LIFE SCIENCES

Does the Development of Cancer Drugs Yield Exorbitant Profits?

A Review of the *JAMA Network Open* Article by Tay-Tao et al.

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MARCH 2019

Good science starts with a well-specified and meaningful hypothesis to test. It then applies known and accepted methods to analyze available data, uses all relevant information, considers previous findings related to the question, and presents its results in a clear analysis of the original question. Moreover, it does this all in an unbiased manner, letting the evidence dictate the answer to the question at hand.

An article by Tay-Teo, Ilbawi, and Hill[1] published on January 4 in *JAMA Network Open* fails the test of good science on multiple counts:

- This article starts from a straw-man version of the relationship between R&D spending and costs. In fact, economics does not dictate that high R&D costs automatically result in high prices. If someone spent money developing a new type of automobile that no one wanted to buy, its price would not be high just because a lot of money went into its development. A new model of car can only command a premium price if it provides something that is not offered by alternative models. Drug discovery and development is the same. Prices of new therapies generally reflect the value they provide to patients and other stakeholders in the healthcare system. Now, it is true that when R&D costs are high, the search for cures is restricted to the highest value treatments. If R&D costs were lower, the investment into new treatments would rise. More therapies would result in increased competition and prices would be lower. That is how economics works. These authors, seeking to write a piece centered in economic principles, should rely upon the basic principles of the discipline.
- The authors ignore long-established facts about the industry. The returns to drug discovery have long been known to be highly skewed (see DiMasi and Grabowski[2] and Grabowski and Vernon[3]). The most successful new treatments make high profits; most do not. Preposterously, this study claims that the median dollar invested in cancer drug development returns $14.50. If that were true, virtually all new investment of all kinds would be pouring into the search for new cancer drugs. It is not. That finding simply cannot be correct. There is a cable television show that takes lottery winners on home buying excursions. Does that mean the typical lottery player gets to buy a new home? Of course not. It would be foolish to judge the economics of playing the lottery by focusing on the money the winners have. Similarly, a careful economic analysis of the return to drug discovery would look not at the most successful drugs, or even the most valuable class of treatments. It would look at the overall returns to the process of drug discovery. What would that show?
    - Industry data[4] indicate that the probability that a new drug in Phase 1 clinical trials makes it to market is 9.6%. For oncology, the estimated probability is about half that. There are many failed companies and many failed products that never make the headlines.

1 Liu Tay-Teo, André Ilbawi, and Suzanne R. Hill, "Comparison of Sales Income and Research and Development Costs for FDA-Approved Cancer Drugs Sold by Originator Drug Companies," *JAMA Network Open* 2, no. 1 (2019): e186875.

2 Joseph A. DiMasi and Henry G. Grabowski, "R&D Costs and Returns to New Drug Development: A Review of the Evidence," in *The Oxford Handbook of the Economics of the Biopharmaceutical Industry*, ed. Patricia M. Danzon and Sean Nicholson, 21–46 (Oxford: Oxford University Press, 2012).

3 Henry Grabowski and John Vernon, "A New Look at the Returns and Risks to Pharmaceutical R&D," *Management Science* 36, no. 7 (1990): 767–885.

4 David W. Thomas, Justin Burns, John Audette, Adam Carroll, Corey Dow-Hygelund, and Michael Hay, *Clinical Development Success Rates 2006–2015* (Washington, DC: Biotechnology Innovation Organization, n.d.).

This policy brief received financial support from PhRMA. The findings, analysis, and opinions expressed represent those of the author and do not represent the views or opinions of Bates White LLC or of other Bates White employees or affiliates.

  - Overall, drug company stocks have underperformed the market for the past 20 years.[5] These companies have earned unremarkable risk adjusted rates of return[6] and the return to R&D investment fell into negative territory over the last five years of data analyzed in a 2015 study.[7]

- The Tay-Teo, Ilbawi, and Hill study takes its measure of revenues from those reported in company annual reports. Companies only report product-specific sales of those products that have a material impact on their overall financial performance, so by definition, these products must be selected among the most successful products.

- The study accepts as its overall estimate of the cost of drug development estimates from a deeply flawed study[8] that does not engage in rigorous analysis and merely asserts that their estimate is comparable to that of the most peer-reviewed, generally accepted, and rigorous academic analysis.[9,10] In fact, the estimates used are very different from those in the established literature. Good science would take the established literature much more seriously.

- In placing its results into context, this study cites an article making the suggestion that a pharmaceutical company could make money by subjecting an inert chemical compound to clinical trials and rely on statistical chance to yield positive clinical trial results, which would then allow it to sell the compound for the high prices that they say characterize successful cancer therapies. These authors give no credit to the regulators that would recognize an inert compound and carefully scrutinize such a hypothetical trial that yielded nonsense results, to the payors that would recognize a useless product and refuse to pay for it, or to the oncologists that would be well educated and sensible enough to know that using the compound would not help their patients. In short, this thought experiment is meaningless. It was not worthy of citation.

- The study focuses its attention on studies that claim to find limited clinical value in new cancer therapies while ignoring the literature that shows increased life expectancy and quality of life from such advances (see, for example, Howard et al.,[11] Philipson et al.,[12] Stevens et al.,[13] and Lichtenberg[14]).

The bottom line is that economics provides that prices are not set on the basis of the sunk cost of developing a product; prices reflect value. Now, there is good reason to think that certain well-intentioned policies may interfere with the competitive forces that could exact greater discipline on the prices consumers face (see, for

5 Richard Manning, "The International Pricing Index for Medicare Part B Drugs" (policy brief, Bates White, February 2019).

6 Richard Manning and Saurav Karki, "Economic Profitability of the Biopharmaceutical Industry" (policy brief, Bates White, September 2018).

7 Ernst R. Berndt, Deanna Nass, Michael Kleinrock, and Murray Aitken, "Decline in Economic Returns from New Drugs Raises Questions about Sustaining Innovations," *Health Affairs*, 34, no. 2 (2015): 245–52.

8 Vinay Prasad and Sham Mailankody, "Research and Development Spending to Bring a Single Cancer Drug to Market and Revenues after Approval," *JAMA Internal Medicine* 177, no. 11 (2017): 1569–75.

9 Joseph A. DiMasi, Henry G. Grabowski, and Ronald W. Hansen, "Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs," *Journal of Health Economics* 47 (2016): 20–33.

10 Christopher Paul Adams and Van Vu Branter, "Spending on New Drug Development," *Health Economics* 19, no. 2 (2010): 130–41.

11 David H. Howard, Michael E. Chernew, Tamer Abdelgawad, Gregory L. Smith, Josephine Sollano, and David C. Grabowski, "New Anticancer Drugs Associated with Large Increases in Costs an Life Expectancy," *Health Affairs* 35, no. 9 (2016): 1581–87.

12 Tomas Philipson, Michael Eber, Darius N. Lakdawalla, Mitra Corral, Rena Conti, and Dana P. Goldman, "An Analysis of Whether Higher Health Care Spending in the United States versus Europe Is 'Worth It" in the Case of Cancer," *Health Affairs* 31, no. 4 (2012): 667–75.

13 Warren Stevens, Tomas J. Philipson, Zeba M. Khan, Joanna P. MacEwan, Mark T. Linthicum, and Dana P. Goldman, "Cancer Mortality Reductions Were Greatest among Countries Where Cancer Care Spending Rose the Most, 1995–2007," *Health Affairs* 34, no. 4 (2015): 562–70.

14 Frank R. Lichtenberg, "The Effect of New Cancer Drug Approvals on the Life Expectancy of American Cancer Patients, 1978–2004," *Economics of Innovation and New Technology* 18, no. 5 (2009): 407–28.

example, Howard et al.[15] and Manning and Selck[16]). Policies that interfere with appropriate competitive forces run counter to overall patient well-being and should be changed.

Nevertheless, we should expect to see highly valuable innovations yielding attractive financial returns. We should hope that continues to be true. We should want the ultimate cure to the various forms of cancer to make its discoverers a lot of money. We should hope that the cure to hemophilia, to Alzheimer's—to any number of serious diseases—makes their creators a lot of money. That is how we will get those things. And of course, after appropriate periods of exclusivity have expired, we should expect that great inventions become widely available at prices driven low by competitive entry.

But misguided studies such as this, published in journals that are supposed to be the bastions of scientific medical inquiry, simply muddy the water and lead to confusion about the facts. We should be disappointed that the authors didn't follow rigorous scientific methods and that JAMA chose to publish this study despite its obvious flaws.

15 David H. Howard, Peter B. Bach, Ernst R. Berndt, and Rena M. Conti, "Pricing in the Market for Anticancer Drugs," *Journal of Economic Perspectives* 29, no. 1 (2015): 139–62.

16 Richard Manning and Fred Selck, "Penalizing Generic Drugs with the CPI Rebate Will Reduce Competition and Likely Increase Drug Shortages" (policy brief, Bates White, May 2, 2017).