

Advance Market Commitments: Insights from Theory and Experience[†]

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Ten years ago, donors committed \$1.5 billion to a pilot advance market commitment (AMC) to help purchase pneumococcal vaccine for low-income countries. The AMC aimed to encourage the development of such vaccines, ensure distribution to children in low-income countries, and pilot the AMC mechanism for possible future use. Three vaccines have been developed and more than 150 million children immunized, saving an estimated 700,000 lives. This paper reviews the economic logic behind AMCs, the experience with the pilot, and key issues for future AMCs.

I. Theory of AMCs

A. Technologically Distant Target

Kremer and Glennerster (2004) proposed AMCs to encourage research on vaccines against diseases such as malaria primarily affecting low-income countries and to promote access to these vaccines once developed. The AMC has donors pledge to top-up payments for newly introduced vaccines meeting technical benchmarks, conditional on the firm setting the price close to marginal cost.

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The AMC is designed to tackle static and dynamic distortions in the vaccine market. The price-cap feature of the AMC is designed to mitigate static deadweight loss from firms exercising market power. Donors' commitment to top-up price above marginal cost is designed to bolster dynamic R&D incentives, which are weak due to a number of factors, including limited purchasing power in low-income countries, free riding by the unvaccinated on the reduction in disease transmission, and political pressure to reduce price once a vaccine has been developed, causing a holdup problem.

AMCs' "pull" funding is meant to supplement, not replace, direct R&D support (i.e., "push" funding) while mitigating problems attendant with trying to pick winning projects ex ante under asymmetric information.

B. Technologically Close Target

The original AMC concept was translated into an actionable proposal in a Center for Global Development working group report (Levine, Kremer, and Albright 2005). The group suggested conducting AMCs for both technologically distant and technologically close targets. There are several important theoretical distinctions between these targets.

First, the further a vaccine is along its development path into clinical trials, the less R&D remains to be undertaken. The key challenge switches from incentivizing R&D to incentivizing adequate capacity to bring usage to socially efficient levels. Vaccine capacity is expensive. Whether to avoid holdup of the substantial capacity investment required (in a bargaining model) or to leverage monopsony power (in a price-theoretic model), a robust theoretical finding is that firms will tend to underinvest in capacity absent an AMC.

Second, the nature of the information asymmetry between firms and AMC funders may

change with technological distance. For a technologically distant vaccine, the funder may know little about the nature and viability of the technology, giving the researchers asymmetric information about its chance of success. For a technologically close vaccine, published clinical trials may inform the funder about the product's viability, closing that information gap. However, as the firm solidifies its production process, it may instead gain asymmetric information about its costs.

Third, product characteristics are more predictable and easily understood for technologically close products. Country co-payments provide an important market test for technologically distant products, preventing resources from being wasted on products meeting technical specifications but not consumer needs. This test may not be needed for technologically close products.

C. Modeling AMC Design

Kremer, Levin, and Snyder (2019) develop a model of AMC design that illuminates many of these issues. The model focuses on the holdup problem: firms invest in R&D and capacity before bargaining with purchasers over price and quantity. Purchasers expropriate some investment returns in bargaining, leading the firm to underinvest. The firm may not develop the vaccine at all; if it does, it will underinvest in capacity to serve low-income countries.

An AMC that commits to a subsidy policy prior to the firm's investment helps address the inefficiency. However, the design matters: if the AMC merely sets a per-dose subsidy, a monopoly supplier can claim the entire AMC fund with its low equilibrium capacity. Increasing capacity merely increases the rate at which funds are received. As Kremer, Levin, and Snyder (2019) shows, a better solution ties AMC funds to capacity commitments.

II. Pneumococcal Pilot AMC

In 2007, five countries and the Gates Foundation pledged \$1.5 billion toward a pilot AMC targeting a pneumococcal conjugate vaccine (PCV). The World Health Organization (WHO) estimated pneumococcus killed more than 700,000 children under five in developing countries annually at that time (WHO 2007). A

PCV covering disease strains prevalent in developed countries already existed, and PCVs covering the strains in developing countries were in late-stage clinical trials, so this was a technologically close target.

In 2009, the AMC launched under the supervision of GAVI (formerly the Global Alliance for Vaccines and Immunizations). The design called for firms to compete for ten-year supply contracts, capping the price at \$3.50 per dose. A firm committing to supply X million annual doses ($X/200$ of the projected 200 million annual need) would secure an $X/200$ share of the \$1.5 billion AMC fund, paid out as a per-dose subsidy for initial purchases. The AMC covered the 73 countries below an income threshold for GAVI eligibility. Country co-payments were set according to standard GAVI rules. Countries were required to have 70 percent coverage with DPT vaccine to obtain pneumococcus vaccine under the program.

In 2010, GAVI set the first tender for 60 million doses. GSK and Pfizer each committed to supply 30 million doses annually at \$3.50 per dose, or \$10.50 for a 3-dose course (these and subsequent facts from AMC Secretariat of Gavi (2019)). GAVI issued subsequent tenders over time, sometimes outpaced by country demand. In each case, the firms expanded their supply commitments in line with the tenders. There has been purchaser and public pressure for the manufacturers to reduce their prices, which currently are down to \$2.90 per dose. In 2019, a third vaccine developed by the Serum Institute of India qualified for the AMC program. The Serum Institute is expected to participate in tenders for the remaining \$262 million of uncommitted AMC funds, reportedly pricing its vaccine at \$2 per dose for low-income countries.

By 2016, PCV was distributed in 60 of the 73 eligible countries, and annual distribution exceeded 160 million doses, enough to immunize over 50 million children per year. As Figure 1 in the online Appendix shows, by 2018, nearly half of the target child population in GAVI countries was covered. While coverage is far from full, it is higher than in non-GAVI countries. A key reason why the fraction of the population covered is smaller than the fraction of countries covered is that India, by far the most populous GAVI country, did not adopt PCV until 2017 and currently runs only a limited program in five states.

Estimates from Tasslimi et al. (2011) suggest that the PCV rollout has been highly cost effective. At initial program prices, the PCV rollout avoided the loss of a disability-adjusted life year (DALY) at a cost of only \$83. The WHO classifies interventions as highly cost effective if a DALY costs less than one GDP per capita.

Evidence on the cost effectiveness of PCV does not prove the cost effectiveness of the overall AMC, because we lack a valid counterfactual. We do not know, absent an AMC, whether and when vaccines would have been developed, how much push funding would have been spent, or what prices would have been set. However, the high cost effectiveness of PCV implies that the AMC would have been worthwhile were there even a small chance that it sped up PCV adoption.

Some insight on the effect of the AMC-promoted capacity and adoption can be gained by comparing PCV to rotavirus vaccine, for which GAVI supported purchases over a similar time period without an AMC. Figure 2 in the online Appendix shows that the rate of vaccine coverage in GAVI countries converged to the global rate almost five years faster for PCV. At the same time, shortages of rotavirus vaccine were more severe than shortages of PCV, suggesting that firms expanded capacity faster for PCV than for rotavirus vaccine.

III. Design Issues

A. Country Co-payments, Pricing, Coverage

AMC designers do not know manufacturers' reservation price for installing adequate capacity to supply needed vaccines or countries' willingness to provide co-payments. Because the benefits of vaccines far exceed their production costs, AMC designers face an asymmetric loss function in setting firm prices and country co-payments. Offering firms less than their reservation value or asking countries to make co-payments greater than their willingness to pay risks children not receiving lifesaving vaccines. This is very costly relative to what the donor can save by paying firms somewhat less or charging countries somewhat more, so maximizing social welfare under uncertainty requires paying firms more than the expected cost of the vaccine and setting country co-payments below the expected marginal cost.

The online Appendix provides a range of calibrations quantifying the asymmetry of the loss function. For example, assuming the AMC designer sought to maximize health benefit with the available funds, correctly anticipated the speed of rollout under the AMC, and used money saved from lower vaccine prices for other health interventions at the WHO threshold for highly cost-effective interventions, the \$3.50 price set in the pilot dominates a \$2 price even if the lower price generated only a 4 percent risk that the firms refuse to participate (although the precise figure is sensitive to assumptions about alternative uses of savings). Analogous calculations can show that if there were even a small chance that lower co-payments would have led India or other countries to adopt sooner, this would have substantially increased the expected number of lives saved through the program.

While some activists have argued that the \$3.50 paid per dose exceeds manufacturing costs, the relevant issue for AMC designers is not manufacturing costs but firms' reservation values. Their reservation values may substantially exceed manufacturing costs for several reasons: the AMC top up may not fully defray their capacity costs, or they may fear that offering a low AMC price would lead higher-income countries to press for price reductions.

While these factors imply ex ante optimal prices will exceed expected production costs, the facts that both firms participated even though one likely had substantially higher manufacturing costs and that both continued to participate at \$2.90 per dose suggests that at least one firm would likely have participated at a lower price.

Still, prices for PCV are much lower under the AMC than outside it. Currently, lower-income countries in the Americas pay \$12 or more per dose (WHO 2019); the US Centers for Disease Control and Prevention (CDC) pay \$137 (CDC 2019). As we show in Figure 3 in the online Appendix, the percentage discount GAVI receives compared to various global price measures is deeper for PCV than for almost any other vaccine.

Extending AMC participation beyond GAVI-eligible countries could have saved more lives, although it is possible that manufacturers would have demanded higher prices for a program covering higher-income countries if they

thought this would have cut into sales at higher prices or put pressure on pricing in higher-income countries.

B. Number of Firms

A program with lower co-payments, more generous country inclusion rules, and faster issuance of tenders for the full AMC amount could potentially have generated greater health benefits up to now.

However, holding back some funds for later tenders may have helped incentivize entry by the Serum Institute (although the product also received substantial push funding). The Serum Institute's vaccine is somewhat cheaper to produce than previous PCVs, but the chief benefit of this entry likely comes from inducing greater competition in the market outside of GAVI countries and in the GAVI-country market after the AMC ends. Another benefit is that India may decide to expand its heretofore limited participation in response to the entry of a domestic supplier.

A key issue for future AMCs will be whether to split the AMC among multiple suppliers and reserve tenders for future entrants, as did the pilot pneumococcus AMC, or to concentrate incentives on a single supplier, as envisioned in Kremer and Glennerster (2004). Sponsors of the AMC pilot prioritized entry of multiple vaccines because they saw competition as essential for holding down long-run prices and avoiding supply interruptions. Kremer and Glennerster (2004) prioritized the development of a vaccine where none currently existed, relying on the price cap, to which the firm agrees to access AMC funds, to keep prices near marginal cost over the long term. Penalty clauses could be specified to mitigate supply interruptions. Development of yet more advanced vaccines could be incentivized through subsequent AMCs.

For distant technological targets, incentivizing a sequence of entrants reduces incentives for the first vaccine to enter. Thus, structuring a program to incentivize multiple entrants may substantially increase total costs. On the other hand, the design and enforcement of long-term contracts that hold prices close to marginal cost and assure consistent supply through penalty clauses for supply interruptions may be difficult.

C. Political Economy of Target Choice

Policymakers may wish to explore future AMCs with different design features. Kremer, Levin, and Snyder (2019) argues that focusing on a technologically more distant target might generate larger overall benefits. However, political factors may favor technologically closer targets. Firms that have a product close to market have stronger incentives to engage politically than firms with early-stage ideas for distant targets. Moreover, while an AMC for a distant product does not impose substantial financial costs unless a product is developed, politicians looking for a "win" may be reluctant to expend significant effort on a project that only pays off once they have left office, if at all.

One solution might be to simultaneously launch a bundle of AMCs that includes some eye-catching long-term targets with some short-term targets that will deliver quick wins. When technologically close targets are chosen, there are further political considerations. There may be strong industry lobbying around product specifications to include their approaches and exclude potential rivals'. If the process involves first selecting a disease target and then designing the AMC details, more weight in the second stage will be put on getting the product to market than saving money that is already earmarked. It may be possible to address some of these concerns by broadening the set of possible targets or having several groups design AMCs targeting different products and using competitive mechanisms to decide which receives funding.

IV. Conclusions

The AMC moved from theory to practice in its first decade, and we now have a decade of learning from the pneumococcal pilot. While aspects of program evaluation are complicated, the best estimates suggest that the introduction of PCV saved 700,000 lives at a highly favorable cost. Iterations likely could improve AMC design, just as market designs have been refined in settings such as school choice and radio spectrum allocation. Policymakers may wish to consider offering a set of AMCs, perhaps each smaller in scale than the pilot pneumococcus AMC, where potential targets could range beyond health to address agricultural or sustainability problems specific to developing countries.

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