Evaluating the Health and Economic Impacts of Potential Policy Reforms to the US Food and Drug Administration's Accelerated Approval Pathway

Authors: Peter Murphy [1,2], Mahnum Shahzad [2,3,4], Anna Kaltenboeck [5], Huseyin Naci [1,2,4,6]

1. LSE Health, London School of Economics and Political Science, London, UK
2. Pharmaceutical Policy Lab, London, UK
3. Division of Health Policy and Insurance Research, Department of Population Medicine, Harvard Pilgrim Health Care Institute, Boston, MA, USA
4. Harvard Medical School, Boston, MA, USA
5. Verdant Research, Oakton, Virginia
6. Department of Health Policy, London School of Economics and Political Science, London, UK

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Introduction and motivation

The U.S. Food and Drug Administration's (FDA) accelerated approval (AA) pathway allows the early approval of drugs based on surrogate measures that are 'reasonably likely' to predict clinical benefit. Until confirmatory trials are completed, the clinical benefit of these treatments remains uncertain, yet payers such as Medicare continue to bear their substantial costs (1). Consequently, considerable expenditure may be directed towards drugs that ultimately fail to demonstrate clinical benefit (2). As such, there is continued interest in reforms to strengthen the AA pathway.

Cancer drug indications have accounted for more than 80% of accelerated approvals (3). Previous studies estimated the survival benefits of cancer drug indications in the AA pathway (3,4). However, cancer patients also value maintaining quality of life, which was not considered in prior studies (5). Further, estimates of health benefits should consider not only the health gains experienced by patients receiving treatment but also the health losses experienced by other patients, since paying for treatment means forgoing the opportunity to provide healthcare to others.

In this paper, we first quantify the costs, quality-adjusted life years (QALYs) and net health benefits (NHB) of early access to cancer drug indications in the AA pathway. Second, we evaluate the health and economic impacts of potential policy reforms to the AA pathway and identify those that can reduce costs while maximizing the benefits for Medicare beneficiaries.

Data and methods

We model the health and cost impacts of gaining access to new cancer drug indications during the period between accelerated approval and conversion to regular approval or withdrawal.

Our sample includes 90 cancer drug indications that received AA between 1 January 2012 and 31 December 2020. Our decision model is structured as a staggered cohort partitioned-survival model with three health states: pre-progression, progressed disease, and dead (Figure 1). The model allows monthly cohorts of patients to start treatment with either the AA drug or the standard of care. We estimate the number of Medicare beneficiaries starting treatment in each AA indication using claims data. To estimate the time individuals receiving treatment spend in each health state, we extrapolate overall survival and progression-free survival data from the pivotal and confirmatory trials. We adopt a payer perspective and estimate the costs to Medicare and the benefits to Medicare beneficiaries. Monthly costs are estimated from the Centers for Medicare & Medicaid Services (CMS) spending dashboards. Utility values are obtained from the Tufts Medical Center CEA Registry and the literature.

To characterize uncertainty, we perform probabilistic sensitivity analyses using Monte Carlo simulations with 10,000 iterations.

We measure the total incremental costs and QALYs of the AA treatments over the standard of care at the population level, as well as the cost per QALY gained over a 10-year time horizon. We also report NHB which captures health gains net of the health opportunity cost, using $100,000 per QALY gained as the US cost-effectiveness threshold.

We consider five potential reforms to the AA program, informed by recommendations in a recent white paper (6). The reforms are:

- P1: Altering the AA eligibility criteria based on severity of illness using proportional shortfall
- P2: Restricting the AA eligibility criteria based on the availability of existing treatment alternatives
- P3: Implementing stricter enforcement of pivotal trial timelines
- P4: Applying a simple cap on drug prices before conversion to regular approval
- P5: Introducing value-based price caps before conversion to regular approval

To contextualize the discounts involved in P4 and P5, we compare the potential forgone manufacturer revenue resulting from the imposed discount with the total global sales revenue achieved by the 90 treatments during each drug's respective AA window. Global sales are extracted from SEC 10-K filings and annual company financial reports.

Results

An estimated 178,000 Medicare beneficiaries had early access to new cancer drug indications during the accelerated approval period. Compared with regular approval, this access was associated with incremental costs of $20.1bn to Medicare and incremental benefits of 66,085 QALYs, corresponding to a cost per QALY gained of $303,665 and a net health loss of 134,592 QALYs (Table 1).

All five reforms improve NHB relative to the base case, but only the two pricing reforms (P4 and P5) produce a net health gain. Restricting eligibility based on severity of illness reduces the number of patients treated by approximately 27,000 (P1) and incremental costs by $7.3bn, and improves NHB to -62,307 (Figure 2). By contrast, P2 and P4 reduce both costs and QALYs, raising the cost per QALY, and only modestly improving NHB.

P4 retains the number of patients treated in the base case while generating savings of $2.3bn to Medicare, making AA treatment dominant over the standard of care, with an NHB of 88,761 QALYs.

Figure 3 shows the distribution of discounts across treatments required to reach value-based prices under P5.

The discounts involved in P4 and P5 are approximately $2.3bn and $10.5bn, representing 13.7% and 6.4% of global sales revenue, respectively. Mega-cap companies (i.e. those with a market capitalization of over $200bn) would lose proportionately more revenue than smaller companies under both P4 and P5 (Table 2). Under P5, small-cap companies would experience the smallest proportionate impact, at 0.2% of sales revenue, compared with 9.1% for mega-cap companies.

Discussion and policy implications

The FDA's AA pathway involves real trade-offs between speed of access and certainty of treatment effectiveness. Across 90 indications, the program generated 66,085 additional QALYs at a cost of $20.1bn, resulting in a net health loss of 134,592 QALYs when the health opportunity cost is considered. Our model allows a transparent comparison of potential reforms, highlighting those with a large impact (restricting eligibility to the most severe conditions and capping prices) and those with a limited impact (restricting eligibility based on availability of existing treatments and enforcing stricter timelines).

Our findings are timely. The Food and Drug Omnibus Reform Act of 2022 strengthened FDA's authority over confirmatory trials and withdrawal, but it did not include several other potential reforms. Our analysis identifies levers that deserve further attention from the FDA and CMS.

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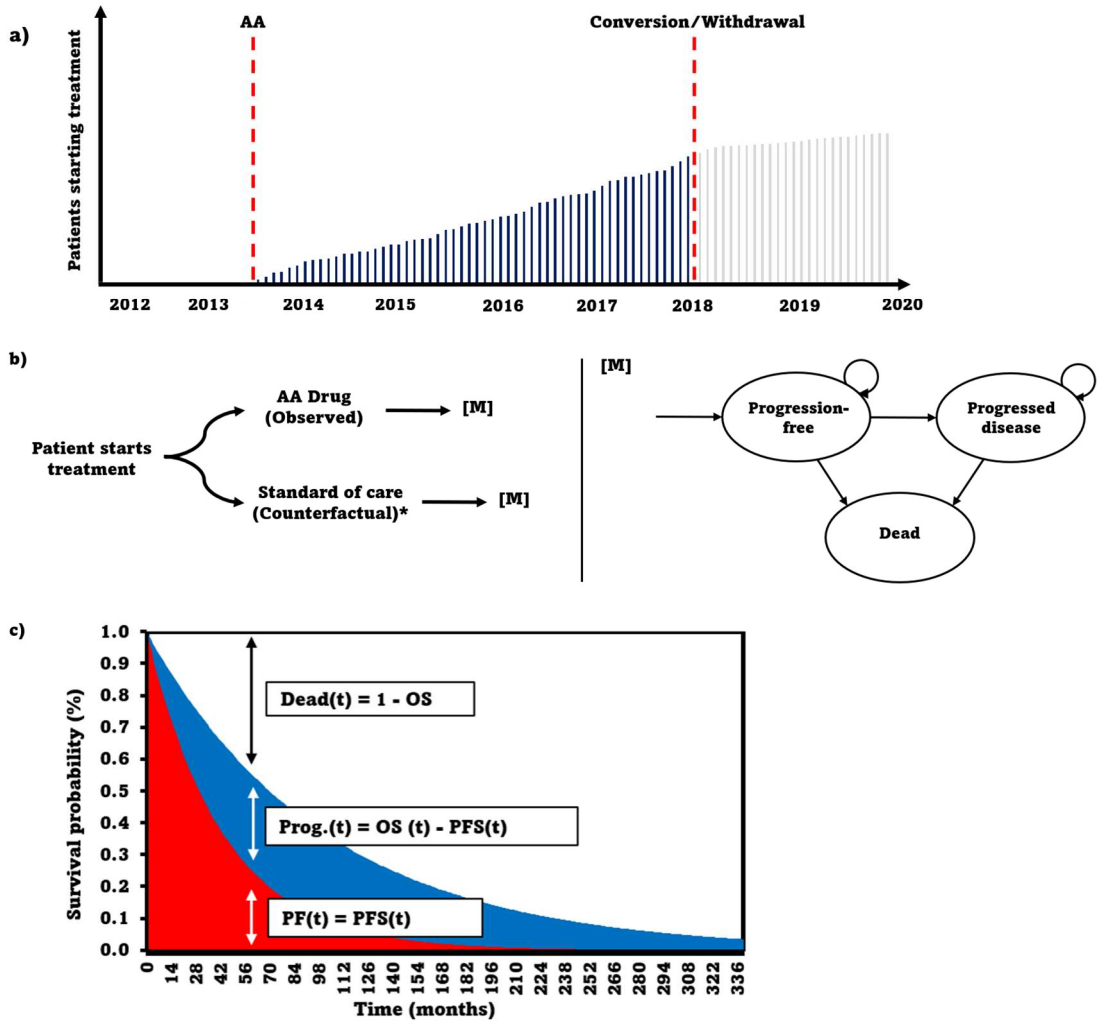
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Tables and Figures

Figure 1 – Model overview



Abbreviations: AA, accelerated approval; M, model; OS, overall survival; PFS, progression-free survival; prog., progressed disease, t, time.

The model can be considered in three-parts: a) Only those individuals that initiate treatment during the AA window (i.e. from the date of AA to withdrawal or conversion) are included in the model. b) When an individual starts an AA treatment within the window, the model considers the lifetime costs and health outcomes for an individual on the AA drug and for an individual on the standard of care based on the clinical trial evidence. To model the lifetime costs and health outcomes the individuals enter the progression-free state and either remain there, progress to progressed disease or move to the dead state over time. c) The time spent in each state over time for each drug and comparator is estimated from modelled OS and PFS curves informed by clinical trial outcomes.

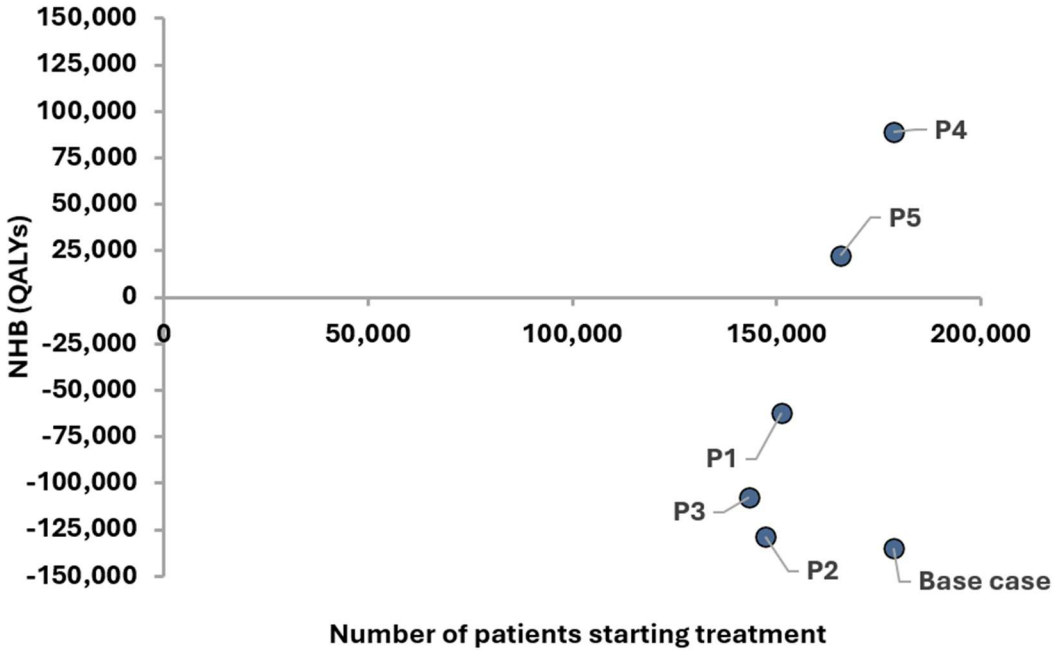
Table 1 - Results of the model and proposed policies

Policy scenario	Incremental costs	Incremental QALY	Incremental cost per QALY	NHB (QALYs)
Base case	$20,067,679,207	66,085	$303,665	-134,592
P1	$12,747,577,438	65,169	$195,608	-62,307
P2	$18,513,496,373	56,349	$328,550	-128,786
P3	$15,366,174,020	46,093	$333,374	-107,569
P4	$2,267,615,294 (saved)	66,085	AA dominates	88,761
P5	$4,395,842,898	66,386	$66,216	22,428

Note, 'AA dominates' means the drugs included in the AA pathway had lower total costs and generated more health than the standard of care therefore representing a dominant strategy.

Abbreviations: AA, accelerated approval; NHB, net health benefit; QALY, quality-adjusted life year.

Figure 2 – NHB – access plane of base case and potential policy reforms



Abbreviations: NHB, net health benefit; QALY, quality-adjusted life year.

Figure 3 – Distribution of discounts required to meet value-based prices

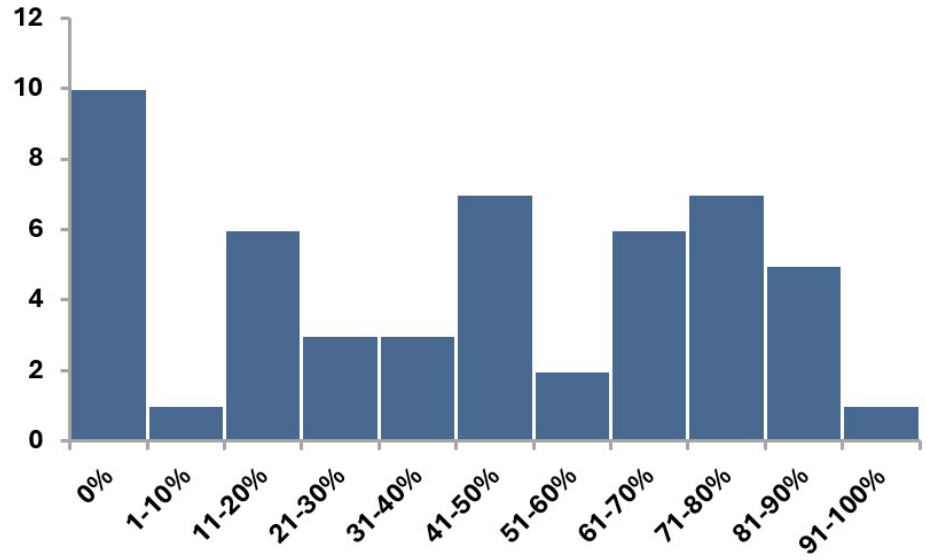


Table 2 – Discounts relative to global sales revenue

Company	Global revenue, USD billions	P4 - Simple discount		P5 - VBP discount	
		Discounted amount, USD billions (i.e. revenue lost)	% of global sales revenue	Discounted amount, USD billions (i.e. revenue lost)	% of global sales revenue
All	163.475	22.335	13.7%	10.457	6.4%
Mega	106.667	17.845	16.7%	9.736	9.1%
Large	56.425	4.449	7.9%	0.720	1.3%
Mid	0.000	0.000	-	0.000	-
Small	0.383	0.041	10.7%	0.001	0.2%

Global revenue is defined as the global sales revenue for the sample of 90 drugs extracted from annual filings and 10-k reports from the manufacturers during the accelerated approval windows.
Note, we define the size of the company using market capitalisation as reported on October 21, 2026 or the last reported market capitalisation prior to acquisition.
Mega companies are defined as >$200bn; large companies are defined as $200bn to $10bn; mid companies are defined as $10bn to $2bn and small companies are defined as <$2bn.
Abbreviations: VBP, value-based pricing.