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Estimated Costs of Pivotal Trials for Novel Therapeutic Agents Approved by the US Food and Drug Administration, 2015-2016

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IMPORTANCE A critical question in health care is the extent of scientific evidence that should be required to establish that a new therapeutic agent has benefits that outweigh its risks. Estimating the costs of this evidence of efficacy provides an important perspective.

OBJECTIVE To estimate costs and assess scientific characteristics of pivotal efficacy trials that supported the approval of new therapeutic agents by the US Food and Drug Administration (FDA) from 2015 to 2016.

DESIGN AND SETTING This study identified 59 novel therapeutic drugs using the annual summary reports from the FDA Center for Drug Evaluation and Research. ClinicalTrials.gov, FDA reviews, and peer-reviewed publications that were publicly available in 2017 were used to identify 52 characteristics of each efficacy trial. Costs were calculated with a global clinical trial cost assessment tool available to contract research organizations and pharmaceutical sponsors.

MAIN OUTCOMES AND MEASURES Estimated mean cost and 95% CIs based on industry benchmark data from 60 countries. Measures of trials' scientific characteristics included trial design (no control group, placebo, and active drug), end point (surrogate outcome, clinical scale, and clinical outcome), patient enrollment, and treatment duration.

RESULTS A total of 138 pivotal clinical trials provided the basis for approval of 59 new therapeutic agents by the FDA from 2015 to 2016, with a median estimated cost of $19.0 million (interquartile range, $12.2 million-$33.1 million). Estimated costs ranged from less than $5 million for trials without a control group for 3 orphan drugs with fewer than 15 patients each to $346.8 million (95% CI, $252.0 million-$441.5 million) for a noninferiority trial with end points assessing clinical benefit. Twenty-six of 138 trials (18.8%) were uncontrolled, with a mean estimated cost of $13.5 million (95% CI, $10.1 million-$16.9 million). Trials designed with placebo or active drug comparators had an estimated mean cost of $35.1 million (95% CI, $25.4 million-$44.8 million). Costs also varied by trial end point, treatment duration, patient enrollment, and therapeutic area.

CONCLUSIONS AND RELEVANCE The highest-cost trials were those in which the new agent had to be proved to be noninferior with clinical benefit end points compared with an agent already available or those that required larger patient populations to achieve statistical power to document smaller treatment effects or accrue infrequently occurring end points.

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Supplemental content

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The US Food and Drug Administration (FDA) relies on pivotal clinical trials to determine whether a new therapeutic agent provides substantial evidence of effectiveness for treating a specific medical condition or indication. These systematically observed patient populations also provide the most authoritative scientific evidence of harms, which the agency must also assess in making a decision whether the benefits of a new drug sufficiently outweigh its risks to allow marketing approval. Since 1962, the standard requirement of the Food, Drug, and Cosmetic Act[1] has been for 2 or more adequate and well-controlled investigations of new molecular entities—clinical trials in humans providing substantial evidence of a treatment effect that can be replicated. Since then, amendments to the Food, Drug, and Cosmetic Act have allowed for exceptions, such as waiving the replication requirement by allowing 1 large single trial in some settings[1] and accelerated approval, which provides provisional approval based on a single trial with a surrogate end point "reasonably likely" to predict benefit.[2] Since 2012, additional changes to the historical scientific standard have been made. For example, agents designated as breakthrough drugs may, in some cases, be approved without a control group, with interim results, or with enrichment strategies that provide a preliminary treatment period to select patients who are most likely to benefit.[3] One study evaluated the characteristics of 448 pivotal trials for 188 new therapeutic agents approved by the FDA from 2005 to 2012.[4] These trials enrolled a median of 446 patients; 48.9% relied on a surrogate end point rather than a clinical benefit or clinical scale, and all but 58 trials used placebo or active drug control. Despite the insights provided by this and previous studies, there has been remarkably little evaluation of the costs of these essential, systematic scientific investigations.

We could identify only 1 peer-reviewed published article that analyzed cost data from individual clinical trials.[5] With selected clinical trial contract data from 2004 to 2012, the authors of that published article estimated that the mean cost of phase 3 clinical trials to establish benefit in a likely patient population ranged from $11.5 million for dermatology drugs to $52.9 million for pain and anesthesia products. In addition, some estimates have been published. For example, Eisenstein et al[6] combined expert opinion with a proprietary clinical trials cost estimation model to estimate that 2 hypothetical, large cardiovascular trials (14 500 and 17 000 patients) would cost from a median of $67 million to $135 million.

In this study, we estimated the costs of the pivotal clinical trials for all new therapeutic agents approved by the FDA in 2015 and 2016 and examined how key features of the trials were associated with these costs.

Key Points

Questions What are the costs of pivotal trials that provide the substantial evidence of effectiveness that the US Food and Drug Administration (FDA) requires to approve new therapeutic agents, and how do these costs vary by the scientific characteristics of their design?

Findings In this study of 59 new therapeutic agents approved by the FDA from 2015 to 2016, the median estimated direct cost of pivotal efficacy trials was $19 million, with half of the trial cost estimates ranging from $12 million to $33 million. At the extremes of the distribution were 100-fold cost differences, and patient enrollment varied from fewer than 15 patients to more than 8000 patients.

Meaning Pivotal clinical trial costs increased if more patients were needed to document treatment benefit, if active drug comparators were used, or to measure clinical end points rather than a change in a surrogate outcome.

Methods

Source Data

We identified the novel therapeutic drugs for this study using the FDA Center for Drug Evaluation and Research annual summary reports on "Novel Drugs."[7,8] We excluded diagnostic and imaging agents, adjuvants to surgical or medical procedures, and new formulations or delivery systems for previously approved molecular entities because these agents require markedly different forms of clinical testing to establish benefits. We also excluded 1 drug (obiltoxaximab for inhalation anthrax) that was not tested in humans and another drug (cholic acid for bile acid synthesis disorders) that did not have a pivotal clinical trial. Novel therapeutic agent approvals that used expedited approval pathways (such as accelerated approval, fast track, breakthrough, and priority review) were identified from the FDA annual reports, as were products approved under the Orphan Drug Act.[9] This study was exempted from review by the Johns Hopkins Bloomberg School of Public Health institutional review board because the source material did not have identifiable human data.

The pivotal trials were identified from those listed in Section 7 of each drug's "Summary Review," the standardized recommendation-for-approval document available from the Drugs@FDA website database.[10] We included the pivotal trials for all the indications associated for each drug's marketing approvals in the study period.

The characteristics of the pivotal clinical trials were obtained through the following publicly available sources: ClinicalTrials.gov[11]; the FDA Summary Review, FDA medical reviews, or cross-disciplinary reviews; and published peer-reviewed studies. In the infrequent cases in which there were definitional differences or minor discrepancies between sources, we normally selected trial data items using the following order of priority: (1) preference to ClinicalTrials.gov because it was a legally required sponsor submission, (2) FDA reviews because they were independently verified data, and (3) peer-reviewed studies.

Estimating Trial Costs

We calculated the overall costs of the pivotal trials using proprietary clinical trial cost estimation software designed to support contract research organizations (CROs) and pharmaceutical sponsors in creating or evaluating contract proposals to conduct trials worldwide. According to the manufacturer (IQVIA Clinical Trial Optimization Solutions, email communications, November 2017), the cost-estimating software, the IQVIA CRO CostPro Mid-Level Tool,[12] produces estimates based

on data from 2000 final awarded proposals for CROs and integrates with cost information derived from clinical trial site contracts from approximately 200 000 sites in 60 countries worldwide. The contracts supporting the estimates were from the previous 2 years and were in unadjusted current dollars, with foreign currencies converted to US dollars at the time of source data contract awards.

To describe each trial, we collected 52 specific items, with 49 variables to support the cost estimates and 3 additional variables to assess scientific characteristics. Trial features included 17 basic variables about each trial's features, starting with the disease target or indication identified through *International Classification of Diseases, Ninth Revision* diagnosis codes. The basic variables also included trial phase, the number of patients screened, the number of patients enrolled, the number of patient visits, the number of site-monitoring visits, and 3 measures of the length of time that sites were involved in these activities: start-up, trial conduct, and close-out. Next, geographic variation in site costs was assessed with the number of countries, study sites, and patients in each of the 8 regions, and these geographic variations were assigned to a 24-item variable matrix. The total costs of other country- or region-specific trial tasks (eg, pass-through, study conduct, site management, and regulatory) were assigned to the 8 regions. Central tasks, such as biostatistics and project management, were assigned to North America or the region with the largest patient total if the trial had no sites in North America. Details of the data inputs are in the eTable and eMethods in the Supplement.

The IQVIA CostPro estimating tool was used to combine these 49 trial characteristics with global industry benchmark cost data to produce 3 estimates for each trial: the 25th percentile, the median, and the 75th percentile reported as the median and interquartile range (IQR).

Study Design Features

We also investigated how trial costs varied as a function of scientific characteristics with 3 additional variables derived from a previous study[5]: end point type (surrogate outcome, clinical scale, and clinical outcome), treatment duration (wks) for efficacy, and form of control (uncontrolled, placebo, or active drug). Total patient enrollment was used both to estimate cost and to assess scientific characteristics.

Assessment of Trial Efficiency

In addition to creating estimates of the median (IQR), we sought to enrich the range of credible estimates by including these contrasting sets of assumptions about the efficiency with which the trial was conducted: shorter or longer study site start-up and close-out periods, centralized or local institutional review board approvals, zero vs 3 protocol amendments, and fewer vs more frequent site monitoring visits by the CRO. Additional detail is provided in eMethods in the Supplement.

Statistical Analysis Plan

The primary cost estimate for each trial was the mean (95% CI) derived from the 6 different trial estimates (the 25th percentile, median, and 75th percentile estimates for more and less efficient trial designs). To characterize the entire group of drugs, where results were not normally distributed, we report the median (IQR). Costs per patient and per patient visit (patients × visits) were estimated by dividing the total mean trial cost by these variables and reporting the median (IQR). The data were collected in a Microsoft Access database (Microsoft Corp) and were input into the IQVIA CostPro estimating program; the results were analyzed using the R Project for Statistical Computing, version 3.3.3 (R Foundation).[13]

Table 1. Characteristics of Novel Therapeutic Agents Approved From 2015 to 2016

Characteristic	No. (%)
Total therapeutic agents	59 (100)
Expedited approval pathway[a]	
Accelerated approval	12 (20.3)
Breakthrough	17 (28.8)
Fast track	21 (35.6)
Priority review	35 (59.3)
None	21 (35.6)
Incentive	
Orphan drug	27 (45.8)
Molecule type	
Biologic	18 (30.5)
Small molecule	41 (69.5)
Pivotal clinical trials per therapeutic agent	
1	27 (45.8)
2	14 (23.7)
3	7 (11.9)
4	6 (10.2)
≥5	5 (8.5)

[a] Therapeutic agents could qualify for multiple approval pathways.

Review and Verification

We reviewed the capabilities of the CostPro estimating tool, our research plan, and key assumptions with 3 experienced clinical trial managers. In addition, we compared cost estimates using the CostPro tool with published results in 3 therapeutic areas as reported in 2 publications[6,7] and obtained approximately similar results after adjusting for inflation based on the Consumer Price Index for Medical Care.[14] We conducted extensive sensitivity analyses to explore the properties of the CostPro tool, its assumptions, and default values and worked with IQVIA staff to insure optimal use of the trial cost-estimating program. We used multiple strategies to verify our data acquisition and entry of the trial characteristics, including comprehensive audits of random samples, double verification of key variables, and statistical assessment to detect unexpectedly large or small values or inconsistencies between related variables.

Results

From 2015 to 2016, the FDA approved 59 new molecular entities for therapeutic use, including 41 (69.5%) small molecule drugs and 18 (30.5%) biological products. The product approval profiles are shown in **Table 1**. Among the 59 approved molecular entities, the most common disease targets were cancer (18 drugs [30.5%]), endocrine and metabolic diseases

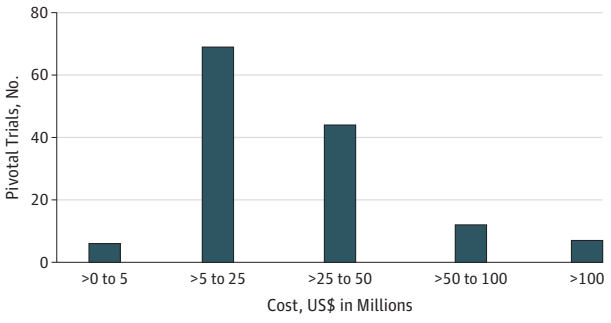
Table 2. Estimated Costs of Pivotal Clinical Trials for Therapeutic Agents Approved From 2015 to 2016

Trial Characteristic	Agents, No.[a]	Trials, No. (%) (n = 138)[b]	Mean (95% CI), US$ in millions[a]
Therapeutic area			
Cardiovascular	5	5 (3.6)	157.2 (113.5-200.9)
Central nervous system disorders	8	21 (15.2)	25.7 (18.4-33.1)
Dermatology	4	9 (6.5)	24.5 (17.0-31.9)
Digestive system	4	7 (5.1)	29.4 (22.2-36.5)
Endocrine or metabolic diseases	9	39 (28.3)	20.8 (15.8-25.9)
Infectious diseases	6	19 (13.8)	22.1 (16.7-27.6)
Oncology	18	24 (17.4)	45.4 (31.5-59.3)
Other	3	7 (5.1)	8.8 (6.4-11.2)
Respiratory	2	7 (5.1)	20.8 (15.7-25.9)
Type of end point			
Surrogate outcome	32	73 (52.9)	24.0 (17.7-30.4)
Clinical scale	15	38 (27.5)	20.5 (14.7-26.3)
Clinical outcome	17	27 (19.6)	64.7 (46.6-82.9)
Trial design			
No control group	18	26 (18.8)	13.5 (10.1-16.9)
Placebo-controlled	33	77 (55.8)	28.8 (21.0-36.7)
Active drug	21	35 (25.4)	48.9 (35.0-62.7)
Patient enrollment, No.			
1-100	6	8 (5.8)	5.9 (4.8-7.0)
101-250	25	32 (23.2)	16.2 (12.2-20.3)
251-500	14	33 (23.9)	18.6 (14.1-23.2)
501-1000	27	44 (31.9)	33.6 (23.6-43.6)
>1000	16	21 (15.2)	77.2 (55.8-98.6)
Treatment duration, wk			
≤26	39	89 (64.5)	19.7 (14.6-24.7)
>26	32	49 (35.5)	51.7 (36.9-66.4)

[a] Therapeutic agents may have trials in multiple categories.

[b] Percentages may not equal 100 because of rounding.

Figure. Pivotal Trial Cost Estimates of Novel Therapeutic Agents Approved by the US Food and Drug Administration From 2015 to 2016



(9 drugs [15.2%]), and central nervous system disorders (8 drugs [13.6%]). Only 16 of 59 agents (27.1%) were approved based on a standard review and 2 or more clinical efficacy trials. Also, 43 therapeutic agents (72.9%) were granted 1 or more forms of expedited reviews or legal exceptions to the primary standard of 2 well-controlled trials. In addition, 27 drugs (45.8%) provided novel treatments for rare diseases with sponsor benefits such as patent exclusivity conferred by the Orphan Drug Act.[9]

Approval of these 59 therapeutic agents was supported by 138 pivotal trials, constituting the study population for our cost estimates. The number of pivotal clinical trials submitted to support approval for each new therapeutic agent varied widely: 27 products (45.8%) were approved with evidence from a single trial, 14 drugs (23.7%) on the basis of 2 trials, and the remaining 18 drugs (30.5%) on the basis of 3 to 11 pivotal trials each. The primary reason for more than 2 pivotal clinical trials was because the sponsor sought multiple indications for approval, with each indication requiring at least 1 trial. Characteristics and estimated costs of the pivotal clinical trials are shown in **Table 2**.

Overall Cost Estimates

Overall, the 138 clinical trials had an estimated median (IQR) cost of $19.0 million ($12.2 million-$33.1 million). The distribution of trial costs is shown in the **Figure**. There were more than 100-fold cost differences at the extremes of the distribution. The lowest was a mean estimate of $2.1 million (95% CI, $1.8 million-$2.5 million) for a pivotal trial that enrolled 4 patients to test uridine triacetate for a rare hereditary metabolic disorder, orotic aciduria. The highest estimated trial cost, a mean of $346.8 million (95% CI, $252.0 million-$441.5 million), was for a noninferiority trial that assessed the efficacy for hospitalization and cardiovascular mortality of a new combination cardiovascular drug for chronic heart failure, sacubitril-valsartan. In addition, we found that the clinical trials cost a median (IQR) of $41 117 ($31 802-$82 362) per patient and $3562 ($2583-$4682) per patient visit.

Type of Trial Control

The type of control in the trial design had an influence on estimated costs, with 26 of 138 trials (18.8%) without a control group with an estimated mean cost of $13.5 million (95%

CI, $10.1 million-$16.9 million) compared with 77 placebo-controlled trials (55.8%) with a mean cost of $28.8 million (95% CI, $21.0-$36.7 million) and 35 active drug–controlled trials (25.4%) with a mean cost of $48.9 million (95% CI, 35.0-$62.7 million). Taken together, the 112 controlled trials (81.2%) had a mean cost of $35.1 million (95% CI, $25.4 million-$44.8 million).

Patient Enrollment

Patient enrollment needed to achieve adequate statistical power to document a treatment effect also influenced trial costs. The pivotal trials enrolled a median (IQR) of 488 patients (230-740 patients). However, at the extremes of the distribution, pivotal trials for 3 orphan drugs (asfotase alfa, eteplirsen, and uridine triacetate) included those enrolling fewer than 15 patients, and 21 pivotal trials for 16 drugs enrolled more than 1000 patients each. Estimated costs increased from a mean of $5.9 million (95% CI, $4.8 million-$7.0 million) for 8 trials enrolling 100 or fewer patients to a mean of $77.2 million (95% CI, $55.8 million-$98.6 million) for the 21 trials enrolling more than 1000 patients.

Duration of Treatment

Costs increased substantially when a longer duration of treatment was required for safety or to accrue enough end points to document a treatment effect. The 89 of 138 trials (64.5%) with a treatment duration of 26 weeks or fewer cost an estimated $19.7 million (95% CI, $14.6 million-$24.7 million) compared with mean costs of $51.7 million (95% CI, $36.9 million-$66.4 million) for 49 trials that were longer than 26 weeks.

Type of End Point

An end point of clinical outcome more than doubled the mean trial cost compared with trials using either surrogate outcomes or clinical scales. The 27 of 138 trials (19.6%) with an end point using a clinical outcome cost a mean of $64.7 million (95% CI, $46.6 million-$82.9 million) compared with a mean cost of $24.0 million (95% CI, $17.7 million-$30.4 million) for 73 trials (52.9%) using a surrogate outcome. The 38 trials (27.5%) using a clinical scale, which provides end point data for every patient, had mean costs of $20.5 million (95% CI, $14.7 million-$26.3 million), similar to those with surrogate outcomes.

Discussion

To our knowledge, this was the first systematic evaluation of the estimated costs of pivotal clinical trials, which provide the primary scientific evidence that supports the approval and medical use of new therapeutic agents in the United States. Our results supported several conclusions about factors that account for the costs of pivotal clinical trials.

First, costs were lowest when the new therapeutic agents were approved by the FDA based on uncontrolled trials without any of the major protections against bias (a comparison group, randomization, or blinding). Our sample included 26 pivotal trials (18.8%) without controls, with a mean estimated cost of $13.5 million. This sample included 3 pivotal trials for rare diseases that enrolled fewer than 15 patients each at an estimated mean cost of less than $5 million per study.

Second, pivotal trials were expensive when the benefits of a new agent were similar to those of agents already available with well-established clinical benefits. The highest-cost trial in this study was for the sacubitril-valsartan combination drug for chronic heart failure, with a mean estimated cost of $346.8 million. The trial was designed to demonstrate noninferiority in cardiovascular mortality and other clinical benefits compared with enalapril, a proven agent in this patient population. Another example was edoxaban for treatment of venous thromboembolism, with an estimated mean cost of $174.3 million. Its higher costs were a result of the requirement for clinical benefit and noninferiority compared with the proven anticoagulants heparin and warfarin.

Third, in most instances, the current costs of pivotal clinical trials appeared to comprise a modest portion of published estimates for overall costs of drug development; recent estimates ranged from a median of $648 million for new cancer drugs[15] to $2.8 billion for broader pharmaceutical company development costs for a wider variety of agents.[16] The intent of this study was to put a realistic price tag on 1 essential component of the drug development process that had not previously been evaluated, not to provide an alternate method to capture the full costs of development or of obtaining approval by the FDA.

Our results were produced with a software tool that incorporated extensive underlying benchmark cost data, and we collected 52 different characteristics of 138 pivotal trials. Because these were estimates rather than actual values, we used CIs and alternate assumptions about trial conduct efficiency to report a realistic range of costs. Alternate approaches to investigating the costs of clinical trials have as many or greater limitations. The analysis of historical CRO contract data presents a risk of using an arbitrary selection of available trial contracts dating back many years that might not characterize the trials being conducted today and might include few pivotal trials. Critical changes that might limit the value of historical data include the widespread use of new approval pathways and the globalization of clinical trial sites. Seeking confidential information from selected drug manufacturers—an approach previously used to estimate overall drug development costs[16]—risks selection bias because of the companies that opt to participate as well as variability in collecting complex information from different corporate information systems. Furthermore, published estimates relating to drug development use arbitrary assumptions, such as a cost of capital, or in the case of 1 published estimate of individual clinical trial costs, the estimate assumed an additional 30% unspecified additional costs.[6] Although our approach has the limitations described below, it has the advantage of focusing on the most important clinical trials, extensive trial data, current FDA requirements, and industry practices.

Limitations

The actual pivotal trials could have cost substantially more or much less than our estimates. Some features of clinical trials that are useful in estimating costs were not available; in these instances, we used default values derived from the underly-

ing contract and proposal data. Our estimates do not include the costs that might be borne by the sponsor, such as the costs of drug manufacturing or of supervision of the CRO. Because we provide only 2 years of data, previous years could provide different estimates. Several drugs had multiple clinical trials for the same or similar indications; we may have overestimated these costs because we could not calculate likely savings from an economy of scale. Nevertheless, a full range of trial characteristics were captured in our study, ranging from orphan drugs tested in a small number of patients to multiyear noninferiority trials enrolling thousands of patients. In addition, these estimates were not intended to capture the full cost of phase 2 or 3 trials, which in some instances, included many additional trials. Finally, these data were not intended to estimate either the overall costs of developing new drugs or to evaluate all of the clinical trials of all types; this study evaluated only the costs of successful clinical trials to document likely benefits.

The characteristics of these pivotal trials also did not capture the full scope of scientific evidence about a new drug, such as pharmacokinetic and safety studies, or from required postapproval investigations. However, other published analyses revealed that postmarket study completion rates were slow and irregular, and results were often unavailable or long delayed.[17,18]

Conclusions

This study identified more than 100-fold differences in the costs of pivotal trials that the FDA required to provide substantial evidence of benefit, with a central cluster of trials with estimated costs of $12.2 million to $33.1 million. Costs were increased when larger patient enrollments were required to detect a difference from placebo or active drug comparator, and costs were highest when a new drug had to be proved to have clinical benefit that was noninferior to another drug already available. Our study provides a different perspective to the widely held assumption that elaborate and expensive clinical trials are the main reason for the high costs of developing a new drug. These data suggest that high-cost trials occur but usually when drug effects are small or a known drug already provides clinical benefit. On the other hand, pivotal trials for novel drugs with substantial clinical benefits can be conducted at a lower cost.

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Concept and design: Moore, Anderson, Alexander.
Acquisition, analysis, or interpretation of data: Moore, Zhang, Alexander.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: Moore, Zhang, Alexander.
Statistical analysis: Moore, Anderson.
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Administrative, technical, or material support: Alexander.
Supervision: Moore, Anderson.
Building database and entry forms: Zhang.

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Editor's Note

Clinical Trials—We Get What We Pay For

Joseph S. Ross, MD, MHS

It is universally agreed that a clinical trial provides invaluable insights and knowledge, particularly when done well, through the use of randomization, blinded allocation, by including a control arm, and by focusing on a clinical outcome as opposed to a surrogate marker of disease. Clinical trials form the basis of many of the most important determinations in medicine and health care broadly, including the US Food and Drug Administration's (FDA's) determination of medical product safety and efficacy, the determination made by the Centers for Medicare & Medicaid Services and other commercial payers to provide coverage for a medical product, and clinical recommendations made by professional societies and government agencies to guide practice. But a common objection to performing a clinical trial is that trials are expensive, requiring extensive time and resources (although such costs pale in comparison to the costs of the health care interventions spent after approval, with or without coverage).

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While trials are costly, few peer-reviewed characterizations of the topic are available, particularly related to the costs of trials needed to secure FDA approval. One study estimated the costs of a phase 3 pivotal trial program to range from $11.5 million for drugs used for dermatologic indications to $52.9 million for drugs to treat pain and anesthesia,[1] while an industry report suggested the median cost of a phase 3 trial to be $21.4 million.[2] In this issue of *JAMA Internal Medicine*, using the proprietary IQVIA CRO CostPro Mid-Level Tool, Moore et al[3] characterized the costs of 138 pivotal trials supporting FDA approval of 59 novel therapeutic agents in 2015 and 2016, estimating the median cost to be $19.0 million. Importantly, there was a wide range in estimated costs, depending on the trial's design and size, use of randomization, inclusion of a control arm, and focus on clinical outcome. This study should not be misinterpreted as an estimate of drug development costs and has important limitations because it was focused solely on pharmaceuticals approved in 2015 and 2016 and on individual pivotal trial costs instead of the aggregate evidence used to secure FDA premarket approval or to satisfy postmarketing requirements. And the IQVIA Cost Tool is not available for public scrutiny. Nevertheless, it suggests that the stronger the evidence that is generated, which is most useful to inform clinical practice, the more it costs. We get what we pay for, and high-quality clinical trial data are well worth the investment to be sure that we prioritize spending our health care resources on therapies that have been shown to benefit patients.

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