factor (F4), producers follow either an 'adjusted' or 'invariant' pricing policy. As stated earlier, producers estimate a minimum price per vaccine dose considering the annualized fixed R&D

production costs to be recovered. With an 'adjusted' policy, if part of a vaccine's supply has been sold to some coordinating entities, the producers determine minimum bounds on vaccine prices for following negotiations that will help them meet their annualized fixed costs goals. This is achieved by updating the value of the annuity to be recovered after each entity negotiation, as shown in Algorithm 1, consequently changing the bounds of Restriction (4). In the 'invariant' policy, at the beginning of the procuring cycle, producers estimate the minimum price needed to recover the entire annualized fixed costs, which remains fixed during the procurement sequence.

The combination of levels for the four factors results in 60 experimental scenarios. For each scenario, we randomize each vaccine's reservation prices at each market from 90% to 110% of their baseline reservation prices. Vaccines that have not been purchased by a specific market had their reservation prices estimated as a function of each market segment's income, as well as of the historical price of other vaccines offering similar antigens, as described in Mosquera [23]. For each experimental scenario, we generate one thousand random instances of the vaccine reservation prices. For each random instance, we iteratively solve the GVA three-stage optimization process for each procuring entity as illustrated in Algorithm 1.

Algorithm 1 Solution Procedure

```
1: for e ∈ E do
2:     Solve the GVA
3:     Define which vaccines to produce
4:     Define vaccine quantities sold to each market segment m ∈ M_e
5:     Define upper and lower price bounds per vaccine dose
6:     for b ∈ Set of Vaccines bought do
7:         if Adjusted policy = true then
8:             C_b ← C_b - revenue obtained from selling b ∈ B to m ∈ M_e
9:         S_b ← S_b - volume of b purchased by m ∈ M_e
10: Generate output metrics.
```

3.3. Output Metrics

This study monitors for all experimental scenarios: the aggregated profits and revenue for the producers, the aggregated savings for all market segments, and savings and profits generated by LIC, LMIC, UMIC, and HIC as they are grouped in different market segments. In each experimental instance, a market' savings in procuring a vaccine (i.e., customer surplus) is reported by the difference between the market's reservation price and the mid-price between the lower and upper price bounds determined in Stage 2 and 3 of the GVA for the instance. Given that the price countries are willing

Metric	Description	Mathematical Expression
Total Customer Surplus (TCS)	Savings received from the vaccine procurement of all market segments of all coordinating entities	$\sum_{e\in E}\sum_{b\in B}\sum_{m\in M}(R_{bm}-Y_{bm})X_{bm}$
Market Value (MV)	The total monetary value in the vaccine market. Sum of all customer savings and all profit.	$TCS+\sum_{e\in E}(X_{bm}Y_{bm}-C_bg_b)$
$\frac{TCS}{MV}$	Total customer surplus across all entities as a fraction of the market values.	$\frac{TCS}{MV}$
$\frac{CS_t}{MV}$	Customer surplus in aggregated market segment $t\in$ (low-income, lower-middle-income, upper-middle-income, high-income) as a fraction of the market value, at the lowest vaccine prices.	$\frac{\sum_{e\in E}\sum_{b\in B}\sum_{m\in L_t}(R_{bm}-Y_{bm})X_{bm}}{MV}$
$\frac{TPF}{MV}$	Total profit across all entities as a fraction of the market value.	$\sum_{e\in E}\left(\frac{\sum_{b\in B}\sum_{m\in M}(X_{bm}.Y_{bm}-C_bg_b)}{MV}\right)$

Table 4 Variables used as performance metrics and their explanations.

to pay is randomized for each experimental scenario, the dollar value of the global vaccine market is also random. Hence, we normalize our metrics over the market dollar value of each experimental instance. Table 4 summarizes the set of metrics used in this study. In Appendix 5 we also show the aggregate savings and profits (i.e., total social surplus), the number of producers who do not cover annualized fixed costs for their vaccines, the number of times in which a market segment does not satisfy all of its vaccine demand, savings for lower-middle-, upper-middle- and high-income countries, and the revenue generated by low-, lower-middle-, upper-middle- and high-income countries.

4. Results

This study considers a vaccine market consisting of 14 producers offering 52 vaccines to satisfy demands for 6 different antigens (Hib: Heamophilus Influenza type B, HepB: Hepatitis B, DTP: Diphtheria Tetanus and Pertussis, V: Varicella, MMR: Meassles, Mumps and Rubella, and IPV: Polio) (see Table 5); 194 countries are grouped by their GNI per capita into market segments for tier-pricing purposes. Rather than having only the usual 4-tier market segmentation (i.e., high-income, upper-middle-income, lower-middle-income and low-income countries based on the World Bank classification [33]), we rank countries in descending order by their GNI per capita and group them in either 2, 4, 8, or 12 market segments (see Table 6). Consequently, each vaccine can have a different average reservation price at each market segment, depending on the member countries of the market segment. Without a loss of generality, in this study, all variations of diphtheria-tetanus-pertussis vaccines and all polio vaccines are considered to offer the same type of antigens and are represented by DTP and IPV, respectively.

For each of the 60 experimental scenarios, resulting from exploring all factors and levels, we compare key metrics with a benchmark in which all market segments receive procurement recommendations from a single coordinating entity. As a result, there is a different benchmark based on

Producer	Vaccine	Antigens
1	6	HepB
	41	DTP, HepB and Hib
2	20	IPV
3	1	DTP
	7	HepB
	32	DTP and HepB
	42	DTP, HepB and Hib
4	2	DTP
	43	DTP, HepB and Hib
5	8	HepB
	14	Hib
6	3	DTP
	9	HepB
	15	Hib
	21	IPV
	25	MMR
	29	V
	33	DTP and HepB
	38	DTP and IPV
	44	DTP, HepB and Hib
	49	DTP, HepB and IPV
	51	DTP, HepB, Hib and IPV
7	10	HepB
	45	DTP, HepB and Hib
8	11	HepB
	16	Hib
	26	MMR
	30	V
	39	HepB and Hib
	40	MMR and V
9	17	Hib
	35	DTP and Hib
10	46	DTP, HepB and Hib
11	4	DTP
	18	Hib
	22	IPV
	27	MMR
	31	V
	36	DTP and Hib
	50	DTP, Hib and IPV
	52	DTP, HepB, Hib and IPV
12	5	DTP
	12	HepB
	19	Hib
	23	IPV
	28	MMR
	34	DTP and HepB
	37	DTP and Hib
	47	DTP, HepB and Hib
13	13	HepB
14	24	IPV

Table 5 Vaccines produced by each producer and the antigens they offer. (Hib= Haemophilus influenzae type B, DTP= Diphtheria-Tetanus-Pertussis, HepB=Hepatitis B, V=varicella, MMR=Measles-Mumps-Rubella, IPV= inactivated polio

the number of market segments in which the global vaccine market is divided (i.e., 2, 4, 8 or 12). Each benchmark mimics a fully coordinated system for a given number of market segments in which there is no need to follow any procurement order, nor adjust the recovery of the annualized fixed costs, and all tenders are synchronized.

For clarity and brevity, and without loss of generality, this section primarily contrasts the results collected for experimental scenarios with countries grouped in 12 and 4 market segments. Results for scenarios with 2 and 8 market segments are available in Appendix 5, and ratify the trends described in this section. In this section the output metrics are computed considering the mid-point prices between the lowest and highest prices per dose for each vaccine in each market segment.

Figure 1 illustrates the Total Social Surplus as a fraction of the dollar value of the global market ($\frac{TSS}{MV}$) for each experimental instance. Figures 3 and 2 illustrate the Total Customer Surplus ($\frac{TCS}{MV}$) and Total Profit ($\frac{TPF}{MV}$) considering the mid-point prices for the feasible price range resulting from

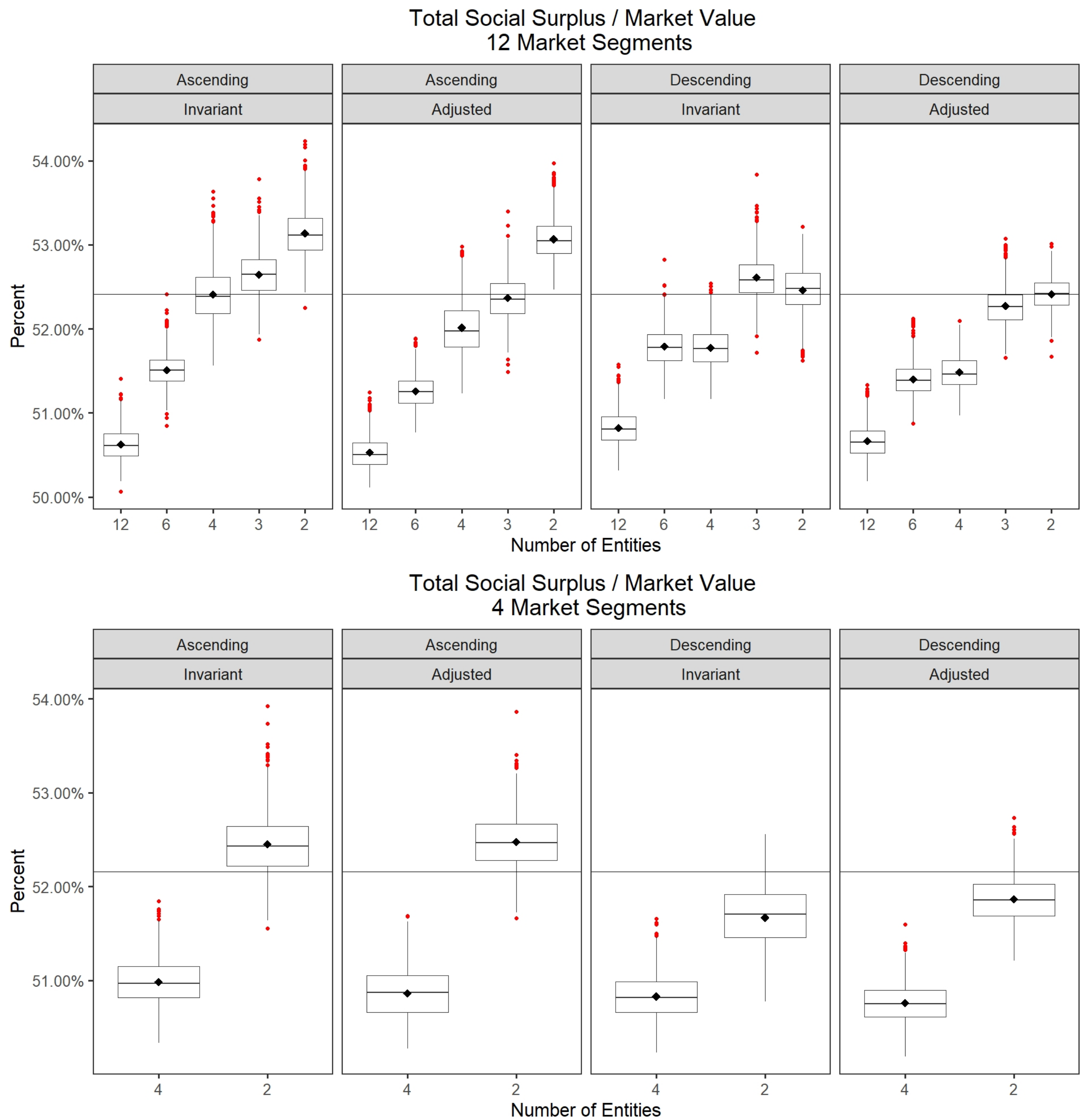

Figure 1 **Aggregated $\frac{TSS}{MV}$ in the global vaccine market for experimental scenarios with 12 and 4 market segments, for a varying number of coordinating entities, different procurement priorities orders, and different choices for the fixed cost recovery policy. For all scenarios, $\frac{TSS}{MV}$ increases as the number of entities decreases. Other factors have smaller impact.**

the three-stage optimization process. Figure 4 illustrates the $\frac{CS}{MV}$ for countries that under the World Bank classification are considered low-income (LIC).

Figure 1 shows that total social surplus ($\frac{TSS}{MV}$) increases as the number of coordinating entities decreases, or since the number of market segments is equally distributed by the number of entities

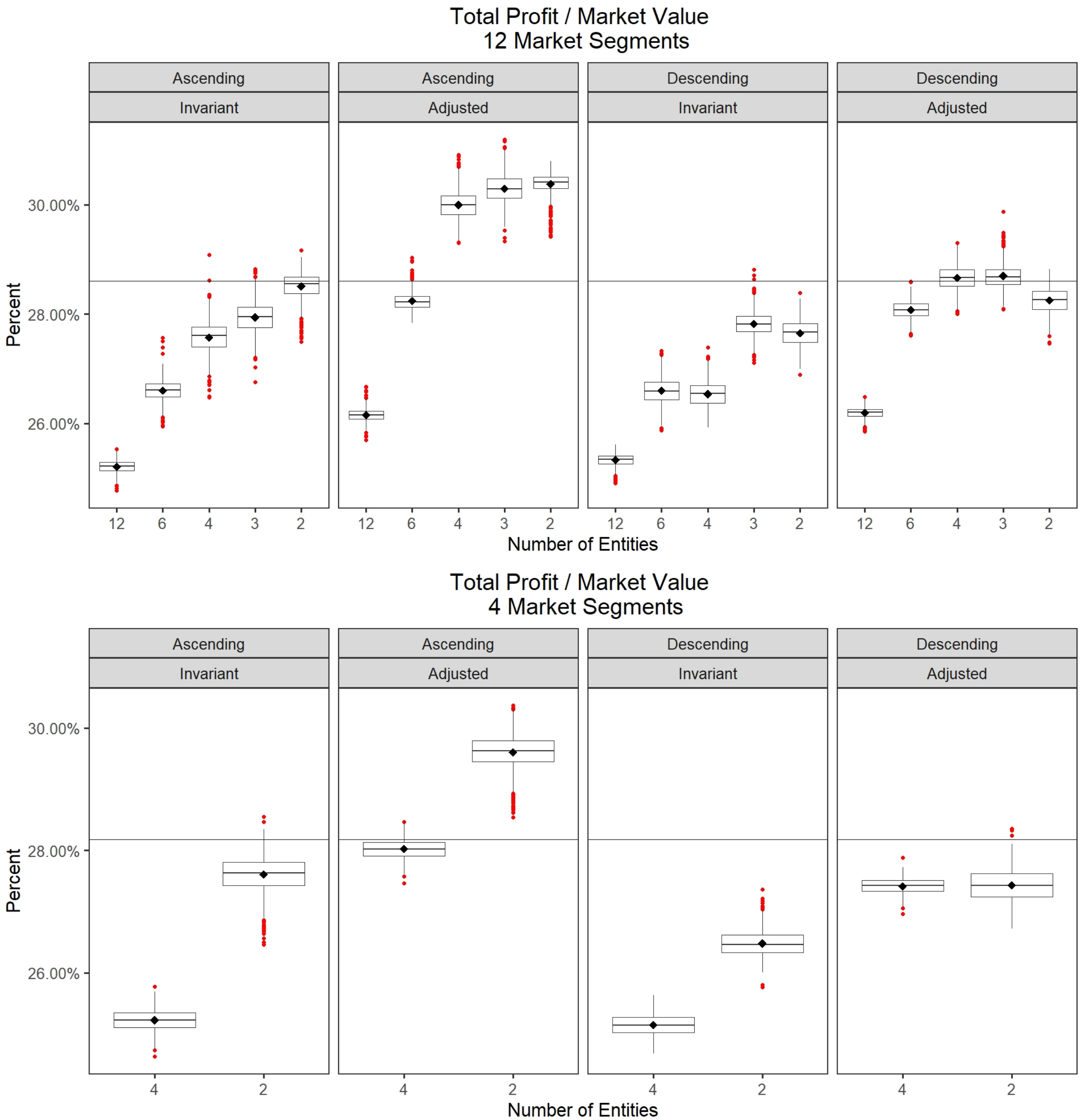

Figure 2 **Aggregated $\frac{TPF}{MV}$ in the global vaccine market for experimental scenarios with 12 and 4 market segments resulting from grouping countries in a varying number of coordinating entities, different procurement priorities, and choice of fixed cost recovery policy. $\frac{TPF}{MV}$ decreases as the number of entities increase. Other factors have a smaller impact.**

in each experiment, as the number of market segments handled by each entity increases. The $\frac{TSS}{MV}$ when countries are grouped into 4 market segments show similar trends. These results illustrate that the $\frac{TSS}{MV}$, and hence the global market's aggregated affordability and profit expand when the

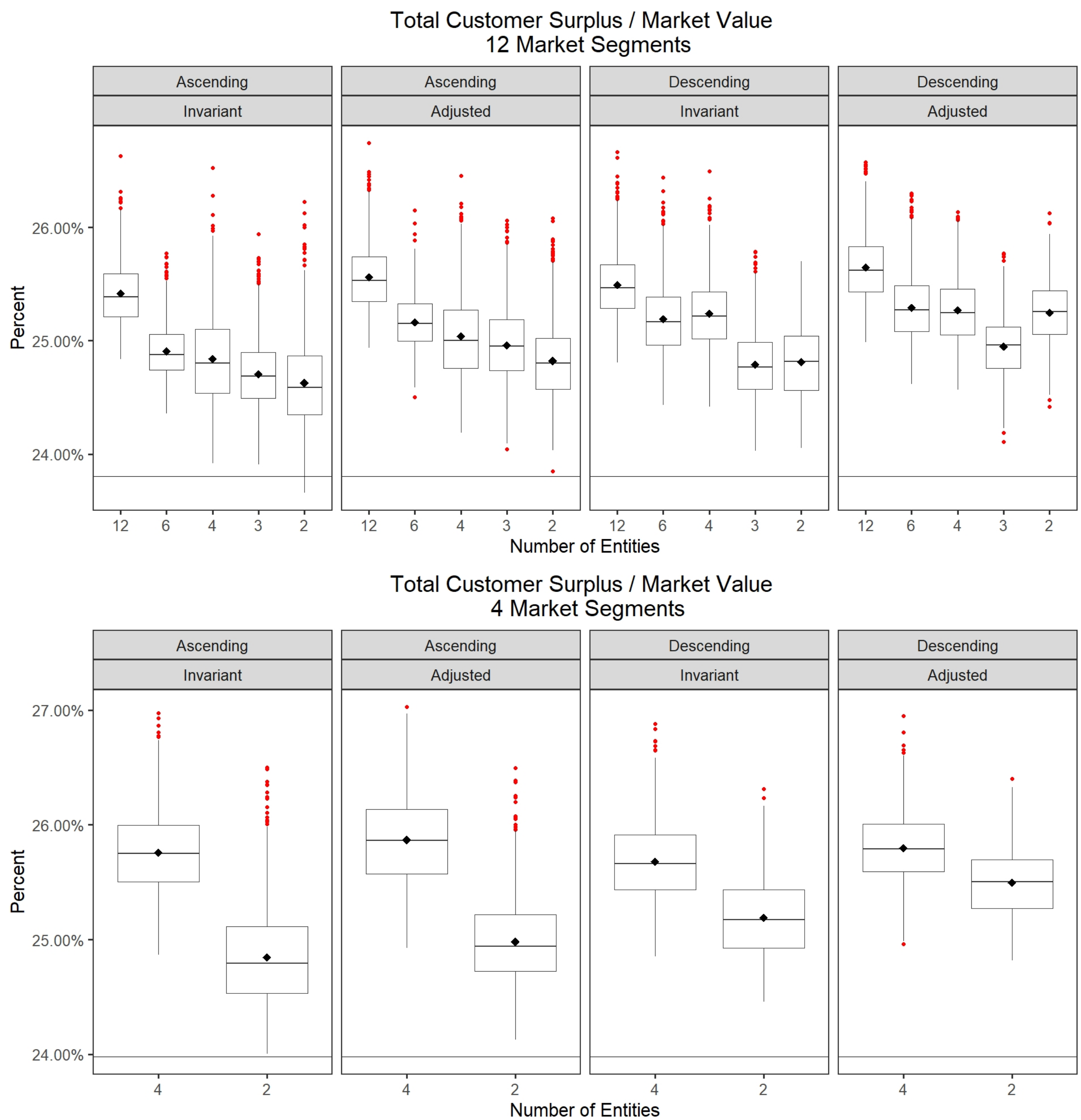

Figure 3 **Aggregated $\frac{TCS}{MV}$ in the global vaccine market for experimental scenarios with 12 and 4 market segments, resulting from grouping countries in a varying number of coordinating entities, different procurement priorities, and choice of fixed cost recovery policy. $\frac{TCS}{MV}$ increases as the number of entities increase. Other factors have a smaller impact.**

market is more cooperative (i.e., fewer coordinating entities), and when entities leverage on tiered pricing opportunities by coordinating a large number of market segments.

Figure 2 shows that the profitability ($\frac{TPF}{MV}$) increases as the number of coordinating entities decreases or equivalently as the number of markets per entity increases. Scenarios following 'ascending' procuring policy dominate those following a 'descending' policy.

Figure 3 shows that market affordability increases when there are more entities, or equivalently when the number of market segments per entity decreases. Additionally, there is little difference in total customer surplus resulting from adopting an 'adjusted' or 'invariant' policy to recover the fixed cost annuities, or from ordering the coordinating entities in an 'ascending' or 'descending' manner.

Under mid-point prices, low-income countries (LIC) can ensure a modest customer surplus, between 3 and 6% of the MV. Figure 4 shows that customer surplus for countries in low-income market segments decreases as the number of entities decrease, or equivalently, as the number of market segments per coordinating entity increases, especially when entities follow an 'ascending' procuring order. This behavior is the same as the one observed when considering the customer surplus across all markets. Entities favor generating affordability for markets with higher saving opportunities, which are market segments with higher reservation price values (i.e., HIC and UMIC).

A decrease in Total Customer Surplus is not necessarily bad news. The GVA framework ensures that vaccine prices per dose are lower than the average willingness-to-pay for a dose in each market. Hence, low Customer Surplus at a market level means that countries are buying vaccines at prices closer to their reservation prices (or willingness-to-pay), and there is no room for savings. In our experimental construction, Customer Surplus is measured as the gap between a vaccine's market price and the market's average reservation price. Consequently, in any market, there are countries for whom a vaccine's price is lower than their reservation prices (i.e., countries with higher income in the market) and those for whom the market prices are higher than their reservation prices (countries with lower gni_p in the market.) Therefore, having a lower customer surplus with fewer coordinating entities means that with higher coordination, countries with lower gni_p are paying vaccines at prices closer to what they can actually pay (i.e., they affordably buy vaccines.)

A practical implication of these results is that organizations that procure on behalf of low-income countries should group their countries in as many market segments as possible, and start procurement negotiations sequentially, in an ascending order, starting with market segments that have lower gni per capita. Additionally, this study suggests that entities procuring on behalf of lower-income countries should try to procure before other market segments during a given time period. This implies that organizations such as UNICEF should try to schedule their tenders before any other market or group of countries with higher income levels.

Traditionally, low-income countries try to negotiate lower prices for the remaining supply after vaccine stocks have been committed to higher-income countries, effectively using a descending priority order with an adjusted price policy. The results in Figure 2 suggest that if an ascending

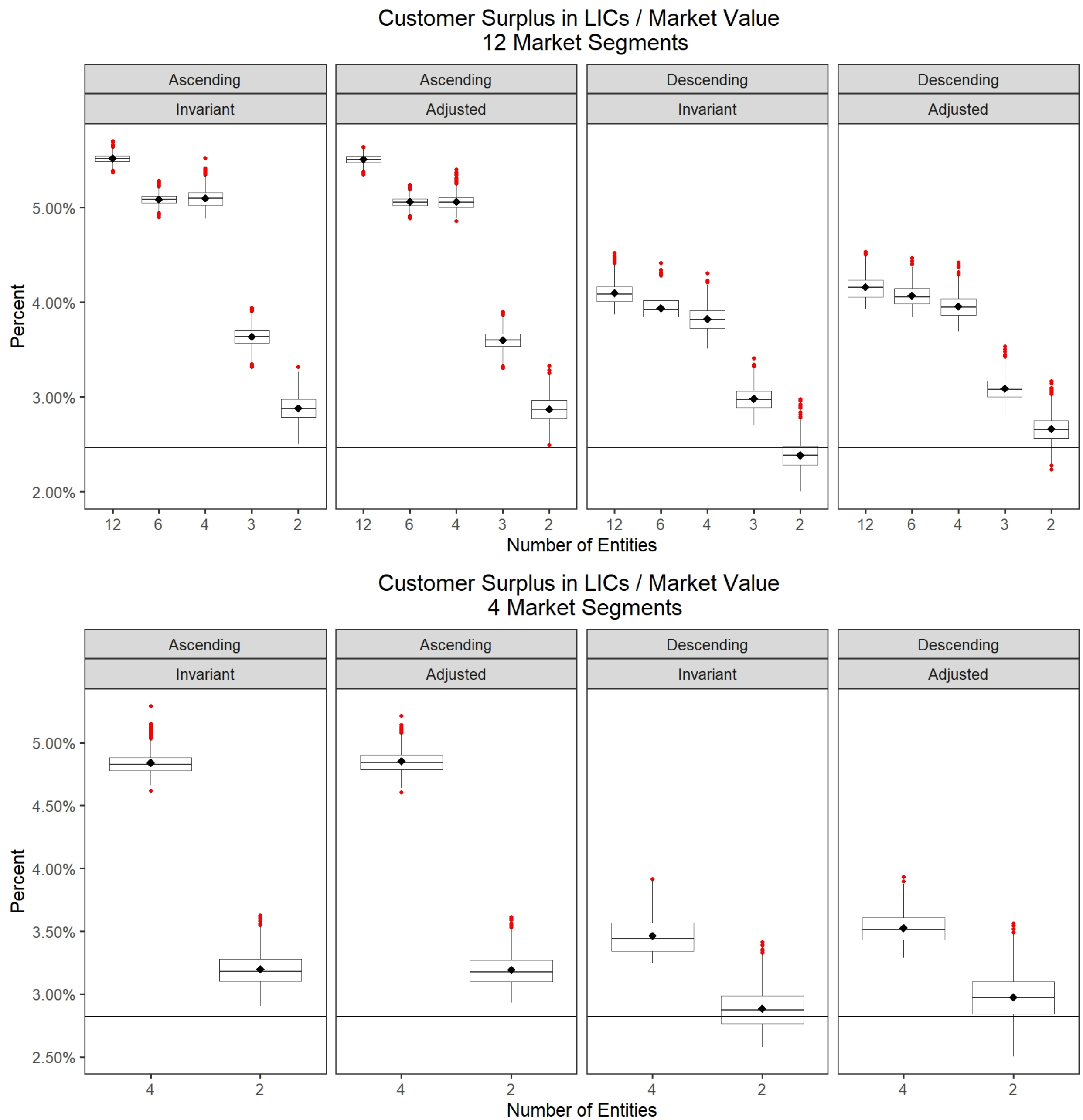

Figure 4 $\frac{CS}{MV}$ **for low-income countries (LIC) in the scenario with 12 and 4 market segments.** $\frac{CS}{MV}$ **for LIC improves as the number of entities increases. Descending priority provides overall worse results. The adjusted cost recovery policy seems to have little impact.**

negotiation order with an invariable price policy were used instead, more profit could be extracted during the negotiation. This reflects the fact that by negotiating first with lower-income countries, producers allocate a larger volume of their supply in the first few rounds of negotiation, meeting their profit goals despite the lower reservation prices. The producers would then have wider latitude to negotiate higher prices with higher-income countries, whose demand tends to be price-inelastic.

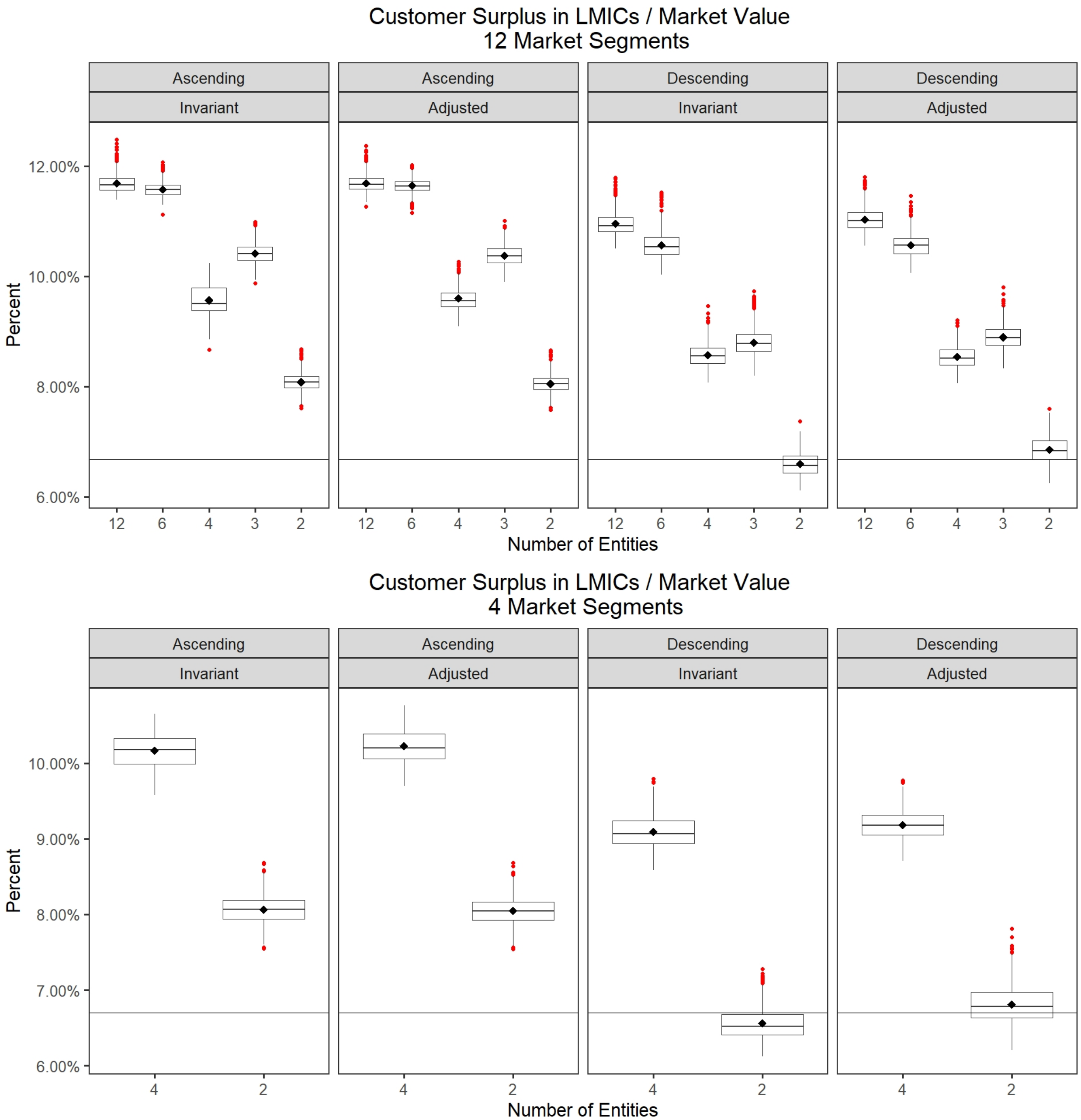

Figure 5 $\frac{CS}{MV}$ **for lower-middle-income countries (LMIC) for scenarios with 12 and 4 market segments.** $\frac{CS}{MV}$ **for LMIC improves with a lower number of coordinating entities. The ascending procuring order tends to generate higher affordability for LMIC. At low prices there is higher variability.**

This analysis is supported by Figures 6 and 7, which show lower customer surplus for higher-income countries under the ascending negotiation order. Conversely, Figures 8 and 9 show that such negotiation order also allows for the extraction of higher revenue from low-income market segments, as countries within their market buy vaccines at prices closer to their own willingness-to-pay.

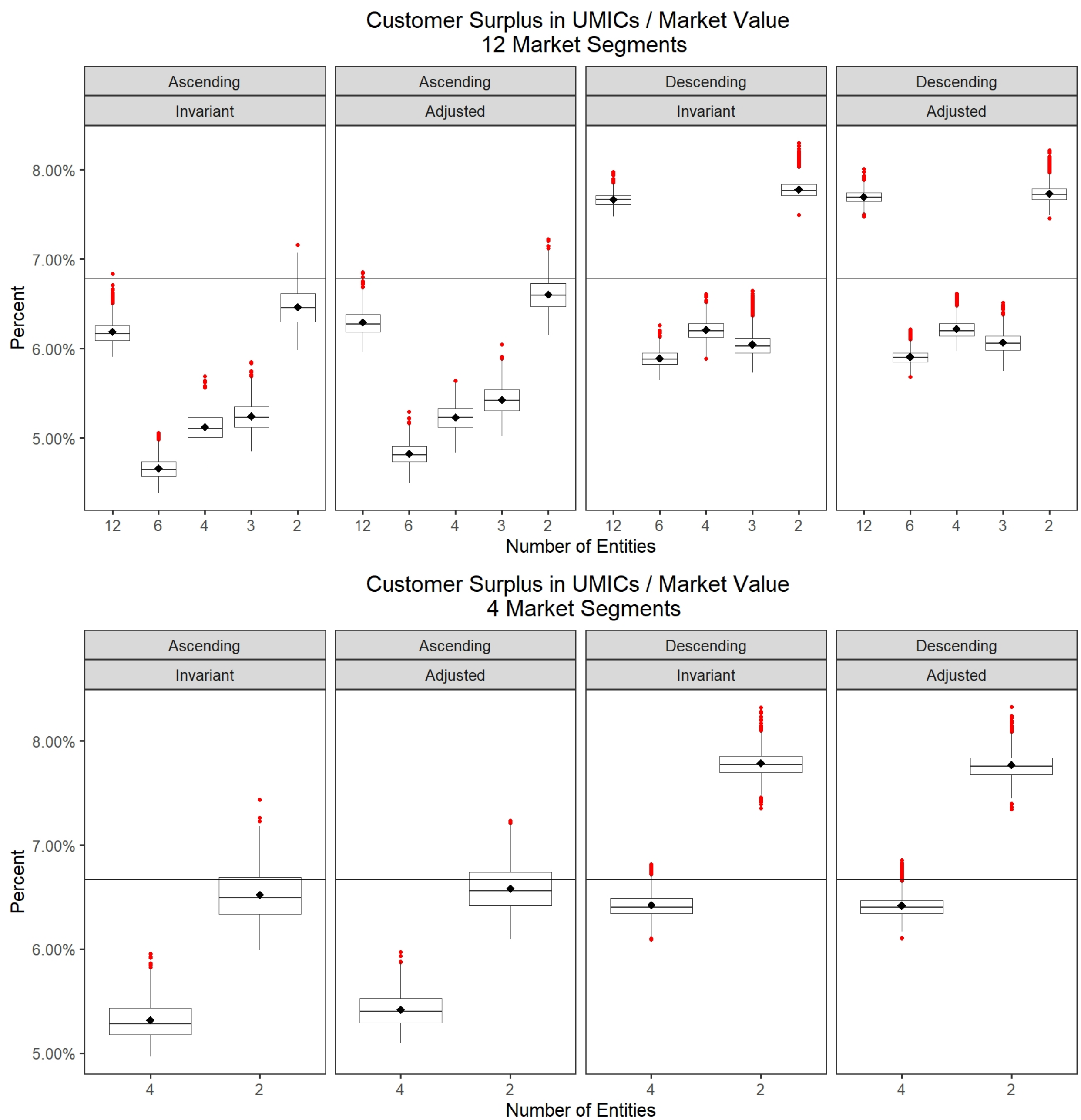

Figure 6 $\frac{CS}{MV}$ **for upper-middle-income countries (UMIC) in the scenario with 12 and 4 market segments.** $\frac{CS}{MV}$ **for LMIC improves as the number of entities increases. Descending priority provides overall worse results. The adjusted cost recovery policy seems to have little impact.**

5. Conclusions

Our results suggest that under a non-cooperative vaccine market, there are opportunities to concentrate affordability on LIC and LMIC and generate profit from sales to UMIC and HIC while maintaining affordable prices for all countries regardless of their income level. This study suggests that affordability at the market level for low-income countries can be more easily improved when

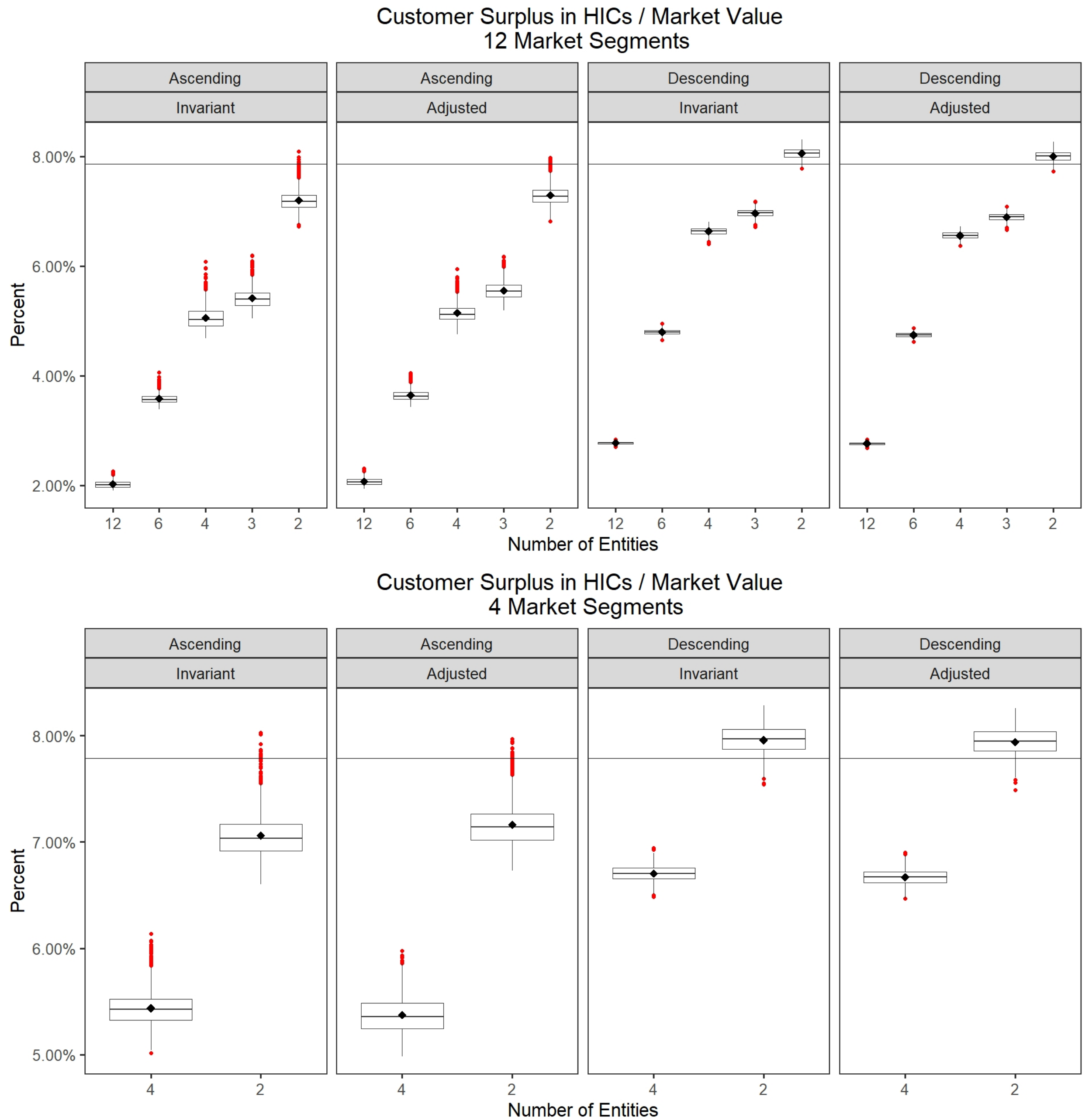

Figure 7 $\frac{CS}{MV}$ **for high-income countries (HIC) for scenarios with 12 and 4 market segments. Affordability decreases as the number of coordinating entities increases. Descending priority dominates results, while there is little impact when using an adjusted pricing policy**

there are more coordinating entities. However, with fewer entities with more market segments countries with lower gni_p pay vaccines at prices closer to their reservation prices. This arrangement also allows for more of the demand to be covered, and hence potentially increasing coverage. However, producers see lower profit levels when negotiating with multiple coordinating entities, mostly due to a revenue decrease from upper-middle-income countries (revenue from sales to LIC increase).

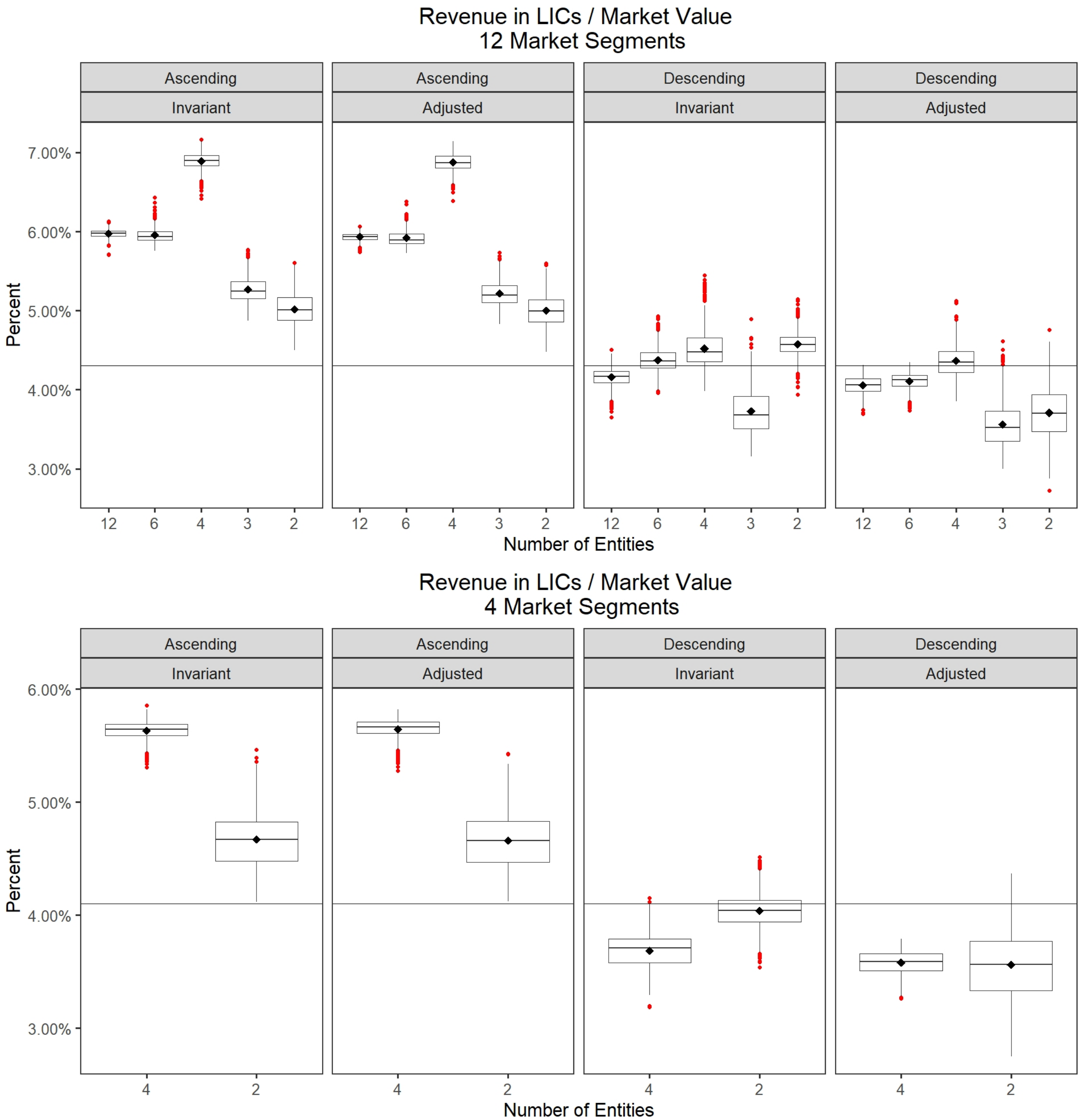

Figure 8 **Revenue obtained from sales to low-income countries (LIC) across all experimental scenarios for 12 and 4 market segments. Revenue tends to increase as the number of coordinating entities increases. The ascending priority order dominates the descending order for LIC.**

This suggests that the value generated by higher-income countries falls at a faster rate than the revenue increase from low-income countries. Results using the highest profitable prices suggest that while some fragmentation in the market is always beneficial, the optimal amount of cooperation may change depending on the final negotiated price.

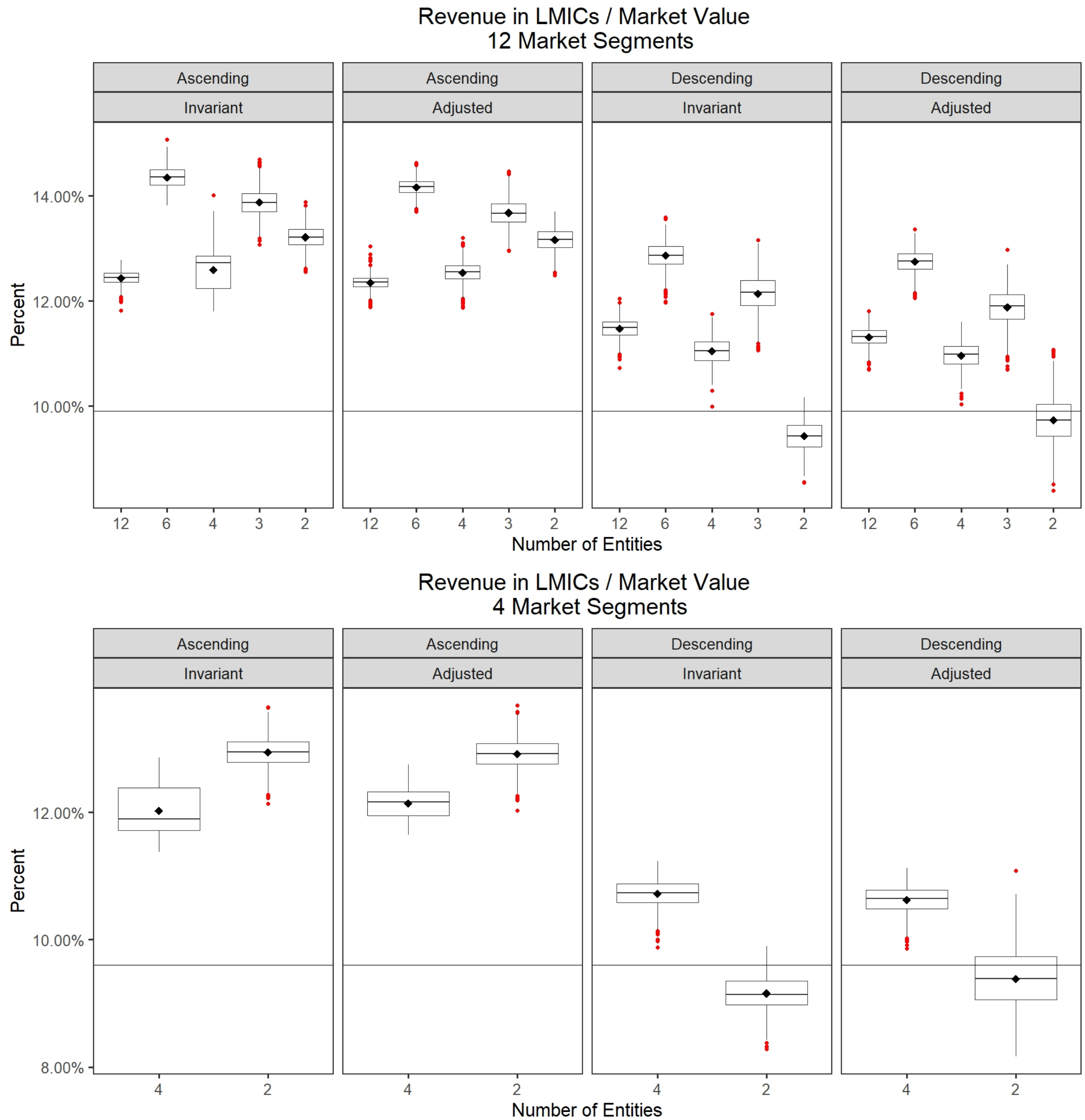

Figure 9 Comparison between the revenue obtained from lower-middle-income countries across experimental scenarios with 12 and 4 market segments. There is a similar pattern to the revenue in low-income countries, indicating interactions between the factors.Ascending order dominates.

Additionally, comparing the fixed costs recovering policies, if producers decide to adjust their annuity based on the volume of vaccines that have already been sold, affordability and profits are not significantly improved. However, maintaining an 'invariant' policy distributes better the profits so that fewer producers face losses, suggesting the 'adjusted' policy is not effective in recovering

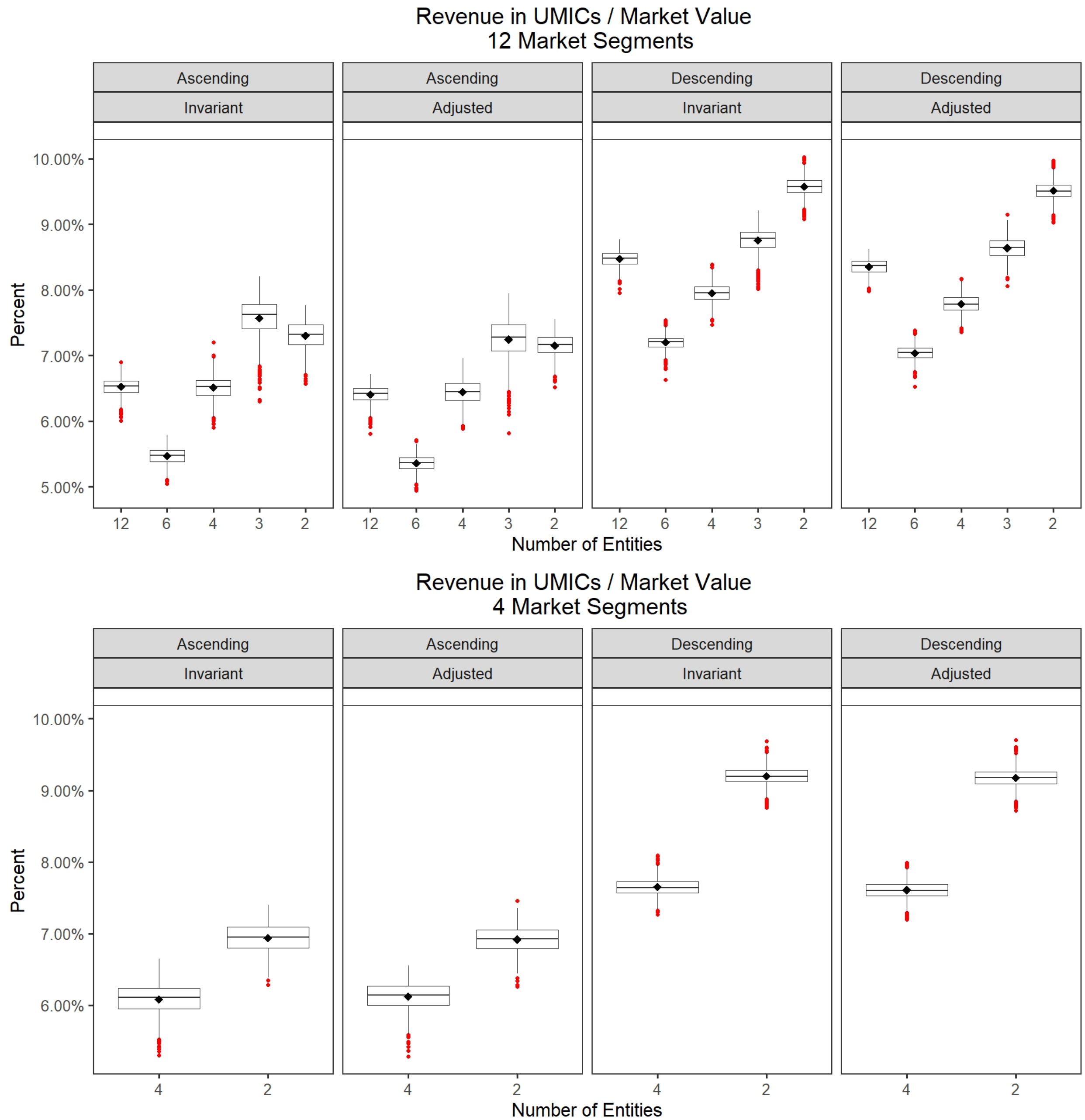

Figure 10 Revenue from sales to upper-middle-income countries (UMIC) across experimental scenarios with 12 and 4 market segments. Revenue tends to decrease as the number of entities increases. A descending priority procuring order offers higher revenue from sales to UMIC than an ascending order.

the annuity of unsold vaccine supply. Furthermore, ordering the entities by descending GNI helps prevent losses for producers.

The trend in Figure 4 suggests that to increase customer surplus while guaranteeing a desired profit level for the producers, the vaccine market should organize low- and lower-middle-income countries into more non-cooperating entities, and high- and upper-middle-income countries in fewer

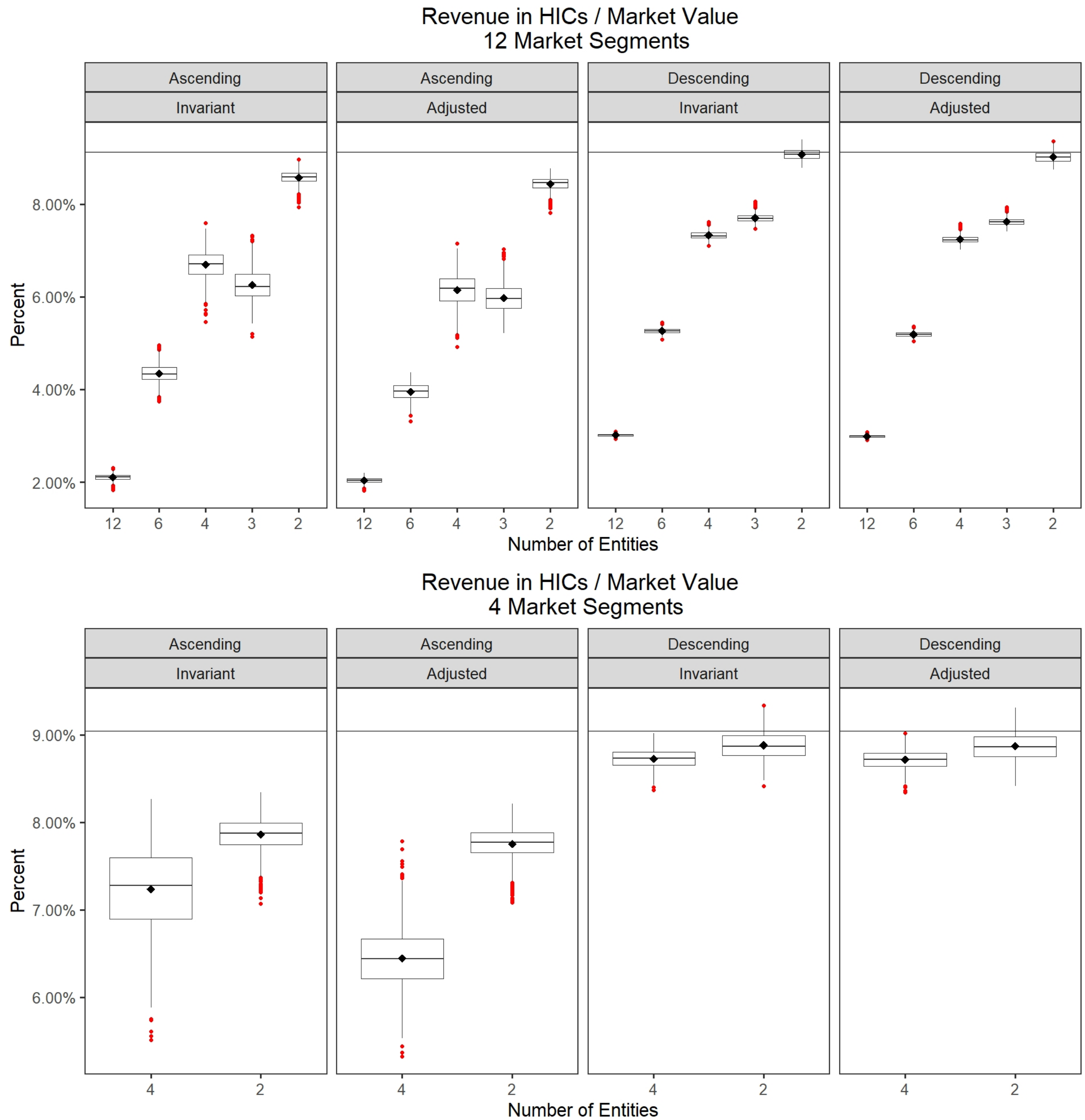

Figure 11 **Revenue from sales to high-income countries (HIC) across scenarios with 12 and 4 market segments. Revenue declines for an increasing number of coordinating entities.**

coordinating entities. In practical terms, this also implies that entities with LIC and LMIC countries grouped them in a higher number of market segments. This is a different organization to what is currently seen in the global market. Lower-income countries are organized into fewer coordinating entities, while higher-income countries negotiate independently.

This study solely shares insights from an academic experiment that assumes that all procuring entities aim to buy vaccines affordably, and yet try to ensure that producers obtained the desired

Total Markets	Market segment	Countries
12	1	1 to 5
	2	6 to 26
	3	27 to 57
	4	58 to 65
	5	66 to 75
	6	76 to 109
	7	110 to 113
	8	114 to 134
	9	135 to 158
	10	159 to 172
	11	173 to 191
	12	192 to 194
8	1	1 and 2
	2	3 to 57
	3	58 to 65
	4	66 to 109
	5	110 to 123
	6	124 to 158
	7	159 to 180
	8	181 to 194
4	1	1 to 57
	2	58 to 109
	3	110 to 158
	4	159 to 194
2	1	1 to 131
	2	132 to 194
1	1	1 to 194

Table 6 Countries grouped into each market segment considered in the experiments discussed in this paper

return on their sales. Under this hypothetically altruistic buying, there are opportunities to enhance affordability. The effort to implement the proposed vaccine procurement mechanism will require that all decision-makers act as coordinating entities that have access to a system that allows them to determine optimal procurement plans, but most importantly, establish a consensus that allows coordinating entities to buy following the recommended order. The challenge to determine the incentives to induce such consensus is not trivial and is beyond the scope of this study.

Appendix A: Other Figures

All figures generating during the study have been uploaded to the GitHub repository at https://github.com/ba8641/ME_General.git.

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