

## Drug development cost estimates hard to swallow

In the March 2003 edition of the *Journal of Health Economics*, a trio of economists from the United States wrote about a number. Soon after, that number began popping up all over the place — in newspapers and political speeches, on television and the Internet. But the figure, despite reaching near-canonical status, drew criticism. Some said it was inflated. Less diplomatic detractors said it was a 9-digit fairy tale.

That number was 802 000 000. It was, according to the 2003 study, the number of US dollars that pharmaceutical companies spent, on average, to bring a new drug to market (*J Health Econ* 2003;22[2]:151-85). Now there are new numbers. Some health economists peg the current cost of drug development at US\$1.3 billion, others at US\$1.7 billion.

These figures have also been questioned, and Donald Light is among the skeptics. “These high estimates are all from industry-supported studies done by industry-supported economists who, as far as I can tell, compete to see who can come up with the higher number,” says the professor of comparative health care at the University of Medicine and Dentistry of New Jersey and coauthor of an article challenging the validity of the 2003 study (*J Health Econ* 2005;24[5]:1030-3).

Most experts agree that the cost of research and development in the drug industry — the cost of clinical trials in particular — is rising significantly. Most clinical trails for drugs are sponsored by pharmaceutical companies, who cite costly development as the primary reason their products are so expensive. A 2004 Glaxo-Kline-Smith ad, for instance, concluded with the message: “Today’s medicines finance tomorrow’s miracles.”

Some researchers fear that the growing expense of developing drugs will stifle innovation. But others claim it’s impossible to determine how far prices are truly rising because drug companies keep a tight grip on their financial data, releasing dribs and drabs on occasion, but only to economists with industry ties.

“They don’t have to make any of this public, but if they want to whine about high costs, they should,” says University



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In Canada, drug prices are not based on research and development costs, but some health economists claim that drug companies exaggerate the cost of developing drugs to justify their products’ high prices.

of Victoria (British Columbia) economist Rebecca Warburton, Light’s coauthor on the article criticizing the US\$802-million figure.

The lead author of the often-cited 2003 study is Joseph DiMasi, director of economic analysis at the Tufts Center of Drug Development at Boston, Mass., who says there is considerable evidence to support it. “Data on clinical trial sizes and clinical trial complexity from other sources were presented in the paper,” he wrote in an email to *CMAJ*. “My Center has looked at even more recent data on clinical trial complexity and found that it has continued to increase.”

Recognizing a trend of rising trial complexity is one thing, critics claim; ac-

curately estimating how that is affecting the cost of research and development quite another. “There’s certainly a lot of debate on the numbers,” says Dr. Joel Lexchin, a professor at York University’s School of Health Policy and Management, in Toronto, Ontario. “The Tufts Center gets most of its money from drug companies, though the people who work there say it is unrestricted funding. Being cynical, I would say the reason drug companies fund the centre is because they know, in general, that the results will be favourable to them. They wouldn’t be putting money into some place to produce reports they didn’t like.”

According to the document, *Become a Corporate Sponsor*, on Tufts’ website,

the centre currently receives funding from “pharmaceutical and biopharmaceutical companies, contract research organizations, trade associations, and other organizations. ... Corporate Sponsors make unrestricted grants to Tufts CSDD to support our research agenda. ...”

The US\$802-million figure was based on the research-and-development costs of 68 drugs at 10 companies. The data, however, were not made available to other researchers, and drug-industry watchdogs say this lack of transparency is typical. Warburton says it is in the best interests of drug companies — who often lobby governments to loosen price regulations and increase patent protection — to overstate costs. “I’d like to see the proof. Let’s get the auditors in. Was it payments to doctors? Was it payments for lab tests and analysis? They have been caught being unscrupulous so many times. Why should we believe them on costs?”

Drug companies are sometimes accused of passing these big numbers on to the media to deflect public criticism about price gouging. But research costs and retail prices in Canada are in no way linked, according to Rx&D, the national face of the Canadian brand-name drug industry. “In a recent study commissioned by the [Patented Medicine Prices Review Board], Professor D.G. McFetridge of the Department of Economics, Carleton University, Ottawa, Ontario, indicates that fixed costs are not a factor in determining the price of a new product,” wrote a spokesperson in an email to *CMAJ*. “Therefore the [board] does not consider costs of clinical trials in determining the price of a new product destined to Canadian patients.”

Another criticism of studies that produce numbers in the billion-dollar range is that large portions of those estimates aren’t out-of-pocket expenses. About half of the 10-figure price tag is an estimate of the profits a drug company might have made, over the course of bringing a product to market, if it had instead invested its capital elsewhere. Calculating forgone profits is, according to Light, a reasonable way for a company

to determine if it should go ahead with a project. “What is not reasonable,” he says, “is to then take that estimate, which is a calculation of investment, and claim it as a cost against society.”

The cost estimate of successful drug development also includes the cost of research that fails to net new products. Again, this is a common practice. But critics claim the pharmaceutical industry misleads the public by claiming it costs more than a billion dollars to overcome the 1-in-5000 odds of a new chemical compound making it to market. About two-thirds of true research and development costs, Light says, are incurred in phase III trials, where the odds of success are about 3 in 5. Earlier trials are relatively inexpensive, and most compounds don’t even make it to the trial stage.

Promoting a link between long odds and big costs, some claim, makes high drug prices more palatable. According to Light, it is just another part of a bigger problem: the growing influence of the marketing department in the lab.



In 2003, economists with ties to the drug industry claimed it cost US\$802 million to develop a new drug. Some say it now costs between \$1.3 billion and \$1.7 billion, but there is much debate about those figures.

This has become a concern for many health researchers, who note that 6 of 7 new drugs offer little, if any, clinical advantage over existing drugs.

“It’s business,” says Light. “It’s not unlike marketing the newest version of a cellphone.”

In their critique of the 2003 economic study, Light and Warburton also note that it only took into account new chemical entities that drug companies had researched, discovered and developed in-

house. These are much more costly to develop than new formulations or combinations, though they account for less than a quarter of the drugs approved by the US Food and Drug Administration.

DiMasi and his coauthors responded by writing that active ingredients are the best units of observation for calculating development costs (*J Health Econ* 2005;24[5]:1034-44). Counting drug approvals is inferior, they wrote, because the new formulations and combinations that drug companies develop are based on their existing novel molecular entities, which required substantial investments to discover. The authors also refuted the challenges on the validity of their industry-supplied data, stating that they had performed numerous internal and external checks.

With regard to an industry bias toward overstating costs, DiMasi and colleagues wrote that this too is false: “Those familiar with the commercial drug development process uniformly recognize that, on average, drug development is in some sense costly, risky, and lengthy. There appears to be little reason for firms to fabricate to achieve particular results when the acknowledged reality supports such basic claims.”

Light and Warburton, however, remain skeptical. Greater transparency is needed, Light suggests, and one way to accomplish this would be to run more publicly funded trails. This could provide greater insight into actual costs and lead to more efficient trail designs. In the meantime, Warburton would like to see health care economists provide cost ranges rather than point estimates, to reflect the huge variability in funds required to bring different drugs to market.

Neither puts much stock in the pharmaceutical industry’s complaints about the rising cost of research and development. Light acknowledges that drug company profits have dipped, but only from “huge to very large.” Warburton concurs: “You can’t say that they are suffering. They spend more on marketing than they do on research.” — Roger Collier, *CMAJ*

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