

Market Shaping and Market Access in the Global Vaccines Market: Approaches for the Future

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Abstract

This paper looks at market access and market shaping in the interest of public health in a post-COVID world. It starts out with a detailed case study of Gavi's market shaping (presented in a snapshot over 20 years), highlighting the key successes in: (i) introducing new vaccines in Gavi-eligible countries successively, (ii) expanding the number of suppliers, and (iii) bringing down prices for immunization in LMICs. Looking closely at how these successes were facilitated, the paper identifies a number of 'behind-the-scenes' factors that helped Gavi achieve these successes in different vaccine categories.

In its second part, the paper moves on to the lessons learned through these experiences, highlighting ways in which these learnings can be used to address the opportunities and challenges for market access and market shaping in the future. Finding that some of these challenges arise directly from the dynamics of the vaccine sector itself, while some others are the outcome of contrasting policy interventions, the paper advocates a more integrated approach to local production, pricing, procurement, and competition given the inter-related workings of many of these incentives. Acknowledging that such market shaping will also require closer monitoring of progress (in terms of greater access) across specific vaccine categories, the paper calls for working closely with more actors in the field including regional agencies and national governments in Africa. Findings suggest that a discussion of how to enable such a wider, more structural approach to market shaping with Gavi's active involvement and coordination with other partners, might be necessary.

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I. Introduction

Health is an established human right, and yet, access to life-saving pharmaceuticals, vaccines and related products continue to be critical problems in low- and middle-income countries (LMICs). According to the World Health Organisation (2011), access to medicines is determined by five variables:

- *Appropriateness*: i.e., mechanisms that focus on strategic selection of essential medical products that are important for local public health needs and are in short supply.
- *Availability and Affordability*: i.e., the supply of medical products to ensure that they are available at prices that match the ability to pay.
- *Quality Assurance*: i.e., the guarantee of strict compliance to quality standards by manufacturers and effective national regulatory authorities.
- *Health Security*: i.e., a continuous availability of essential medicines at various levels of the health system from a long-term perspective.
- *Continued Innovation*: i.e., provision of incentives not only for R&D leading to new drug discovery, but also for the development of products that are incremental improvements, or locally adapted products, suitable for local conditions in developing countries.

In any well-functioning pharmaceutical and healthcare market, active competition would be the best means to strike the balance between these variables to promote the supply of goods (through R&D, innovation, and production) and to maximize global welfare (through affordable and reliable access). Such a well-functioning market, that could provide the right incentives for innovation for pharmaceutical products, and fully internalize the social costs and benefits of innovation, requires: (a) ease of entry and exit of firms; (b) the absence of significant monopoly power; (c) easy access to information on market parameters, such as demand, and (d) an absence of (information and other) externalities.²

But the global pharmaceutical and healthcare sector does not match this description easily. Successful pharmaceutical innovation requires large-scale R&D investments, with the result that successful companies are regularly large concerns (Cockburn and Henderson, 1996) and market imperfections related to monopolistic/ monopsonistic/ oligopolistic competition persist widely. This includes high-risk aversion and large uncertainties amongst innovating firms, high barriers to entry for new firms, predatory business models to sustain market positions (with effects on pricing) and the prevalence of other market stabilizing strategies that require governmental intervention (Mendoza, 2019; Fossett and Wunnava, 2019).

So, although consumer demand should automatically stimulate pharmaceutical research and development (R&D) investments, this remains far from the truth in many categories, such as for diseases that disproportionately affect the poor in LMICs, with direct impacts on the availability of drugs (Kyle and McGahan, 2012). Even when drugs are available, they often remain unaffordable due to high prices,³ the low or no 'ability-to-pay' in specific user-groups,

² As an example of 'other' externalities influencing decisions of firms, consider the first-mover advantage in several therapeutic categories where drugs and vaccines are high in demand. The first mover advantage in capturing markets creates an automatic negative externality for entry of other companies. The magnitude of this negative externality may not be as high for the first few firms but can become significant for other firms discouraging them from investing into R&D after the first few products have been successfully introduced in the market.

³ Whether prices are too high or too low have static and dynamic considerations, but in general, a number of studies show relatively high prices in product categories across countries irrespective of their income status. See for example, Babar et al (2019) for a discussion on insulin pricing; Goldstein et al (2016) and Gyawali (2017) for a discussion on cancer drugs across all countries.

and the late introduction of drugs in many jurisdictions worldwide (Ahonkhai et al, 2016). Current evidence from the global pharmaceutical sector suggests that these trends are often reinforced by low competition across new and generic pharmaceutical categories for drugs, vaccines and other medical products (Ladkawala, 2018; Knox, 2020).

A similarly complex set of issues in health systems' organisation in LMICs impacts the market. Weak institutional and regulator capacity for health contributes to delayed introduction of products, high prices, low access, and often also poor quality. Of particular relevance are supply chain issues, such as unregulated intermediaries and excessive mark-ups, faulty/fluctuating public procurement mechanisms, low regulatory capacity and poor and ineffective policy frameworks. In the economic interplay of all these peculiar factors, the global pharmaceutical sector fails to create the requisite balance between innovation, availability, and affordability within countries, negatively impacting the achievement of public health objectives.

However, markets evolve as they allocate resources (Stiglitz, 2017), offering a glimmer of hope to address the situation. In any given instance, formal institutions such as intellectual property, trade law and policy, and competition law, and informal institutions, such as habits and practices of agents, and the behaviour of individual companies tend to have a 'shaping' influence (Schumpeter, 1947: 153) on markets. Tweaking the incentives on the supply side (especially those influence innovation funding) and on the demand side (those that signal consumer demand) can influence how markets get sliced over time and also help mitigate the divergences between profit interests of private firms and global health objectives. There is now a strong consensus amongst actors working in public health that this could offer a way to promote healthier competition on a global scale, especially in markets where one or a few buyers persist.

Over the past two decades, national and international agencies have worked together to shape markets toward public health objectives, particularly to promote the supply of vaccines and some drug classes that have high significance to public health in LICs (particularly HIV/AIDS). Thus far, these market shaping efforts have focused on interventions aimed at ironing out market imperfections that dominantly impact pricing and access. Broadly speaking, they operate along a three-way axis:

- (a) Assessing the market landscape and identifying bottlenecks;
- (b) Identifying ways to reduce supplier and buyer risks;
- (c) Promoting security of supply by bringing together public, private, and non-profit actors, including, *inter alia*, creating a 'marketplace', or other such instruments.

By closely coordinating demand with supply, on the one hand, and by bringing together public sector actors with those in the private sector, existing market shaping approaches seek to minimize adverse outcomes for public health and expand the number of total manufacturers that supply or produce products (Vargo and Lusch, 2017; USAID, 2014: 9). A predominant focus of current approaches, however, has been to optimize the market in sectors that have certain shortcomings to achieve immediate and tangible public health outcomes.

This paper looks at market shaping as a tool to promote public health objectives in a contemporary context to offer some thoughts on lessons learned and a way ahead for funders, international agencies, national governments, and pharmaceutical companies. It begins with a discussion of the Gavi Alliance's market shaping experience in Section II, with a sharp focus on the evolution of the global market shaping approach to vaccines, and the key milestones achieved up until now. In Section III, the paper moves on to identify the reasons for success achieved in individual vaccine categories, zooming in on a number of 'behind the scenes' factors that have helped achieve these market shaping successes.

The market shaping analysis of the Gavi Alliance (hereafter, Gavi) conducted in this paper covers all Gavi vaccine categories over a period of 2000-2021 using available data. The analysis highlights that the experience and success of market shaping strategies are different in each and every vaccine category, and has depended on alleviating several structural constraints faced by companies in the vaccines sector. In the second half of the paper, the paper addresses the extent to which we might build on these experiences in the future. In this part of the paper, the additional challenges for market shaping in the current context are discussed, with specific attention to the need to align market shaping better with the dynamic evolution of supply and innovation in the sector, including through local production. The paper concludes with feasibility considerations and policy recommendations.

II. Gavi's Market Shaping Approach: A Discussion

Gavi was set up in 2000 to address the low and lagged introduction of vaccines in low- and middle-income countries (LMICs), widely acknowledged by then to be a function of low purchasing capacity and low availability (no or few introductions). Gavi's role in pooling demand from LMICs and offering financing for vaccines for the Gavi 74 countries (now reduced to 57) has changed the market in several ways.⁴ Gavi's market shaping initially set out to: (a) improve demand forecasting for vaccine introductions in LMICs; (b) incentivize new vaccine manufacturers to supply to the GAVI market, and (c) obtain the lowest possible prices (Gilchrist and Naani, 2013).

While the ambition to bring down prices in the Gavi 74 market was not met immediately in its phase I (2000-2006) (Chee et al, 2008; Gilchrist and Naani, 2013: 840), by Phase II (2007-2010), several developing country manufacturers such as Shantha Biotech (India), Panacea Biotech (India) and the Serum Institute of India (SII, India) started supplying to Gavi (Gehl Sampath and Pearman, 2021). Over time, the number of companies supplying to Gavi has expanded, along with the progressive introduction of new vaccines to the Gavi-eligible countries. Gavi's salient achievements have been:

- a. The introduction of greater competition in several product categories, with the result that it has moved to 17 initial suppliers across all product categories between 2000 and 2021 (table 1 below).
- b. The offer of financial and technical assistance support structures to producers and an expansion of the market shaping approach include systemic parameters.
- c. Significant price reductions of the weighted average vaccine price per child for Gavi-eligible countries.

1. New and Steady Product Introductions

Following the introduction of the pentavalent vaccine, Gavi has introduced a range of new vaccines in Gavi eligible countries expanding access in a steady manner. Table 1 maps the evolution showing the introduction of the Pneumococcal Conjugate Vaccine (PCV) and Rota vaccines in 2009, followed by vaccines for Rubella, Human Papilloma Virus (HPV) and Japanese Encephalitis from 2011, and Typhoid and Cholera and Inactivated Polio Vaccines (IPV) from 2015. New vaccines to be funded include those for Ebola, Rabies, Hep-B (birth dose) and Diphtheria-Tetanus (DT) boosters. Gavi has also been steadily increasing the

⁴ Of the original Gavi 73, 16 countries have transitioned to full self-financing status in 2019. As a result, Gavi's priority countries have now been reclassified to a group of 57. See <https://www.gavi.org/types-support/sustainability/eligibility>

supplies of COVID-19 vaccines through the COVAX Facility, created in April 2020.⁵ The COVAX Facility aims to ensure that at least twenty percent of high-risk populations in all countries (frontline health workers, the elderly and those exhibiting co-morbidities) – but particularly in the 92 low- and middle-income countries (LMICs) that form part of the COVAX-AMC - are prioritized for vaccines access.⁶

2. Evolution of a Broader Market Shaping Approach

Gavi's market shaping approach has evolved to include a per category approach (roadmaps) for individual vaccines with due consideration to healthy market assessment tools and systemic factors.⁷ In 2016-2020 (Phase IV), Gavi's market shaping listed its objectives as (Gavi, 2019):

- a. Ensuring adequate and secure supply of good quality vaccines;
- b. Supporting the evolution of prices of vaccines and other immunisation products to appropriate, sustainable levels;
- c. Saving money for countries to the tune of US\$ 1.3 billion between 2016-2020;
- d. Incentivising the development of suitable, good quality vaccines and related immunisation products; and
- e. Maximising the number of healthy vaccine markets.

The Supply and Procurement Strategy 2016-2020 identified ways in which to taper off market interventions from markets that reach the healthy market goals, including long term competition.⁸ Gavi's market shaping approach has been fine-tuned once again in 2020, as part of the Gavi V (or 5.0 approach).⁹

3. Increases in the Number of Manufacturers and Lower Prices

Between 2000 and 2020, Gavi has contributed to increasing the number of suppliers in almost all vaccine categories that it supplies (see table 1) with significant impacts on lower prices. A large share of this success can be traced back to the fact that the Gavi model has offered a guaranteed pool procurement mechanism with stable demand of over 1 billion vaccines and reliable financing (unlike the unpredictability of national procurement in LMICs) for its priority countries. This guaranteed pool procurement mechanism has been instrumental in providing the requisite confidence for pharmaceutical companies to invest into technological upgrades to produce a wide variety of vaccines (Gehl Sampath and Pearman, 2021). It has also helped foster the emergence of several suppliers such as Serum Institute of India (SII, India), Panacea (India), Biologicals E (India), Bharat Biotech (India), SK Bioscience (South Korea), Chumakov (Russia), Biomanguinhos (Brazil), Chengdu (China), Biofarma (Indonesia), who now supply to Gavi in several vaccine categories. These suppliers now form a growing group of companies that are members of the Developing Country Vaccine Manufacturers Network (DCVMN) (see Jadhav et al, 2008).

⁵ The acronym stands for the COVID-19 Vaccines Global Access (COVAX) Facility, led by the by the World Health Organization in collaboration with Gavi, The Vaccine Alliance and the Coalition for Epidemic Preparedness Initiative (CEPI).

⁶ 182 countries are in the COVAX Facility since 15 December 2020. 90 are fully self-financed, and 92 are LMICs that form part of the COVAX-AMC, of which 58 Gavi-eligible countries form part of the core COVAX-AMC, and 34 countries that are transitioning out of, or have already transitioned out of Gavi. See https://www.gavi.org/sites/default/files/covid/pr/COVAX_CA_COIP_List_COVAX_PR_15-12.pdf

⁷ In 2015, Gavi also introduced its healthy market framework in collaboration with UNICEF and the Gates Foundation which identifies the relevant characteristics of healthy markets, and costs to be assessed according to each of the attributes, and vaccine categories. <https://www.gavi.org/sites/default/files/document/healthy-markets-framework--public-overviewpdf.pdf>

⁸ <https://www.gavi.org/programmes-impact/our-impact/evaluation-studies/gavi-supply-procurement-strategy-2016-20>

⁹ <https://www.gavi.org/our-alliance/strategy/phase-5-2021-2025>

Gavi has now diversified its supply across different vaccine categories, from 5 companies in 2000 (Gavi, 2020a) to 17 in 2021.¹⁰ Table 1 below summarizes Gavi's entire market shaping story in a snapshot. It provides the timelines of introductions of new vaccines, the amount of financing provided by Gavi, the number of suppliers in each vaccine category (and how the supply security has increased per vaccine category).

Gavi's total vaccine funding (currently close to USD 1 billion per annum) has lent the organization significant leverage to negotiate better prices with pharmaceutical companies. This, along with the entry of new suppliers, has fostered an overall dynamic supply side evolution with significant price reductions in some categories. For instance, Gavi brought down the weighted average vaccine price per child for full immunization using the pentavalent, pneumococcal conjugate and rotavirus vaccines from US\$35 in 2010 to US\$20 in 2015: a 43% reduction in the total price (Gavi, 2020a; 2020b). Such direct price decreases in vaccine costs are often just the tip of the iceberg. Global strides in immunization have several long-term benefits that are not easily quantifiable. A recent study notes that USD 1 spent on immunization can save USD 21 in health care costs and productivity declines (thanks to illness or death) between 2021 to 2030, lending significant support to Gavi's overall mission (Sim et al, 2020).

Currently, pooled procurement continues to act as a relevant incentive for investments by pharmaceutical companies. In 2021, Gavi has already procured over 1.4 billion vaccines for routine immunizations (Table 1), in addition to those that are expected to be delivered through the COVAX Facility.

Table 1: GAVI's Market Shaping Story in a Snapshot: 2000-2021

Date from which funding/supply started	Vaccine	Number of suppliers in each vaccine category		2021 volume of doses funded in millions (Gavi 73)*	2021 derived value of doses funded in million USD (Gavi 73)	2021 volume of doses (millions) in graduated countries (Gavi 73-Gavi 64)*	2021 value of doses transitioned in million USD (Gavi 73-Gavi 64)
		At start	In 2021				
2000	HepB, Hib	1	6	239	\$203	85	\$72
2000	Yellow Fever	3	4	81	\$97	0	0
2008	Measles	1	1	67	\$21	0	0
2009	PCV**	2	3	161	\$470	34	\$99
2009	Rotavirus	2	4	118	\$283	49	\$117
2011	Rubella	1	1	168	\$109	71	\$46
2011	HPV**	2	2	13	\$58	1	\$4
2011	JE**	1	1	35	\$17	28	\$14
2015	Typhoid (TCV)**	0	1	47	\$71	0	0
2015	Cholera	1	2	5	\$9	0	0
2015	IPV***	3	5	78	\$192	12	\$30
2016	Ebola	0	1	1	\$5	0	0
2021	Total	17	31	1013	\$1535	280	\$383

¹⁰ Table shows a total count of 34, but these are counted per vaccine category. In total, 17 companies supply multiple vaccines.

2021	COVID	0	10	2 billion	≅ \$14 billion****
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Source: Calculated by author. Volumes projected use GAVI public demand forecast. Value projections have been derived / estimated at unit price from UNICEF procurement data (using a calculation of weighted averages to arrive at derived value).

Table Notes:

*Gavi 64 represents all Gavi 73 except India, Indonesia, Ukraine and six PAHO countries, and includes the Gavi 57 countries that are still eligible include those as determined by their GNI per capita below or equal to US\$1,630 over the past three years (based on World Bank data on the topic published annually) including all low income countries.¹¹

**Expanded abbreviations: PCV is the pneumococcal conjugate vaccine, HPV refers to the human papillomavirus vaccine, JE is the Japanese encephalitis vaccine, TCV is the typhoid conjugate vaccine, and IPV refers to the inactivated polio vaccine.

***OPV (oral polio vaccine) is funded by the Global Polio Eradication Initiative (GPEI), not by Gavi. BCG, DTP and Measles is also funded by donors on a case by case basis, and not by Gavi.

****For COVID19 vaccines, price computed at 7 USD per dose as per Gavi documents, might need revision given the latest deals.

****Table does not contain Meningococcal A vaccine that was introduced by Gavi in 2016. The total of 31 suppliers listed in the table is computed per product category, but supplied by 17 companies.

III. What Worked, and How: The ‘Behind the Scenes’ Factors in Gavi’s Success

Markets take time to evolve, even in the presence of market shaping interventions. The real factors that determine market shaping successes – from that perspective - are the overall vaccine portfolio (the total number of vaccines that demand is forecasted for, and their production characteristics), and product maturity (i.e., lifecycle and continued demand). These two factors can work in favour of competitive markets if adequately bolstered by incentives that provide technical and financial support.

At closer look, Gavi’s assistance for product introductions during these years has been wide ranging. It has included technical and financial assistance, market assurances (through advance market commitments and demand forecasts) as well as other kinds of risk-sharing arrangements in certain instances. These, however, have had differentiated impacts on the market evolution in individual vaccine categories. A deep dive into market shaping successes per vaccine category suggests that in each instance where Gavi has been successful, interventions have been aimed at alleviating structural impediments to competition in the vaccines’ sector. These were either shaped by Gavi directly or were enabled by way of incentives and partnerships fostered through other agencies, including the WHO. This section identifies these factors by looking at individual vaccine categories to generate a clearer account of how these markets transitioned over the years.¹²

1. Supply Alternatives Take Time to Emerge

GAVI’s experience shows that supply alternatives take time to emerge. A good example is the pentavalent vaccine where it took over ten years, and demonstrates the role played by mature *lifecycle and competitive demand*. When Gavi first started out, the pentavalent vaccine was procured from GSK, which was producing HiB and had the volume capacity to produce for

¹¹ For the current list of Gavi 57 (as of 2020), see: <https://www.gavi.org/types-support/sustainability/eligibility>

¹² See Malhame et al (2019) for a similar detailed analysis based on the pentavalent vaccine.

Gavi. Sanofi, on the other hand, did not have capacity to accommodate Gavi's demand, despite being a producer of HiB. During the initial years, the volumes procured from GSK remained insufficient to meet the growing demand for large birth cohorts across LMICs. Consequently, even as countries such as Uganda, Kenya and Tanzania introduced the vaccine, countries with large birth cohorts such as India, Indonesia and Nigeria had no access to the pentavalent vaccine as of 2008. This began to change only when Berna Biotech and Novartis formed a joint venture (with the latter providing the capacity for HiB, one of the antigens in the pentavalent vaccine). Soon thereafter, Shanta Biotech (India) and Panacea Biotech (India) started supplying the pentavalent vaccine to Gavi in 2008, followed by the Serum Institute of India (SII, India) in 2011. The market evolved further with the emergence of Bio Farma (in 2014), two Korean producers (including SK Pharma), and then the exit of GSK and Berna Biotech.

In the case of the rotavirus vaccine, similarly, it took over eight years for the entry of Rotavac (Bharat Biotech) and Rotasil (SII), after the initial introduction of Rotarix (GSK) and Rotateq (Merck) respectively. As a result, Gavi's rotavirus introductions suffered when Merck decided to withdraw Rotateq from some African countries (Douceff, 2018; see also, MSF, 2015). The same is true of the pneumococcal adjuvant vaccine (PCV), where competitors only emerged after a decade. A reason for the slow development of alternative manufacturers is that it takes significant finances and technical expertise to set up production facilities, apart from the need for technology, in some instances. Past studies have contended that developing country manufacturers typically lag anywhere between 5 and 15 years in production capacity (WHO, 2011, Thomassen et al, 2013). Although this is fast changing, investments into large scale production facilities while overcoming technical requirements often requires time despite the presence of future markets.

2. Mature lifecycles and Competitive Demand Play an Important Role

Mature lifecycles and competitive demand play important roles in the emergence of competition. In the case of the pentavalent vaccine, it was the long lifecycle and steady demand that jointly enabled the emergence of competition over a 10+ year period. In the period 2001–2018, Gavi disbursed US\$3.5 billion to support the administration of the vaccine, and the demand remained steady at 300 million doses annually between 2005 and 2016 (Malhame et al 2019). This led to large scale investments in building production capacity by several manufacturers in LMICs, approximated roughly at around USD 100 million per facility (Malhame et al 2019). Amongst the suppliers that emerged over time, some companies, notably, Bio Farma (Indonesia) had supply capacities mainly to meet their domestic demand, but many others, such as SII and Biologicals E (the latter entering the market in 2012 after Gates push funding), first increased production to supply to India, who was forecast to account for 20% of the global pentavalent market in 2014 (MSF, 2015) and also began supplying to Gavi. Over time, the growing demand for the vaccine in India led to greater domestic price competition between SII and Biologicals E, and also helped Gavi negotiate better prices with SII in keeping with its roadmap for the pentavalent vaccine (Gavi, 2013).

3. Technology Transfer and Vaccine Development Partnerships Remain Critical

In cases where competition was successfully introduced, the pull incentives of financial rewards to companies was categorically supported by push programs that included R&D funding and technology transfer. In particular, technology transfer remains a highly relevant factor in the introduction of competition. In the pentavalent market for example, technology transfer by several sources, played a critical role in supply diversification. The pentavalent vaccine, for example, is a conjugate of five antigens, whose production was constrained by a lack of technical know-how related to production and the presence of conjugation patents for one of the antigens (HiB) in the early 2000s. To overcome this hurdle, the Netherlands Vaccine

Institute (NVI) used the PRP-T conjugation method to circumvent competing conjugation patents (Buerett et al, 2012; Hamidi et al, 2014). The technology necessary to produce conjugate Hib (*Haemophilus influenzae* type B) vaccines was then transferred by the NVI to Biologicals E and SII in India,¹³ Bio Farma in Indonesia, Glovax in South Korea and the Shanghai Institute for Biological Products (SIBP) in China (Buerett et al, 2012) and by GlaxoSmithKline (GSK) to a Brazilian manufacturer (WHO, 2011:11). This technology transfer was instrumental in the entry of Shanta Biotech, Panacea Biotech and SII from India between 2008 and 2011 and helped Bio Farma to enter as a Gavi supplier in 2014.

During this time, in addition to the technology transfer for production from NVI, technical assistance was provided by the WHO for pre-qualification (WHO, 2013) and facilitated through PATH and funded by the Gates Foundation to several new suppliers with the intent of furthering investment into building capacity (Malhame et al, 2019). Gavi implemented and coordinated these market interventions, consistently improving market information, promoting transparency, securing risk-sharing agreements and facilitating innovative procurement with a view to building a competitive market.

Similarly, the rotavirus vaccine supply was initially dominated by two companies – GSK and Merck, with supply disruptions until two other companies – SII and Bharat Biotech introduced rotavirus vaccines. Bharat Biotech's rotavirus vaccine, Rotavac, is the product of a long-term R&D partnership in India, that started with the isolation of an attenuated strain at the All-India Institute of Medical Sciences, New Delhi in the 1980s. This was later built on by the Department of Biotechnology (Government of India), Bharat Biotech, the US National Institutes of Health, the US Centers for Disease Control and Prevention, Stanford University School of Medicine, and PATH (Path, 2018). The vaccine development partnership was facilitated from 2000 onwards with the support of the Indian Department of Biotechnology, the Bill & Melinda Gates Foundation, the Research Council of Norway, and the UK Department for International Development (Path, 2018; DCVMN, 2018).

More generally, the WHO estimates that between 1990 and 2010, eleven developing countries actively participated in vaccine technology-transfer agreements. India was the recipient of twenty-six such agreements, followed by China (eighteen) and Brazil (ten) (WHO, 2011:12). On closer look, there is a relationship between these technology transfer initiatives and the net observed effect of expanded manufacturing capacity in LMICs (WHO, 2011:12) in general, and the increased capacity of Indian suppliers, in particular. The latter now account for a large share of the global vaccines supply by volume (see Gehl Sampath and Pearman, 2021; and Figure 2 below).

4. Introduction of Vaccines into Immunization Guidelines and Protocols

Supply expansion, in a few cases, has been facilitated by the introduction of vaccines into immunization protocols. Measles production (when the big pharma switched from Measles to trivalent MMR combinations) by SII was well-timed with the prioritization of elimination of measles in immunization programs, which helped the company consolidate to emerge as the largest producer in volume terms. SII remains the sole WHO pre-qualified supplier of the vaccine globally to LMICs today (table 1).

¹³ Technology transfer commenced formally in 2002 and ended with a pentavalent DTwP–HepB–Hib fully liquid market license in 2009.

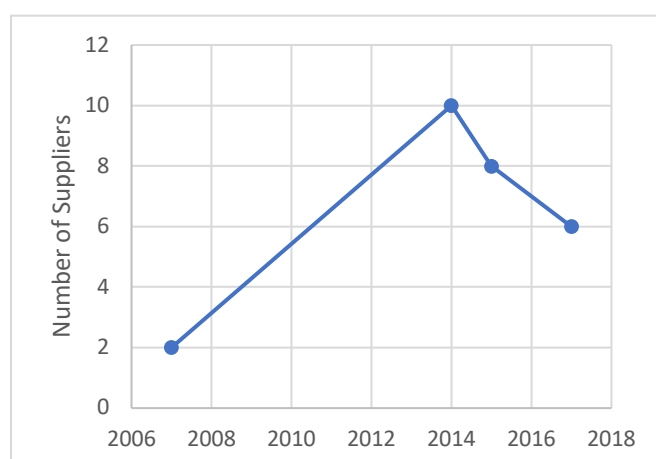
IV. Expanding Market Entry and Sustaining Supply: Lessons Learned

The discussion in Section III helps to carefully locate Gavi's market shaping successes, also highlighting its imbrication with other structural levers for market transformation that were ongoing in specific vaccine categories. These other structural levers included push funding from the Gates Foundation and other national/ international agencies, and parallel technology transfer initiatives under the auspices of the WHO, and played an important role in expanding the pool of suppliers over time. In this process, Gavi's additional financial and technical assistance played an important role in bringing actors together, aligning the supply of technology and finance with global demand for vaccines. While the process of market entry and expansion depends also on the specificities of the vaccine in question, the following general observations stand out.

1. Ensuring Diversity of Supply in the Long Run: The Market Retention Challenge

Promoting market entry remains distinctly easier than retaining companies in the market over time. The expanded market entry successes listed in Table 1 help to highlight that it takes time for competition to emerge. Across vaccine categories where competition emerged over the past two decades, the average timeline for 1-2 competitors to emerge remained around 6 years, with another 3 or so years for the market to grow to around 4 players, and then an average of another four years for the introduction of more competition. This indicates a timeline of over 10 years to build a market from 1-2 suppliers to anywhere between 4-8 suppliers. Gavi's market shaping experience also shows that the emergence of 4 or more suppliers is critical for large price reductions, as was the case in the pentavalent and the rotavirus categories. At the same time, supply security depends on retaining a wide number of companies engaged in production over time, which is often not as easy as it seems. The pentavalent vaccine experience helps showcase some of these difficulties (figure 1).

Figure 1: Pentavalent Vaccine: Supply Evolution¹⁴



The pentavalent vaccine supplies began to diversify thanks to Gavi's forecasted demand, and companies that invested included Berna Biotech, Bharat Biotech (India), Bio Farma (Indonesia), Panacea (India), SII (India) and Bio E (India) taking the total to 10 suppliers at the peak (around 2015). While significant competition between players at the peak of the supply expansion pushed the price below \$1 per dose, the extreme low prices also led to the exit of GSK and Berna Biotech over time, with Sanofi remaining only in the 10-dose liquid presentation. Many other companies

have not managed to sustain the price competition (Gehl Sampath and Pearman, 2021). For instance, of the companies that entered from the DCVMN category, Bio Farma and Bharat Biotech now mostly cater to national markets only (with the latter focused on private sales). This has left three companies (Panacea, SII and Biologicals E) as the dominant suppliers in the pentavalent category.

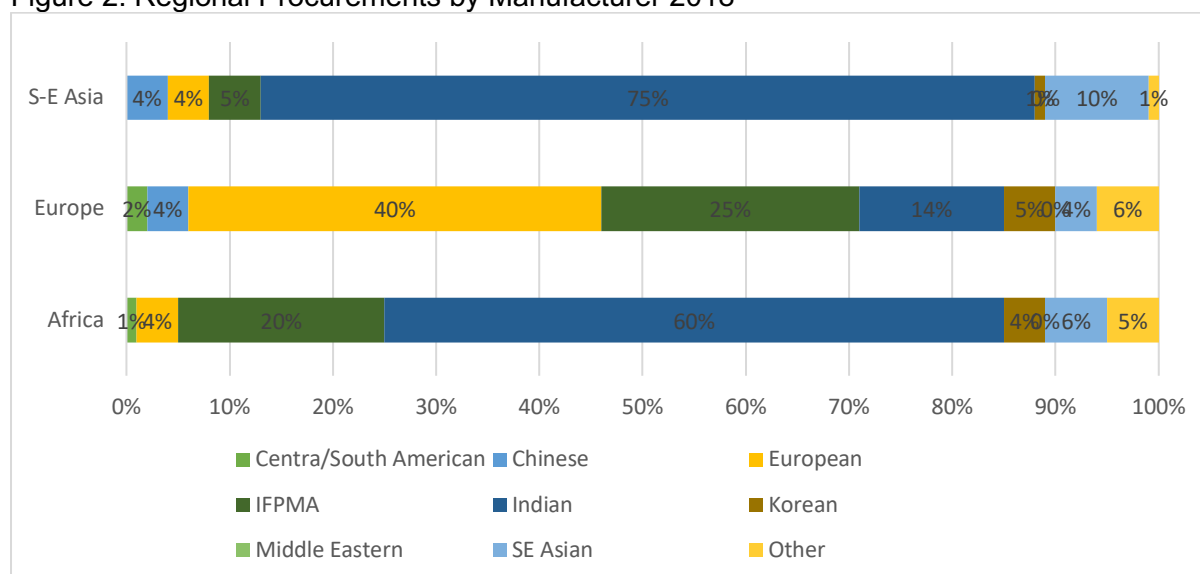
¹⁴ Figure Source: Author.

2. Beating the Vaccine Sector Tendency Toward Concentration

Similar trends persist in other vaccine categories, with a widespread tendency toward concentration of supply. As a result, despite significant market inroads and expansion work by Gavi, working alongside UNICEF and PAHO to pool procurement over the years, market retention (i.e., retaining market presence of the companies that enter) has not been easy. The listing of suppliers across vaccine categories in Table 1 shows that although there has been an expansion of companies on the whole (17 in total, supplying across several product categories), each of the vaccine categories currently operates with one or two dominant players. For example, SII has the market monopoly on Measles and Rubella in Gavi and UNICEF procurement. Sanofi and Chumakov (the latter being a more recent market entrant) supply the largest shares of Yellow fever vaccines globally followed by Biomanguinhos, Brazil and Institute Pasteur de Dakar, Senegal (Gehl Sampath and Pearman, 2021). Japanese encephalitis supply to Gavi has been dominated by Chengdu, a Chinese company, and Merck (USA) has dominated HPV supply when compared with GSK (Belgium). More broadly, the big pharma suppliers dominate PCV, Rotavirus and HPV, although the Rotavirus situation is transforming slowly.

A primary reason explaining this market structure is that vaccine production costs only decrease with production scale and scope, so the sector lends itself toward companies with the largest scale operations (see also Munira et al, 2019; Nguyen and Schwalbe, 2019). This demonstrates a central dilemma in balancing out the focus on low prices on the one hand and maintaining supply security on the other (see also Keller and Glassman, 2019). Currently, Indian companies have large shares of the market by volume, accounting for almost 60% of the global market supplied in 2018 (Gehl Sampath and Pearman, 2021). A cursory distribution of regional procurements by supplier type (Figure 2) helps to underscore this, and points to the difficulties in expanding the pool of suppliers using pooled procurement as a main driver in the vaccine sector. This raises interesting and significant questions for market shaping in the future (see next section).

Figure 2: Regional Procurements by Manufacturer 2018



Source: Computed by author using WHO's MI4A database and sales in high income countries by manufacturer.

3. Building Production Capacity Sustainably Requires Addressing Structural Barriers

The problem, however, is not created by a focus on price-based competition alone as some recent studies identify. There are often multiple, structural constraints that impact the emergence of alternatives, dictating how companies survive over time. Some of these remain product or vaccine category-specific, while many others relate to the complexity of vaccine R&D and vaccine production.

An important learning from Gavi's experience is that it is almost impossible to shape markets in short timelines such as the next two-three years. An ideal market shaping strategy rather, is not just one that matches supply and demand in the short-term by pooling demand and bringing potential suppliers together who can produce currently, but also expands to addressing the structural factors that prevent competition from emerging easily in the vaccine category in question. This would imply a more calibrated matching of instruments that go beyond supply calibration to those that address unequal distribution of capabilities for production, and market access. This lends strength to a different, but more nuanced theory of change: namely, that, when markets do change, they do so, because several other binding constraints that act as barriers to entry – such as the unavailability of finance and technology access – worked in tandem along with routine market shaping incentives such as technical assistance to improve quality of production or market forecasting – to enable those market transitions.

A review of each of the DCVMN companies helps underscore this point more effectively, given that each of them have relied on such drivers to survive and grow in different ways. SII (India) made a huge bet on high volume Measles production around the time it was introduced in the immunization guidelines, which helped the company consolidate to emerge as the largest producer in volume terms. Panacea (India) set up a diverse product portfolio to diversify risks, and after some initial hurdles, managed to find a secure footing in the market. Shanta Biotech (India) followed a different path by focusing on a single therapeutic area (Hep B) in which large cost efficiencies could be achieved in the initial years by expanding production (Chakma et al, 2011).

Other companies that emerged to compete globally have similarly found different ways to survive and grow, but in general, two factors: push funding for product developments, and technology access have been instrumental in the growth of some of these companies. A good example is Biological E (India), which has been supported by the Gates Foundation for pentavalent capacity expansion. A closer look shows that other sources of funding have also been critical for the DCVMs. Panacea has financed its expansion from its other businesses and from private shareholders (which includes SII). Shanta Biotech was financed and eventually purchased by Sanofi. Bio Farma (Indonesia) is a parastatal company with support from the Indonesian Government, like Brazil's Biomanguinhos and Senegal's Institute Pasteur de Dakar. Korean vaccine companies are significantly different in this respect. Being part of large conglomerates, they are able to lean on the other divisions of the company during the investment periods, and have different risk diversification strategies.

In this process, commonly acknowledged factors – such as demand forecasting and financial incentives, as well as technical assistance for quality production *work more closely with other important structural incentives*, such as lifecycle and steady demand, steady financing for production expansion, technology sharing and product development partnerships to create long-lasting shaping influences by:

- (a) offering new opportunities to incrementally increase profitability,
- (b) paving the way for market disruptions of existing markets with one or a few suppliers (by expanding newcomer entry, particularly through R&D and push funding), and

(c) creating the basis for more broad-based market transformation (where the demand guarantees through Gavi help companies to increasingly penetrate markets outside of Gavi processes, through country-specific purchases).

The differences in the theory of change relate to how far-reaching the instruments are in addressing the underlying issues in the vaccines market (Table 2 illustratively provides three examples).

Table 2: Illustrating market shaping influences of different instruments

Instrument	Theory of Change	Benefits
Pooled procurement	Aggregates demand. Reduces transaction costs in purchases. Increases market information	Greater accuracy offers incentives for investment. Suppliers can compete on volume and achieve economies of scale.
Push funding	Acts on increased market information, and supplier identification to build capacity.	Suppliers can compete on volume and achieve economies of scale. New entrants.
Technology transfer or vaccine development partnerships.	Reduces transaction and production costs. Incentivizes suppliers to invest more into vaccine production.	Leads to greater investment. More competition. Lower prices. Might also lead to R&D.

Source: Author.

V. What Next: Market Access and Market Shaping Concerns for the Future

COVID-19 has transformed the global vaccines' market significantly. Active governmental and international support toward financial and market guarantees has created a promising environment for private companies to make large scale investments into other experimental technology platforms. Estimates suggest that the global vaccines market has grown more than 250 per cent in terms of volume, and 550 per cent in terms of value in 2021 when compared to what it was in 2018 (Gehl Sampath and Pearman, 2021). This, coupled with the fact that the perceived value of vaccines (not just for COVID-19, but also for other diseases including future pandemics) has never been higher than it is now for both consumers and policy makers, should be expected to lead to a steady expansion of vaccines R&D and production in large companies, and steady entry of new vaccine candidates.

Against this backdrop, expanded market shaping activities across the vaccine supply chain – through initiatives such as the COVAX Market Place recently launched by CEPI¹⁵ – offers immense possibilities to expand the market, and increase the entry of new players across entire supply chains. At the same time, several challenges abound, calling for a closer look at market access and market shaping in the future. Some of these challenges, as this final section highlights, arise directly from the dynamics of the vaccine sector itself, and some others, are the outcome of contrasting policy interventions.

¹⁵ https://cepi.net/news_cepi/cepi-launches-covax-marketplace-to-match-buyers-and-sellers-of-critical-manufacturing-supplies-and-speed-up-global-access-to-covid-19-vaccines-through-covax/

1. The Challenge of Market Shaping with First-Mover advantages in Vaccine R&D

Vaccines, across different categories, tend toward even more supply concentration in the presence of R&D. Once again, table 1 shows the difficulty in R&D intensive vaccine categories such as HPV. In these categories, a core focus of Gavi's market shaping has been to facilitate product introductions in LMIC markets and negotiate reduced prices. As a result, although tiered pricing by Gavi has brought down the price to 4.55 USD for supply in Gavi-eligible countries, only two suppliers continue to exist for HPV supply even after ten years. Supply of HPV is far below the overall demand for the vaccine in LMICs (Gavi, 2018)¹⁶ and new companies have found it hard to enter the market due to existing patent protection (Chandrashekar et al, 2015).¹⁷ Market foreclosure – a commonly observed flipside effect of tiered pricing in some markets where one or two companies become sole suppliers globally, expanding their presence and market power at the expense of new market entrants, remains a real concern in such instances.

Current dynamics with the mRNA vaccine, where Sanofi recently pivoted its mRNA candidate out of the 'crowded' COVID-19 vaccine market, toward other markets where promising market entry can be made, underscores this point further.¹⁸ This is not to say that other companies will not invest in mRNA vaccines for COVID-19, but that there is need to consider the role of market access in a more rigorous way. Clover Pharmaceuticals, for instance, which also has a mRNA vaccine in the making, should be expected to enter the market relying on its ability to also access the Chinese national market.

Building on the lessons emerging from Gavi's experience comprehensively, and taking into account the structural issues identified in this paper, it remains critical that market shaping strategies in a post-COVID world employ a wider range of instruments. This would imply, in general, an expansion of market shaping from price and supply based indicators, to more dynamic market shaping instruments in different combinations for established and new companies. For established companies, market shaping for the future will have to include a strong focus on market access to secure new entrants at the global level across all categories. Promoting new firms from other regions will also call for mediated technology transfer (especially for proprietary vaccines and related products), and a more broad-based push funding that goes beyond the more programmatic and narrowly focused approaches of the past.¹⁹ Figure 3 below tries to map these across the continuum of vaccine innovation, production, and distribution, highlighting their relevance.

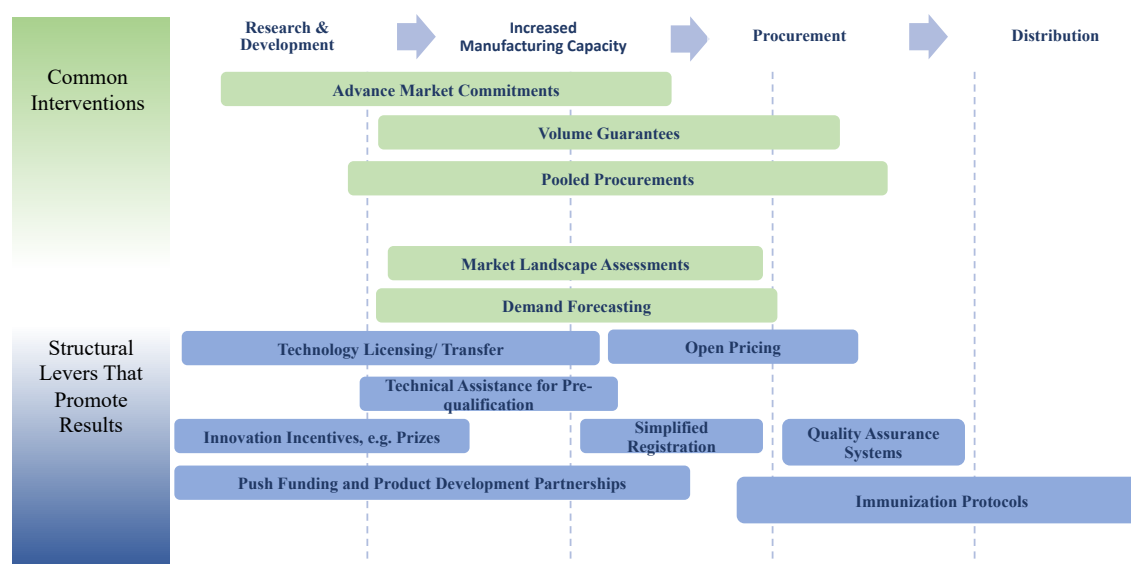
¹⁶ The US CDC prices are at USD 178 per dose for a HPV for cervical cancer prevention as opposed to 4.55 USD for HPV procured by UNICEF for supply to Gavi-eligible countries (WHO, 2019).

¹⁷ Gavi's current strategic period (2021–2025) forecasts that the supply situation for HPV is expected to improve with new manufacturers expected to enter the market, but other scholars note intellectual property as a major impediment for supply expansion (see Songane and Grossman, 2021).

¹⁸ <https://www.genengnews.com/news/sanofi-pivots-mrna-vaccine-program-from-covid-19-to-flu-pathogens/>

¹⁹ As a result, although three manufacturers from developing countries that have managed to break into vaccines R&D (Bharat Biotech's new rotavirus vaccine (Rotavac) and SII's new rotavirus vaccine (Rotasil) and pneumococcal vaccine (Pneumosil)), DCVMs have not had the ability to invest into R&D in a more broad-based way until recently.

Figure 3: Structural Levers to Shape Markets



Source: Author, based on USAID (2014).

2. Aligning Price and Value of COVID-19 Vaccines

In the past, all new suppliers of vaccines in market shaping efforts have produced almost perfect substitutes of the same vaccine. Hence, there have been no issues in aligning price and quality. The COVID-19 vaccines market, however, does not share this characteristic. So although from a market expansion perspective, the market shaping effort has been to increase the entry of as many vaccine suppliers into the procurement ambit as possible including through the COVAX Facility, from an epidemiological perspective, all vaccines – existing and new ones – are not perfect substitutes. This poses new challenges of aligning price and value in market shaping efforts. Epidemiologically, a vaccine with 60% efficacy is different from one with 90% efficacy. Other characteristics, such as cold chain requirements and dosage (single versus two doses), and ease of reproduction in other regional sites, are important for negotiating price and engaging in market shaping. These are not yet accounted into bargaining metrics and call for new approaches to think about market shaping in the future.

3. Expanding Market Access to COVID-19 Companies Along the Supply Chain

Another significant hurdle in leveraging the demand for COVID-19 vaccines to expand market access. A key issue, and a larger part of the puzzle that remains unaddressed currently, is the market forecast for COVID-19 vaccines. Current production projections available until end of 2022 peg production at over 10 billion doses (Taylor et al, 2021) with the likelihood that supply will exceed demand by then. Additionally, a volatile market that has multiple new entries forecasted, and a two-year campaign mode for procurement, and a lack of information on how the demand curve for COVID-19 vaccines will look like in a steady state beyond 2022, increases the financial risks for investments by new companies, and also raises the important issue of sequencing supply expansion and local production initiatives for COVID-19 vaccines.

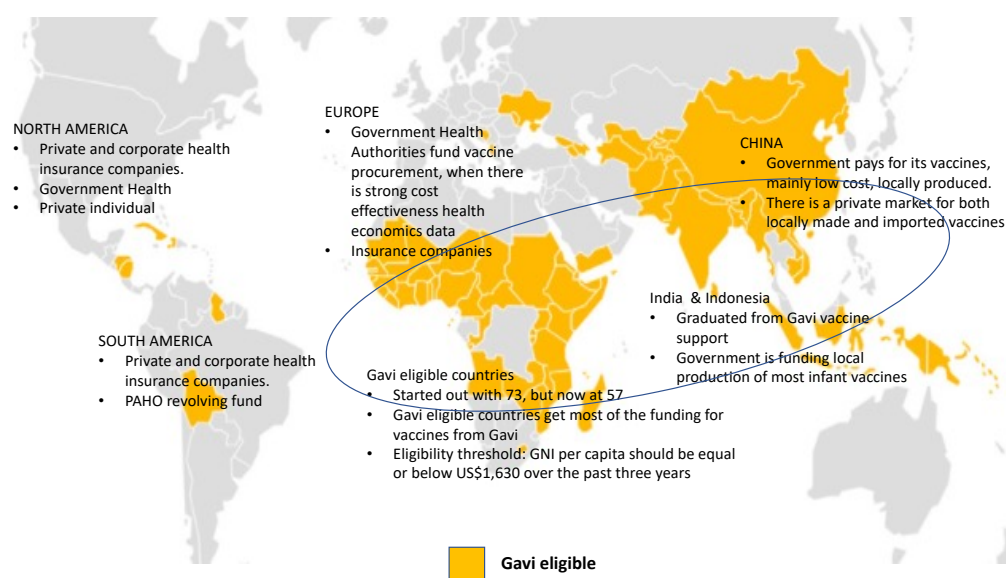
That is, given the short timelines for COVID-19 vaccines' demand as we know it currently, an important issue will be to ensure coordination between supply expansion by large firms, and ongoing efforts to boost local production of COVID-19 vaccines. One way to diversify risk would be to diversify and build production capacity in a way that it can easily be used beyond

COVID-19 to safeguard a new cohort of producers against the risk of entering a saturated market.²⁰ A second question is how to shape markets effectively for the future, looking beyond supplies for COVID-19 vaccines, to promote vaccines access in all categories.

4. Guarding Against Political Risks: Retaining and Strengthening Pooled Procurement

When Gavi started out, 73 countries were fully eligible for its support. But since 2007, Gavi has been operating on a “co-financing” policy that works in four stages – initial self-financing, preparatory transition, accelerated transition and fully self-financing – and guided by the GNI per capita status of countries.²¹ In the initial self-financing, countries share a small proportion of the share of the vaccines (0.20 cents per dose increasing to 15% of the cost and beyond) provided (to UNICEF) each year.²² Broadly speaking, as countries develop and their GNI per capita increases, they enter a transition phase in Gavi, when over a set 5-year term, their share of the co-payment increases up to 100% of the cost for the vaccine. After this period, the country is responsible for payments for the vaccine.²³ Today there are 16 countries which have completely transitioned from vaccine support, and another group of 8 countries are in the accelerated transition phase (see Figure 4). Low-income countries with GNI per capita below US\$995 as of 2019 qualify for initial self-financing and continue to get most of the funding from Gavi for their vaccines. In the event that new vaccines are introduced in new categories such as Dengue and Malaria, these countries are automatically eligible for access. The fully transitioned countries, and others in accelerated transition, are likely to get tailor-made support specifically designed for these new vaccines as well.²⁴

Figure 4: Pooled Procurement as a Market Shaping Incentive



Source: Author.

²⁰ For a detailed discussion of how this could be facilitated see Gehl Sampath and Pearman (2021).

²¹ Based on World Bank Data.

²² For Gavi purposes, low-income countries with a GNI per capita below US\$ 995 in 2019 are classified as initial self-financing.

²³ For details of preparatory transition and accelerated transition see: <https://www.gavi.org/programmes-impact/programmatic-policies/co-financing-policy>; <https://www.gavi.org/vaccineswork/how-gavis-co-financing-model-works>

²⁴ The co-financing policy is not applied to the IPV vaccine which is part of the Global Polio Eradication (GPEI) program, and not to Ebola – which is an epidemic, and also to COVID-19 vaccines for the 92 AMC-eligible countries.

In the coming years, the 57 Gavi-eligible countries – particularly those in Africa – will continue to offer a significant market for producers in the coming years (see figure 4). But recent discussions on creating markets for locally produced vaccines have tended to hanker on using demand in countries transitioning out of Gavi as a means to pool procurement at the regional or national level.

Such a proposal carries some risks. First, it overlooks the fact that almost all countries that have transitioned out of Gavi support continue to procure the vaccines which were introduced with Gavi support at Gavi negotiated prices, including through the PAHO Revolving Fund.²⁵ Gavi also has specific post transition engagement policies to engage with countries post-transition.²⁶ Many countries, such as India, Nigeria and Papua New Guinea, that do not fit Gavi's GNI per capita thresholds continue to have tailored strategies for engagement with Gavi for vaccine supplies and health systems strengthening. Second, these engagements have a symbiotic dimension. On the one hand, Gavi still offers valuable support to countries beyond the Gavi 57 aimed at meeting global immunization goals. On the other, the inclusion of these countries into Gavi's demand forecasts strengthens Gavi's negotiating power by expanding markets for those products in a wider range of countries than those that Gavi primarily funds. Separating these markets for vaccine procurement (even for some vaccines), therefore, can end up balkanizing the pooled procurement processes and thus weaken some of Gavi's power to negotiate prices of vaccines from producers by reducing the total demand that Gavi caters to. At the same time, if regional or national procurement is sliced too thin (too many countries negotiating individually), it could lead to intransparent pricing with no wins for anyone at all.

A better way to facilitate the entry of new producers might be to assess and slice markets not by procurement alone, but by vaccine category and forecasted demand. There is intense price-based competition in existing vaccine categories that are being sourced by large DCVMs, such as SII, Panacea Biotech, Bharat Biotech, among others. These companies focus on the needs of birth cohorts globally, and intrinsically, such vaccines have a one-time requirement (or limited dosage demand), and do not need to be administered repetitively. Targeting such a market from a production perspective, even beyond COVID-19 will be difficult particularly for African producers, given the advantages of incumbent firms in those vaccine categories. To introduce new suppliers in these categories, an option would be to work within Gavi's current pooling capacity to market shape with supply for countries that have transitioned out of Gavi, or will transition out of Gavi in the coming years, but to do so in conjunction with specific incentives/ sourcing quotas for vaccines produced from new suppliers in certain regions (especially Africa).

To be clear, to facilitate the entry of newcomers, new manufacturers particularly from Africa could be given secure market access that is based not just on the 'cheapest cost' calculations but includes a '*price incentive*' that enables them to compete in global markets in the initial years of production. Such price incentives might need to be calculated for each vaccine in question, based on a combination of price and supply diversity metrics, and also be accompanied by pricing benchmarks (that offer some stability to newcomers in the initial phase only, but do so without shifting the costs of production to consumers in the long run). Arguably, such a change in procurement guidelines at Gavi and UNICEF more generally could also help new firms supply to some extent even in the birth cohort vaccine categories offering them some space to settle into the market before they diversify to other categories.²⁷

²⁵ <https://www.paho.org/en/revolvingfund>

²⁶ <https://www.gavi.org/types-support/sustainability/transition>

²⁷ Such a price incentive is now often provided by national policy makers, where the enhanced use of quotas for local producers is becoming increasingly visible. In the Russian Federation, for example, preferences can be given to locally produced finished dosage forms for pharmaceutical production through the government procurement system. See for example, Resolution 1289 (Nov 30, 2015) of the Russian Federation, which

Even now, the transition of countries out of Gavi eligibility can create the fluctuations in Gavi's total vaccine funding each year. When countries lose their eligibility for Gavi funding, a way to maintain levels is to approve the introductions of new vaccines through Gavi, so that the overall purchasing power remains constant and can be leveraged for negotiating and intervening in the interest of secure supplies. This option – of expanding the vaccines introduced through Gavi - could be reinforced more categorically if pooled procurement mechanisms are considered more widely at the national/ regional level to facilitate the entry of local producers. This would retain overall funding to Gavi and to maintain Gavi's capacity to continue to market shape with national and regional actors globally by introducing new vaccines into immunization protocols in Gavi-eligible countries.

5. Enlarging the Size of the Market Pie: Market Shaping by Expanding Markets

Another important market shaping objective, particularly in light of current uncertainty related to the demand for COVID-19 vaccines post-2022 and the relatively well-supplied market for birth cohort vaccines, should be to find ways to expand the overall market to promote the entry of new suppliers in other vaccine categories. This can be done in two ways. First, the increased investment into new technology platforms can be creatively linked with demand pooling in new categories, such as for Malaria vaccine. Such demand facilitation focused on epidemiological profiles in certain regions such as Africa, Latin America and Asia for which vaccine development has been slow and neglected can also help open up markets. Especially relevant here are diseases such as Dengue, Zika, Chikungunya, West Nile Virus and River Blindness. Signaling some of these as priorities for future immunization protocols could pave the way for the private sector to refocus their vaccines R&D activities in this direction, thus expanding the size of the total global vaccines market and, possibly, paving the way for new entrants.

Second, the emphasis of market shaping for new and emerging companies in new regions of the global South could be explicitly placed on vaccine categories that offer opportunities. The predominant focus for new suppliers in the DCVMN category has been the pediatric market. While being large in volume (81%), the pediatric market accounts for only 29% of the total sales value globally (Gehl Sampath and Pearman, 2021). Other vaccine categories, such as joint pediatric and adult vaccines (e.g., influenza) or mainly adult vaccines still account for a large share of the global market in value. New companies seeking to enter the market from Africa, for instance, could build on a combination of vaccines in these categories to secure some operating space.

VI. Concluding Remarks

This paper has looked at market access and market shaping in the interest of public health in a post-COVID world. It has conducted a case study of Gavi market shaping (presented in a snapshot over 20 years) highlighting its successes by: (i) introducing new vaccines in Gavi-eligible countries successively, (ii) expanding the number of suppliers, and (iii) bringing down prices in some categories. Looking closely at how these successes were facilitated, the paper has identified a number of 'behind-the-scenes' factors that helped Gavi achieve these successes in different vaccine categories.

In its second part, the paper has presented the lessons learned through these experiences, highlighting ways in which these learnings can be used to address the opportunities and challenges for market access and market shaping in the future. Finding that some of these

provides what is widely known as the “three is a crowd” approach. In this case, discussions should focus on how to systemically factor this into procurement of vaccines at the national, regional and international levels.

challenges arise directly from the dynamics of the vaccine sector itself, while some others are the outcome of contrasting policy interventions, the paper advocates a more integrated approach to local production, pricing, procurement and competition given the inter-related workings of many of these incentives. Acknowledging that such market shaping will also require closer monitoring of progress (in terms of greater access) across different vaccine categories, the paper calls for working closely with more actors in the field including regional agencies and national governments in Africa. The findings suggest that a discussion of how to enable such a wider, more structural approach to market shaping with Gavi's active involvement and coordination with other partners, might be necessary.

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