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Economic Perspectives On The Advance Market Commitment For Pneumococcal Vaccines

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ABSTRACT Pharmaceutical companies have long been reluctant to invest in producing new vaccines for the developing world because they have little prospect of earning an attractive return. One way to stimulate such investment is the use of an advance market commitment, an innovative financing program that guarantees manufacturers a long-term market. Under this arrangement, international donors pay a premium for initial doses sold to developing countries. In exchange, companies agree to continue supplying the vaccine over the longer term at more sustainable prices. This article provides a preliminary economic analysis of a pilot advance market commitment program for pneumococcal vaccines, explaining the principles behind the program's design and assessing its early performance. Spurred by the advance market commitment—and other contemporaneous initiatives that also increased resources to vaccine suppliers—new, second-generation pneumococcal vaccines have experienced a much more rapid rollout in developing countries than older first-generation vaccines.

The GAVI Alliance—a partnership formed in 2000 by governments, nongovernmental organizations, foundations, and vaccine manufacturers that was formerly known as the Global Alliance for Vaccines and Immunization—supports immunization programs in more than seventy countries (to be eligible for assistance from GAVI, a country must have an annual per capita national income of less than $1,500). GAVI consolidates funds from public- and private-sector donors in industrialized countries; then, as procurement agents for GAVI, the World Health Organization and UNICEF purchase vaccines for developing countries with the funding. The prices that these organizations pay for the vaccines are a fraction of the prices charged in industrialized countries—often not much more than production costs.

GAVI, the World Health Organization, and UNICEF have greatly increased access to traditional vaccines in developing countries. However, they have been less successful in inducing manufacturers to build sufficient capacity to supply new vaccines to poorer countries as quickly as these vaccines are rolled out in industrialized countries.

The organizations have also had less success in providing pharmaceutical companies with incentives to develop new vaccines for diseases such as malaria and yellow fever, most of whose victims live in developing countries. Manufacturers need to be able to price vaccines and other drugs high enough so they can recoup not just their production costs, but also their investments in capacity and in research and development, which could amount to hundreds of millions of dollars for a new vaccine.

The so-called advance market commitment is an approach that is designed to address this pricing problem.[1] The commitment is a long-term agreement between donors—such as GAVI's pub-

lic- and private-sector funders—and a manufacturer, in which the donors pay a premium above the incremental production cost—the manufacturer's cost of producing one additional unit of the product. This premium gives the manufacturer an economic incentive to invest in producing the product.

In this article we provide a preliminary economic analysis of a pilot advance market commitment, announced in 2007 for pneumococcal vaccines. In a conceptual analysis, we construct an economic model in which the pneumococcal vaccine is supplied by manufacturers whose sole goal is to maximize their profits. A detailed description of this model appears in the online Appendix.[2] We use this model to simulate vaccine supply under various designs for the advance market commitment program. We also include an empirical analysis that provides a preliminary assessment of the pilot program. We compare the rollout of the pneumococcal vaccines supported by the program in countries eligible for GAVI's assistance to the rollout of earlier-generation pneumococcal vaccines, which received much less support from donors.

First we provide some background on the history of the pilot program.

The Pneumococcal Vaccine Advance Market Commitment Program

MILESTONES IN THE PROGRAM'S HISTORY In 2003 the Center for Global Development convened a working group to explore the merits of advance market commitments and to consider design details for a pilot program.[3] Initial interest in the commitments had focused on creating incentives for research and development for malaria vaccines. For two reasons—the severity of the disease, and the potential to see rapid results from the program—the focus shifted to pneumococcal vaccines that were already in the late stages of development. Pneumococcal disease is the leading killer of young children worldwide that is preventable by vaccines. According to recent estimates, each year the disease is responsible for the deaths of more than 800,000 children under age five, with over 80 percent of the deaths occurring in countries eligible for assistance from GAVI.[4,5]

A vaccine protecting children against seven strains of pneumococcal disease had already been launched in the developed world. This vaccine, known as PCV-7 or Prevnar, was originally manufactured by Wyeth.

When the working group convened, two second-generation vaccines—one from GlaxoSmithKline that protected against ten strains of the disease (called PCV-10 or Synflorix) and one from Wyeth protecting against thirteen strains (PCV-13 or Prevnar-13)—were in late stages of development. Each of these vaccines covered strains that are relatively rare in industrialized countries and that are beyond the seven strains covered by Prevnar-7. However, these other strains are responsible for 12–25 percent of serious pneumococcal infections in poor countries.

Given the status of these second-generation vaccines, the working group believed that it would be possible to use them as a test case of the advance market commitment, both accelerating their production for the developing world and quickly demonstrating the feasibility of the approach.[3] In February 2007 the Bill & Melinda Gates Foundation and the governments of Canada, Italy, Norway, Russia, and the United Kingdom collectively pledged $1.5 billion for a pilot pneumococcal commitment program (all monetary figures are in US dollars, not adjusted for inflation). In March 2009 GlaxoSmithKline received approval from the European Medicines Agency, the European counterpart of the US Food and Drug Administration, to sell PCV-10. Soon afterward the company opened a $411 million plant in Singapore with the capacity to produce 300 million doses annually.[6] That same month Wyeth applied to the US Food and Drug Administration for a license to sell PCV-13.[7]

In October 2009 GlaxoSmithKline, Pfizer (which by then had acquired Wyeth), the Serum Institute of India, and Panacea Biotech filed expressions of interest with the advance market commitment program—meaning they expressed a desire to participate in such an arrangement on a nonbinding basis. GAVI used its forecasts of demand for pneumococcal vaccines to set a goal of obtaining and providing 200 million doses of the vaccines annually by 2015.[8]

In March 2010 GlaxoSmithKline and Pfizer each agreed to supply thirty million doses of their second-generation pneumococcal vaccines annually for ten years through the advance market commitment, starting in 2013.[8] Since each supplier's commitment was 15 percent of GAVI's 200 million-dose target, GlaxoSmithKline and Pfizer were each allocated 15 percent ($225 million) of the $1.5 billion fund. In addition, the companies agreed to provide collectively seven million doses in 2010, twenty-four million in 2011, and twenty million in 2012 to countries eligible for GAVI's assistance. Exhibit 1 provides data on the approved shipments and introductions of second-generation pneumococcal vaccines to countries eligible for assistance from GAVI. As of September 2010, nineteen countries had been approved to receive PCV-10 or PCV-13.

FUNDING STRUCTURE

▶ **SOURCES OF FUNDS:** Exhibit 2 shows an

EXHIBIT 1

Scheduled Shipments And Introductions Of Second-Generation Pneumococcal Vaccines To Countries Eligible For GAVI Assistance

			Number of doses approved for shipment in		
Country	Vaccine	First shipment	2010	2011	Status of introduction
Kenya	PCV-10	Sep. 2010	1,200,000	5,874,700	Introduced Jan. 2011
Sierra Leone	PCV-13	Oct. 2010	388,800	388,200	Introduced Jan. 2011
Nicaragua	PCV-13	Nov. 2010	149,400	538,200	Introduced Dec. 2010
Yemen	PCV-13	Nov. 2010	970,650	2,395,800	Introduced Jan. 2011
Guyana	PCV-13	Dec. 2010	19,800	33,300	Introduced Jan. 2011
Honduras	PCV-13	Dec. 2010	199,800	651,500	Introduced Apr. 2011
Dem. Rep. Congo	PCV-13	Feb. 2011		5,409,300	Introduced Apr. 2011
Gambia	PCV-13	Feb. 2011		174,700	Switch from donation
Mali	PCV-13	Mar. 2011		2,062,800	Introduced Mar. 2011
Cameroon	PCV-13	Apr. 2011		1,542,300	Expected Jul. 2011
Central African Rep.	PCV-13	Apr. 2011		302,400	Expected Jul. 2011
Rwanda	PCV-13	May 2011		1,002,600	Switch from donation
Rep. Congo	PCV-13	Oct. 2011		309,600	Expected Jan. 2012
Benin	PCV-13	TBC		TBC	Expected Jul. 2011
Burundi	PCV-13	TBC		TBC	Expected Jul. 2011
Ethiopia	PCV-10	TBC		TBC	Expected Sep. 2011
Malawi	PCV-13	TBC		TBC	Expected Oct. 2011
Madagascar	TBC	TBC		TBC	TBC
Pakistan	TBC	TBC		TBC	TBC

SOURCES Authors' communications with GAVI staff. UNICEF. GAVI/VF shipments [Internet]. New York (NY): UNICEF; [cited 2011 Apr 29]. Available from: http://www.unicef.org/supply/index_gavi.html. **NOTES** "Switch from donation" means the country received donated vaccine through a different program before being supplied through the Advance Market Commitment Program. TBC means to be confirmed.

example of the program's final funding structure. The example assumes that there will be demand for all thirty million doses that GlaxoSmithKline agreed to supply of its second-generation vaccine annually over the ten-year period. After tapping its entire allotted subsidy from the Advance Market Commitment Program at the end of 2014, the manufacturer is guaranteed not $7.00 per dose, but $3.50 for the remaining eight years.

The later price, called the "tail price," is intended to cover incremental production costs. The initial "topped-up" price is meant to give the manufacturer extra revenue, to recoup some of the fixed costs of research and development, and of constructing manufacturing capacity.

▶ **RISK:** The agreements with the Advance Market Commitment Program obligate manufacturers to supply whatever amount is demanded up to the supply commitment (in the GlaxoSmithKline example in Exhibit 1, thirty million doses annually for ten years). In contrast, GAVI has the option, but not the obligation, to purchase any amount up to that supply commitment. Manufacturers therefore bear substantial risk if the forecasted demand does not materialize.

This risk is tied to the inherent difficulties in predicting the demand in countries eligible for assistance from GAVI, as well as the uncertainty over whether GAVI will have sufficient donor funds to sustain its contribution. To offset the risk in this case, UNICEF—GAVI's procurement agent—agreed to purchase a minimum of 20 percent of GlaxoSmithKline's committed supply in the first year, 15 percent in the second, and 10 percent in the third, regardless of whether demand materializes in those years.[8]

▶ **RESERVE FOR FUTURE SUPPLY REQUISITIONS:** With only 30 percent of the $1.5 billion fund allocated to the two participating manufacturers so far, 70 percent remains in reserve. The reserve funds can be used to obtain commitments from the participating manufacturers or new suppliers to meet more of GAVI's target of 200 million doses in future years.

Design Principles Of The Program

We turn to an economic analysis of various program design features—including the fund size and the tail price—to investigate how important each feature is to the overall performance of the advance commitment program. We employ an

economic model calibrated to the market for pneumococcal vaccines in countries eligible for GAVI assistance (a detailed presentation of the economic model is provided in the online Appendix).[2] Our goal is not to provide an exact calibration but to use round numbers to illustrate the underlying principles and trade-offs of the commitment program.[9]

The notes to Exhibit 3 list the specific numerical values assumed in the analysis. Values were set to reflect the actual program terms where possible, but two require further consideration. First is the monetary value on the health benefits from a dose of the vaccine administered in countries eligible for GAVI assistance. Based on a study of the cost-effectiveness of the pneumococcal vaccine in African trials and on the thresholds that donors use to judge highly cost-effective projects, we set this health benefit to $8.50 per dose.[10–12]

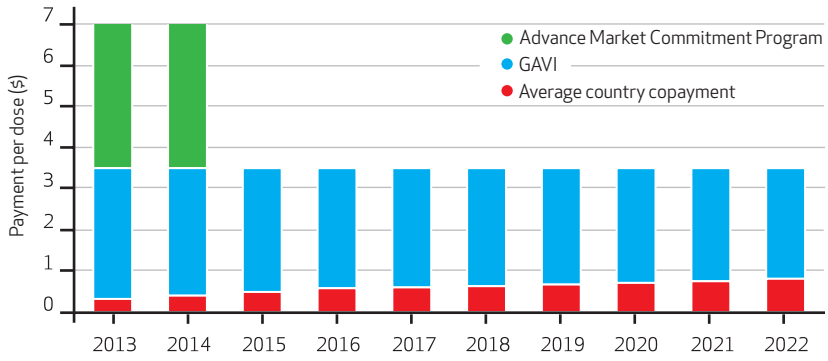
Second is the supplier's fixed cost of installing a unit of capacity. This fixed cost includes the cost of constructing a factory (about $1.40 per dose for GlaxoSmithKline's Singapore facility). It can also include a loss of bargaining power vis-à-vis higher-income countries entailed by excess capacity. The loss of revenue from these higher-income markets could dwarf construction costs. We assumed fixed costs were $4 per unit, but we performed a sensitivity analysis around this and the assumed value of health benefits.

BENCHMARK SCENARIO Our benchmark scenario assumed some of the same terms as the Pneumococcal Vaccine Advance Market Commitment Program used: a subsidy fund of $1.5 billion; a tail price of $3.50 per dose and an upfront subsidy from the program of another $3.50; demand for 200 million doses annually; and a program length of ten years. It also assumed that a single firm participated in the advance market commitment—instead of the two actual participants—and supplied the number of doses that would maximize its profit stream (revenue minus cost, discounted to reflect interest rates). Exhibit 3 shows that, given these assumptions, the manufacturer would supply the entire 200 million doses annually. The net social benefit in the benchmark scenario is $9.1 billion, a figure computed by adding up the dollar value of the health benefits from all vaccine doses supplied over the duration of the program, subtracting all payments to manufacturers (the subsidy and the tail price), and discounting to reflect interest rates.

This benchmark result differs from the experience to date with the pneumococcal vaccine pilot program. The two manufacturers so far have agreed to supply only 30 percent of the target 200 million doses annually. We have been unable to ascertain whether the manufacturers, GAVI, or both balked at committing to make more doses available. It is possible that a larger supply of vaccines would have been forthcoming had GAVI requested it. GAVI may have considered this smaller commitment level to be suitable for demands based on current forecasting, or it may have faced uncertainty regarding future donor funding.[8] Future requisitions from GAVI may provide more evidence on how much supply an advance market commitment can generate.

EXHIBIT 2

Pneumococcal Vaccine Advance Market Commitment Program Financing Structure For GlaxoSmithKline's Second-Generation Vaccine



SOURCES Advance Market Commitment Program and GAVI contributions from Note 8 in text. Country copayment policies from Note 16 in text. Classification of countries into three GAVI categories from GAVI Alliance. Board meeting, 30 November–1 December 2010: doc #11.d, cofinancing policy revision [Internet]. Geneva: GAVI Alliance Secretariat; 2010 Nov 12 [cited 2011 Apr 29]. Available from: http://www.gavialliance.org/resources/DOC_11d_Co_financing_Policy_Revisions.pdf. **NOTES** GlaxoSmithKline's guaranteed price of $7.00 per dose for the first two years consists of $3.50 from the Advance Market Commitment Program; copayments from countries eligible for GAVI assistance; and GAVI funds to make up the difference. The average country copayment is a weighted average of the GAVI copayment levels for the three classes of eligible countries: low-income countries, which pay $0.20 per dose; intermediate-income countries, which pay $0.20 per dose plus a 15 percent increase each year; and graduating countries, which pay a linearly increasing amount over time, reaching $3.50 after five years. Weights are based on the number of people under age fourteen in each group of countries.

SUBSIDY CAP One feature of the advance market commitment was not part of the original design but was added later on the recommendation of the Economics Expert Group, a body of economists and experts from other fields asked to study the economic issues involved in implementing the Pneumococcal Vaccine Advance Market Commitment Program.[13] The group recommended capping the subsidy available to any one manufacturer. The cap was tied to the percentage of the program target that the manufacturer committed to supply. For example, if a manufacturer committed to supply 15 percent of the target of 200 million doses (30 million doses annually), it could earn no more than 15 percent of the $1.5 billion fund ($225 million over the duration of the program). There was no cap in the original design; thus, a single manufacturer could receive the entire $1.5 billion

EXHIBIT 3

Economic Analyses Of The Advance Market Commitment Model

Analysis	Cap on subsidy		No cap on subsidy	
	Quantity (millions of doses/year)	Net social benefit[a] (billions of dollars)	Quantity (millions of doses/year)	Net social benefit[a] (billions of dollars)
SCENARIO				
Benchmark	200	9.1	55	1.7
Competition				
Two manufacturers	200	9.1	187	8.5
Three manufacturers	200	9.1	200	9.1
Cost uncertainty				
Benchmark tail price ($3.50)	164	7.5	85	2.8
Increased tail price ($3.75)	200	8.7	114	4.5
Demand uncertainty	0	0.0	37	0.4
SENSITIVITY ANALYSES				
Fixed costs increased to $10[b]	0	0.0	32	0.8
Fixed costs reduced to $2[b]	200	9.1	81	3.1
Health benefit increased to $20[c]	200	33.4	55	8.4
Health benefit reduced to $5[c]	200	1.7	55	−0.4

SOURCE Authors' calculations. **NOTES** The analyses are described in the text. In addition to the assumed values stated in the text, the interest rate is assumed to be 5 percent, and the lifespan of a manufacturing facility fifteen years. [a]Net social benefit adds the dollar value of health benefits over all vaccine doses, subtracting payments to manufacturers, and discounting to reflect interest rates. See the text for further details. [b]In other scenarios, fixed cost is $4 per dose. Fixed cost includes factory construction costs and possible bargaining costs discussed in the text. [c]In other scenarios, health benefit is $8.50 per dose. Note the distinction between the health benefit from a single vaccine dose and the marketwide sum of these benefits, embodied (along with other adjustments) in net social benefit.

fund, whether or not it met the full target.

Exhibit 3 shows that the lack of a cap in the original design might have weakened supply incentives. The benchmark scenario shows that removing the cap reduced both the annual supply and the social benefit. The manufacturer reduces the supply so dramatically when the cap is removed because it then saves on construction and other upfront costs but still receives the entire fund, just over a longer period of time.

COMPETITION SCENARIO The advance market commitment functions better with more competition among manufacturers (Exhibit 3). The increase in competition does not change the outcome when there is a subsidy cap, because in that case even a single manufacturer meets the target of 200 million doses annually. But it does change the supply and the social benefit in the absence of a cap. When there is no cap on what manufacturers can receive from the total subsidy fund, they compete with each other for a larger share.

An optimistic view of these results is that, if there is enough competition, advance market commitments appear to function quite well regardless of design details. Yet in the pilot program, policy makers ended up agonizing over design details. They feared that sufficient competition would not materialize: Few manufacturers had suitable products in the late stages of development, and the fear was that even fewer manufacturers—perhaps just one—had low enough costs to be a viable supplier.

COST UNCERTAINTY SCENARIO One difficulty in designing an advance market commitment for products in late stages of development, such as the second-generation vaccines in the Pneumococcal Vaccine Advance Market Commitment Program, is that suppliers may have more accurate estimates of costs than program designers do. The problem is particularly acute with pneumococcal vaccines because the complex technologies required to combine protection against multiple disease strains into a single dose entail a great amount of cost uncertainty.

Designing an advance market commitment when suppliers have private cost information involves a delicate balance.[14] Making the program's terms more generous increases the probability that manufacturers will participate and will produce a substantial amount of the desired

supply. But it also increases the overall cost of the program. Even the most carefully designed program may be spurned by all manufacturers if costs turn out to be much higher than expected. Conversely, if manufacturers do end up participating in such a program, they inevitably profit from it, and they receive more profit than the program would like if costs turn out to be much lower than expected. Neither of those outcomes is proof of a design flaw. Rather, they are natural consequences of a program designer's incomplete information about costs.

To gauge the role of cost uncertainty in the model, we assumed once again that there was only one manufacturer (Exhibit 3). Whereas in the scenarios described above, we assumed that each dose of vaccine cost $3.50 to make, in this case we assumed that only the manufacturer knew the precise cost, and that the program designer knew only that the cost was between $3.00 and $4.00.

Consider the commitment program with a subsidy cap. The supplier commits to supply the full target of 200 million doses annually for most cost realizations in the model. Only for costs in the high range ($3.80 or more) does a problem arise: The supplier then rejects the commitment and supplies nothing. But it is unlikely the supplier's costs would end up being that high, and so supply and net social benefit are still fairly high on average across the range of possible costs.

Instead of setting the tail price at the average value of unit cost ($3.50), setting a higher tail price raises net social benefits. Exhibit 3 shows the results from increasing the tail price to $3.75. This higher tail price induces the manufacturer to supply the whole 200 million doses annually even for the highest assumed costs. The health benefits from meeting the target number of doses even when costs are high more than compensates for the increased program expenditures, raising net social benefits from $7.5 to $8.7 billion.

It should be noted that although we have so far focused on advance market commitments for products in the late stages of development, advance market commitments were originally conceived for a different purpose: to provide incentives for research and development of new products. The problem of private cost information is less severe for products in these early stages because drug makers themselves face considerable uncertainty about the costs of products that are a long way from production. Nonetheless, advance market commitment programs will still need to provide a margin over production costs to induce manufacturers to undertake research, with higher margins generally inducing more research effort.[15]

DEMAND UNCERTAINTY SCENARIO Requiring countries to pay a copayment for vaccines serves several purposes. One of these is to ensure that new vaccines "meet the market test," meaning that they have attributes—such as covering particular strains of a disease—that are attractive to their end users. But copayments also have drawbacks, the most serious of which is that countries with small national health budgets may not take up a vaccine.

GAVI mitigates this drawback to some extent by tailoring countries' copayments to their per capita income.[16] But countries may have other reasons to resist introducing a new vaccine, such as a lack of understanding of the health benefits and risks, and the need to invest in clinical infrastructure—for example, cold storage for the vaccine. These barriers contribute to uncertainty regarding the demand for a vaccine. Our conversations with representatives of the pharmaceutical industry and nongovernmental organizations revealed that demand uncertainty was one of their chief concerns about program participation.

The demand uncertainty scenario in Exhibit 3 assumes that a demand for the full 200 million doses and a demand for no doses are equally likely. When there is a cap on the subsidy, manufacturers find committing to a supply of vaccine unprofitable, so no doses are available. Even when there is a cap, only 37 million doses are available annually. To compensate for this demand uncertainty, the total fund amount, tail price, or some other terms could be made more generous. An economic argument can be made for yet another alternative: a guarantee to purchase some of the committed supply regardless of what level of demand materializes.

Economic logic suggests that the party with the most control over an uncertain situation should insure other parties against risk, because the insurer will then exercise its control to mitigate the risk and reduce its costs. Given that the quality of vaccines in the late stages of development is already well established, the manufacturer can do little to affect demand. Rather, demand may depend more on investments by parties such as GAVI and donors to the Advance Market Commitment Program in facilitating rollout. This provides a rationale for these parties to include some form of purchase commitment in the program to insure manufacturers against demand fluctuations.[17]

As noted above, the pneumococcal pilot program included guarantees from UNICEF to purchase 20 percent of the supply for the first year, 15 percent for the second, and 10 percent for the third, even if sufficient demand did not materialize. In our model, these modest guarantees

were enough to overcome the demand uncertainty and induce the manufacturer to commit to producing the entire supply of 200 million doses annually (results not shown).

Perhaps the greatest source of demand uncertainty lies with GAVI's ability to meet its financial obligations under the program. To understand the magnitude of the problem, assume that manufacturers eventually commit to meet the target of 200 million doses annually for the full ten-year duration of the program. Based on Exhibit 2, one can show that GAVI would end up spending $6.3 billion—four times as much as the $1.5 billion that donors committed to the program, commonly mentioned as the program's level of funding.

The problem is inherent in advance market commitments for any complex vaccine involving high production costs. High tail prices are required to cover these production costs, which end up dwarfing other program expenses over the long run. Future programs could increase manufacturers' confidence in the availability of financing by setting aside funds to cover not just the subsidy but also the tail prices.

SENSITIVITY ANALYSES The lower rows of Exhibit 3 show that the main conclusions from the model held even when we used different numerical values. In most of our scenarios, the advance market commitment with a cap on the subsidy resulted in a supply of the full 200 million doses annually. However, if costs increase to a certain point, the manufacturer will deliver no doses. This happens, for example, when the assumed fixed cost of $4 per dose is increased to $10 (an admittedly extreme increase, putting fixed costs at roughly seven times the actual cost of GlaxoSmithKline's Singapore plant per dose).

The figure for the health benefit that we used in our analyses is $8.50 per dose. Changing the health benefit in the sensitivity analyses did not affect supply, but it did have a large effect on the social benefit of that supply. Reducing the health benefit to $5, a level near the $3.50 cost per dose, caused the program's net social benefit to essentially disappear, while increasing the health benefit led to an explosive increase in the net social benefit.

Evaluating The Pilot Program's Performance

The pilot program has not been operating long enough to permit a comprehensive assessment. We provide our preliminary impressions and offer suggestions for subsequent assessments when more data become available.[18]

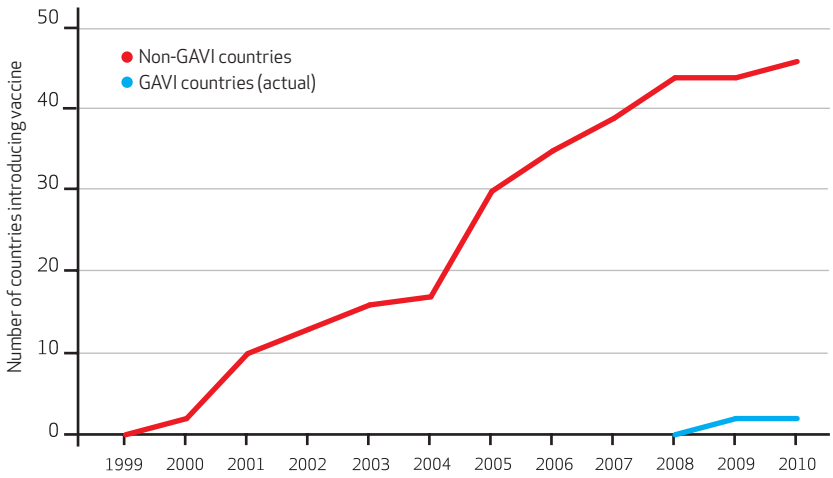
Judging whether the program has been a success requires choosing an appropriate standard for comparison. Did the advance market commitment result in faster and broader rollout of the second-generation vaccines than if no initiative had been undertaken? What if traditional procurement methods and resources had been employed? What if similar resources had been expended but typical procurement methods had been used?

Exhibits 4 and 5 provide one useful comparison, between the rollout of the first-generation PCV-7 and the rollouts of the second-generation PCV-10 and PCV-13 under the advance market commitment. The earlier rollout is an example of a complex vaccine introduced without the benefit of a well-endowed initiative. Exhibit 4 shows the nine-year lag between the introduction of PCV-7 in industrialized countries and its first introduction in a country eligible for GAVI assistance, as well as the widening gulf between the number of countries adopting the vaccine in the two groups.

Exhibit 5 presents a contrasting picture for the introduction of two vaccines under the pilot program of similar complexity to the first-generation vaccines. The lag between rollout in the two groups of countries was virtually eliminated, and the gap in the number of countries in the two groups that introduced the vaccines was reduced. (When we analyzed the quantities of vaccines shipped rather than number of countries to

EXHIBIT 4

Rollout Of First-Generation Pneumococcal Vaccine (PCV-7)



SOURCES Data on non-GAVI countries are from IMS Health. MIDAS. Danbury (CT): IMS Health; 2000–2010. Data on GAVI countries are from UNICEF. GAVI/VF shipments [Internet]. New York (NY): UNICEF; [cited 2011 Apr 29]. Available from: http://www.unicef.org/supply/index_gavi.html. **NOTES** GAVI countries are those eligible for GAVI assistance; non-GAVI countries are not eligible. The horizontal axis has been scaled to make Exhibits 4 and 5 comparable: They span the same number of years, starting with the year before the respective generation of vaccine was introduced. IMS Health data do not cover all vaccine distribution channels (such as clinics, hospitals, and pharmacies) for all countries, but coverage for PCV-10 and PCV-13 is similar to that for PCV-7, so results should be comparable across vaccine types.

introduce the vaccines, we saw similar results.) We cannot conclude that the advance market commitment alone accelerated the introduction of pneumococcal vaccines to countries eligible for assistance from GAVI because other programs with the same goal were initiated around the same time. But the initiatives collectively had a dramatic effect.

More difficult is to determine whether the advance market commitment had more effect than would have been the case if the same resources had gone to more traditional procurement channels. No previous experience is closely comparable to the pneumococcal pilot program. Some authors have suggested comparing the program to the introduction of Hib or rotavirus vaccines, for meningitis and diarrheal diseases, respectively.[18,19] Although this comparison provides useful insights, the introduction of a Hib vaccine may have been slowed by inadequate initial funding,[20] and the introduction of a rotavirus vaccine by a shift in funding priority and initial concerns about the vaccine's safety in developing countries.[21]

Conclusion

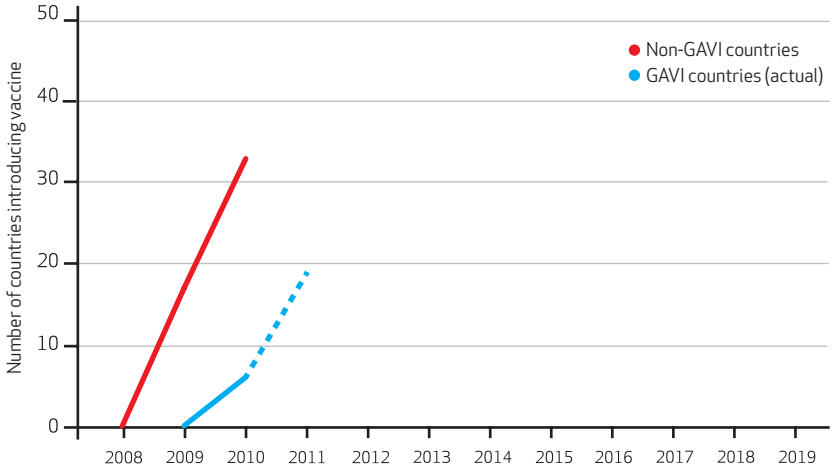
We analyzed an economic model of the supply of pneumococcal vaccines under the Pneumococcal Vaccine Advance Market Commitment Program. In a variety of numerical examples, we found that making the program's terms more generous, thereby increasing the supply of vaccines in developing countries, generated large social gains.

Compared to the experience with first-generation pneumococcal vaccines such as PCV-7, which was rolled out in those countries with no concentrated initiative such as the advance market commitment program, the rollout of second-generation vaccines has been rapid. However, it is not clear whether this change can be attributed to the use of an advance market commitment or simply to the level of resources involved.

The broader question addressed by the pilot program for pneumococcal vaccines was not whether suppliers would respond to an increase in market resources—basic economic principles tell us to expect that—but whether donors have the appetite for a new way of procuring vaccines although it involves a new set of challenges. So far it appears that donors do. ■

EXHIBIT 5

Rollout Of Second-Generation Pneumococcal Vaccines (PCV-10 And PCV-13)



SOURCES Data on non-GAVI countries are from IMS Health. MIDAS. Danbury (CT): IMS Health; 2000–2010. Data on GAVI countries are from UNICEF. GAVI/VF Shipments (various years) [Internet]. New York (NY): UNICEF; [cited 2011 Apr 29]. Available from: http://www.unicef.org/supply/index_gavi.html. **NOTES** GAVI countries are those eligible for GAVI assistance; non-GAVI countries are not eligible. The dotted part of the line for GAVI countries is a projection based on GAVI's approvals of future introductions of vaccines. The horizontal axis has been scaled to make Exhibits 4 and 5 comparable: They span the same number of years, starting with the year before the respective generation of vaccine was introduced. IMS Health data do not cover all vaccine distribution channels (such as clinics, hospitals, and pharmacies) for all countries, but coverage for PCV-10 and PCV-13 is similar to that for PCV-7, so results should be comparable across vaccine types.

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NOTES

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2 To access the Appendix, click on the Appendix link in the box to the right of the article online.

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9 A more detailed model and calibrations are provided in Kremer M, Levin J, Snyder C. Designing advanced market commitments for new vaccines. Paper presented at: International Industrial Organization Conference; 2009 Apr 4; Boston, MA.

10 Accounting for mortality benefits and some reduction in hospitalizations, vaccination with PCV-7 would have a cost-effectiveness ratio of $80 per disability-adjusted life-year, a standard measure of health benefits, assuming Gambian efficacy rates held across countries eligible for GAVI assistance. The assumed cost per dose was around $5.62 (adding the $5 price and the sixty-two-cent midpoint of the range of administration costs considered by the study). See Sinha A, Levine O, Knoll MD, Muhib F, Lieu TA. Cost-effectiveness of pneumococcal conjugate vaccination in the prevention of child mortality: an international economic analysis. Lancet. 2007; 369(9559):389–96.

11 To arrive at our final estimate of an $8.50 health benefit from a dose of the vaccine, two additional steps are needed, described in this note and in Note 12. First, if a vaccine that costs $5.62 generates a $80 per disability-adjusted life-year cost-effectiveness ratio, as the study in Note 10 found, then a vaccine generating a $100 per disability-adjusted life-year cost-effectiveness ratio must therefore cost $7.03. We can interpret the $7.03 as a donor's willingness to pay for the vaccine because this cost-effectiveness ratio is the threshold for highly cost-effective health interventions. See World Health Organization. World health report 2002: reducing risks, promoting healthy life. Geneva: WHO; 2002.

12 We scaled up the $7.03 willingness to pay by 1.2 times, to account for the greater coverage of PCV-13 relative to PCV-9 in countries eligible for GAVI assistance. The 1.2 coverage ratio is based on computations from GAVI Alliance, PneumoADIP. Pneumococcal global serotype project: summary report of stage 1/version 1 analysis [Internet]. Geneva: GAVI Alliance; 2007 Oct 18 [cited 2011 Jul 18]. Available from: http://www.preventpneumo.org/pdf/GSP_Summary_for_SAGE_Nov6-8_2007_Oct_19-07.pdf

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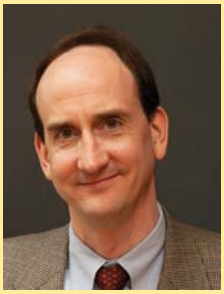

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In this issue of *Health Affairs*, Christopher Snyder, Wills Begor, and Ernst Berndt provide a preliminary economic analysis of a pilot advance market commitment for vaccines against pneumococcal disease, the leading vaccine-preventable killer of young children worldwide. They conclude that the advance market commitment, an innovative financing program that guarantees manufacturers a long-term market, was one of several initiatives that helped to spur rapid rollout of second-generation pneumococcal vaccines in developing countries, compared to the rollout of first-generation vaccines.

Snyder and Berndt have long studied the economics of vaccines and other pharmaceutical markets. They hope that their research can make the discussion and evaluation of advance market commitments "as informed and productive as possible," Snyder says. He characterizes the financing program as "one of the most important and novel global health initiatives ever taken."

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