

Investing in informative trials

How much does it cost pharmaceutical companies to conduct the clinical trials submitted to regulatory agencies in order to obtain marketing authorisation for a new drug?

Marketing authorisation applications contain a variety of data, but most importantly the results of pivotal clinical trials that are crucial for documenting the drug's harm-benefit balance in the clinical situation in question. A group of authors from several public health institutes in the United States has estimated the cost of the 138 pivotal trials conducted on the 59 drugs licensed by the US Food and Drug Administration (FDA) in 2015 and 2016 (1). The cost of these trials was estimated using a modelling tool commonly employed by pharmaceutical companies and contract research organisations, based on a large body of data on actual trial costs from 60 countries.

This study estimated that the median cost of a trial is US\$19 million. The lowest estimate was \$2.1 million for a trial of an orphan drug in 4 patients, and the highest was \$347 million for a non-inferiority trial that compared a drug with standard treatment, focusing on a clinical endpoint. Half of the trials cost between \$12 million and \$33 million each.

Incidentally, these figures show that the frequent claim that the total cost of research and development for new drugs runs into billions of dollars appears improbable and questionable.

Unsurprisingly, the mean estimated costs of these trials increased with their duration and size. It was also influenced by the nature of the comparator and the use of clinical endpoints. Trials with no control group cost \$13 million, versus \$29 million for placebo-controlled trials and \$49 million for trials with an active drug comparator. Trials based on surrogate endpoints cost only \$24 million on average, versus \$65 million for trials using a clinical endpoint.

More informative trials are therefore more expensive. It is the price that must be paid to help patients and healthcare professionals make better treatment decisions (2).

In a context in which most drugs introduced to the market do not constitute a real therapeutic advance for patients, it is unlikely that pharmaceutical companies will, of their own volition, choose to conduct costlier but more informative trials that may well provide results that are unfavourable to the drug they are seeking to market. The system has been broken for decades.

It is high time regulators start putting it right.

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Sources 1- Moore TJ et al. "Estimated costs of pivotal trials for novel therapeutic agents approved by the US Food and Drug Administration, 2015-2016" *JAMA Intern Med* 2018; 10.1001/jamainternmed.2018.3931: 5 pages.
2- Ross JS "Clinical trials-We get what we pay for" *JAMA Intern Med* 2018; 10.1001/jamainternmed.2018.3930: 1 page.

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