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**Corruption of Pharmaceutical Markets: Addressing the Misalignment of Financial Incentives and Public Health**

Marc-André Gagnon

### **The Disconnection between Health Ethics and Business Models**

This article argues that the misalignment of private profit-maximizing objectives with public health needs causes institutional corruption in the pharmaceutical sector and systematically leads firms to act contrary to public health. The article analyzes how financial incentives generate a business model promoting harmful practices and explores several means of realigning financial incentives in order to foster therapeutic innovation and promote the rational use of medicines. These means are:

1. Fines and criminal penalties for illegal conduct.
2. Tax policy to promote specific corporate activities.
3. New forms of prescription drug pricing, such as reference-based pricing (RBP) and value-based pricing (VBP).

Over the last two decades, the dominant business model of major pharmaceutical companies has been characterized by massive spending on promotion. In particular, there has been an explosion of pharmaceutical promotion directed towards physicians.<sup>1</sup> At the same time, little therapeutic innovation has been coming out of these firms' research labs.<sup>2</sup> According to Bill Burns, chief of Roche's pharmaceutical division, the dominant business model in pharmaceuticals can be characterized as the "me-slightly-different-marketed-like-hell" model.<sup>3</sup> It is a model based on the overpromotion of "blockbuster" drugs, many of which do not even provide any therapeutic advance.<sup>4</sup>

Drug promotion is not objectionable *per se* if its use simply disseminates information and evidence in order to promote the rational use of medicines. But in fact, it regularly involves illegal off-label promotion of prescription drugs,<sup>5</sup> kickbacks and financial incentives to influence physician prescribing,<sup>6</sup> and the dissemination of biased information to health care professionals.<sup>7</sup> This state of affairs should not be surprising if we look at the economics of this sector. While drug companies supply new medicines, demand comes from physicians prescribing products without paying for them. This is one of the rare economic cases in which demand has no budget constraints. It was estimated that, in the United States, the pharmaceutical industry spends up to \$42 billion in promotion towards physicians every year, which is, on average, \$61,000 per physician to influence their prescribing habits and generate profits.<sup>8</sup>

Moreover, a growing body of evidence demonstrates that promotional activities are not confined solely to marketing, but are becoming an integral part of how medical research is being organized in the private sector. Research and development are often organized to create a sales argument for drug representatives in order to increase the sales

of products with little therapeutic benefit and sometimes with undisclosed adverse effects.<sup>9</sup> This dominant business model relies on several corporate strategies, including systematic ghostwriting and publication planning,<sup>10</sup> leveraging systemic conflicts of interests of key opinion leaders,<sup>12</sup> seeding trials designed to introduce a new product instead of testing a scientific hypothesis,<sup>13</sup> failing to disclose negative results from studies,<sup>11</sup> and sometimes even bullying independent researchers who arrive at unfavorable conclusions.<sup>14</sup>

It is of little use to blame the pharmaceutical companies for lacking corporate social responsibility if current financial incentives promote such practices. In fact, because these incentives are systemic, the concept of institutional corruption<sup>15</sup> can be used to describe the dynamics of influence at work in the drug industry, leading the institutions underpinning medical research and physicians' prescribing behavior away from their ethical purposes, even when quid pro quo corruption itself is not involved.<sup>16</sup> To tackle this problem, then, one must change the systemic financial incentives at work.

### **Pharmaceutical Markets and Financial Incentives**

Pharmaceutical markets are among the most regulated markets. Regulations oversee how drugs are discovered, produced, marketed, and dispensed.<sup>17</sup> A set of institutional devices supports investment in pharmaceutical research and development, including patent protection, data exclusivity, tax credits, special programs to support research for orphan drugs, and state financial incentives to promote business-university partnerships. The sale of pharmaceutical products is also heavily regulated, with an approval process requiring a series of clinical trials to prove that the product is nontoxic and that it provides greater

benefit than a placebo. Most pharmaceutical products can be accessed only with a prescription from a health care professional and must be dispensed by a pharmacist, each following an extensive set of regulations governing their respective professions. The content of pharmaceutical advertising, both to professionals and to consumers, is also heavily regulated.

Physicians' indifference to price when prescribing pharmaceutical products makes them profitable targets for promotion. Furthermore, when patients buy pharmaceutical products, they rarely pay the full price themselves. Drug coverage is often provided through third-party payers: insurance companies in the case of private health benefits (normally negotiated collectively by employers) or the state in the case of public drug coverage. Most drug coverage systems specify which drugs will be reimbursed; for example, by managing drug formularies or by requiring substitution when generic products are available. Drug pricing and reimbursement varies greatly from one country to another, with most countries using some form of price regulation for prescription drugs.<sup>18</sup> For many drug plans, health technology assessment—comparing drug costs with therapeutic benefits—has become central in determining the price of pharmaceutical products and establishing the modalities for access and reimbursement.<sup>19</sup>

Pharmaceutical markets can be compared to a dinner for three: the first person (the physician) orders the meal (from a heavily regulated menu), the second person (the patient) eats it, and the third one (the third-party payer) pays for it.<sup>20</sup> While the third person might want to have a say about which meal is being ordered, the waiter is pretty aggressive in promoting the newest (patent-protected) meals—which also happen to be the most expensive.

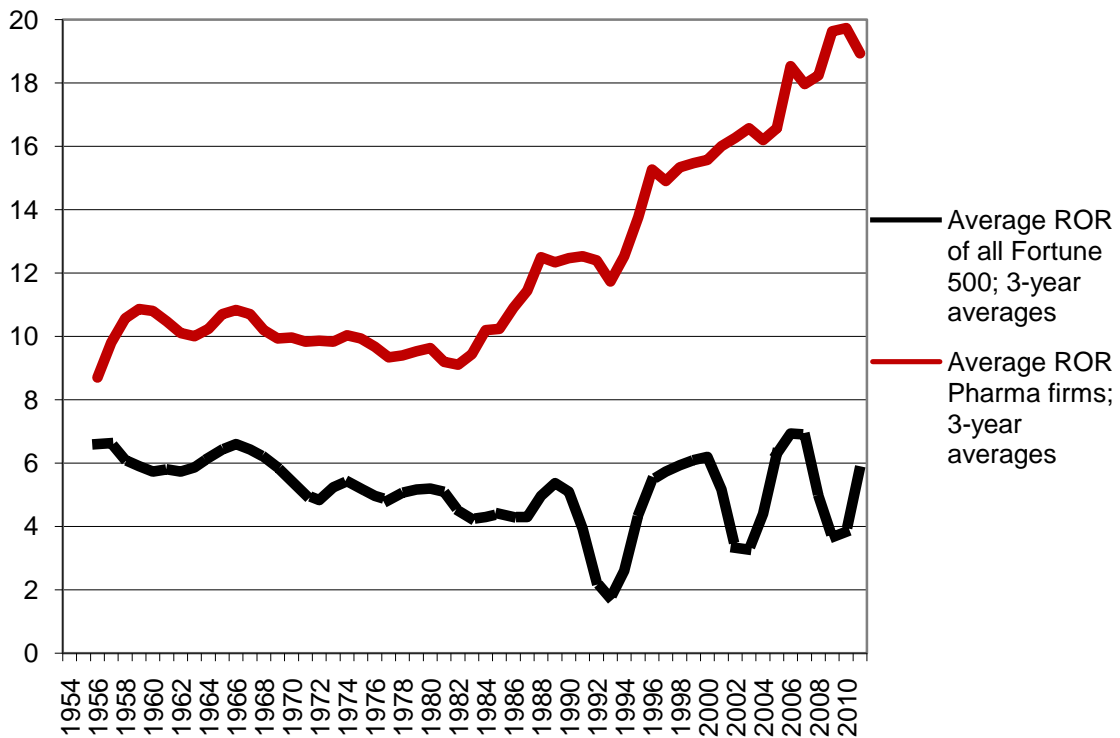
Pharmaceutical firms not only produce new medicines, they also help shape demand and the rules of the game in several ways. For example, they engage in massive lobbying to extend patent protection,<sup>21</sup> increase tax credits, reduce the standards in the drug approval process, and maintain secrecy over clinical trial data. The major pharmaceutical firms, like the dominant corporations in any industrial sector, use their concentrated private power to influence the political process in order to shape markets in accordance with their economic interests. Through massive marketing and promotional campaigns, drug firms also shape and intensify the demand for their products.

The dominant pharmaceutical business model can increase a firm's earning capacity by distorting medical research and medical practice. Objectionable corporate strategies are the product not of rogue corporations, but rather of systemic market incentives. Individual companies are left with little choice but to use these objectionable practices in order to survive in the corrupt market structure.

The importance of institutional corruption in the pharmaceutical sector can be easily established: in the last 20 years, fewer new molecular entities (compounds without precedent among regulated and approved drug products) have been launched on the market every year,<sup>22</sup> with the vast majority of new drugs offering little or no therapeutic advance over existing products.<sup>23</sup> The National Institute of Health is addressing the innovation crisis, in part by creating a major public research lab to develop new drugs.<sup>24</sup> Nevertheless, dominant pharmaceutical companies continue to make record profits in spite of the lack of therapeutic innovation. Figure 1 shows the evolution of profit rate for major U.S. pharmaceutical companies compared with that of major U.S. companies in other sectors.

**Figure 1**

**Net Return on Revenues (ROR) of an Average U.S. Major Pharmaceutical Company Compared with That of an Average *Fortune 500* Company (1954-2011, three-year averages)**



Source: *Fortune 500* database<sup>25</sup>

If we keep in mind the context of the innovation crisis since the 1990s, Figure 1 shows clearly that a pharmaceutical firm does not need to come up with new beneficial drugs to increase its earnings. In fact, it becomes clear that the profit motive in the

pharmaceutical sector does not encourage the development of new drugs as the main way to increase earning capacity. One can thus infer that the industry's business model does not rest on therapeutic innovation and the rational use of medicines and might instead rest on the institutional corruption of medicine through the further entrenchment of harmful practices.

This business model encourages physicians to prescribe newer and more expensive products that may provide less therapeutic benefit or inflict more harm than older and cheaper products. For example, the new generations of antihypertensive drugs<sup>26</sup> and antipsychotic drugs<sup>27</sup> are dominating their respective markets despite being less efficacious and more expensive than older generations of those drugs. Furthermore, for 70 percent of patients taking antidepressants, the drug has been shown to be no more efficacious than a placebo.<sup>28</sup> Another example is that, for decades, the industry has used ghostwriting and the nondisclosure of negative studies to promote the widespread prescription of hormone replacement therapy during menopause in spite of significant adverse effects outweighing the benefits of the treatment.<sup>29</sup> It appears that physicians' prescribing habits are informed not only by clinical evidence, but also by marketing and by the corruption of science, both in terms of lavish promotional campaigns and ghost management of medical science.<sup>30</sup> In many ways, one can say that evidence-based medicine has been replaced by a marketing-based medicine in which research is often organized to provide tailored truths for marketing purposes.<sup>31</sup>

In the United States, authorities have already started to react to the institutional corruption of the pharmaceutical sector. For example, in 2008, Senator Charles Grassley (R-IA) investigated ghostwriting and illegal promotion. Since 2007, all clinical trials are

required to disclose their protocols and results in a national registry in order to reduce the systematic selective reporting of clinical trial results. Some states now require the full disclosure of every payment received by physicians from drug companies. While these reforms increase transparency, they do not change the institutional architecture of the market and therefore do not change the dominant business models.<sup>32</sup> The roots of institutional corruption lie first and foremost in the fact that financial incentives are misaligned so as not to drive companies to achieve optimal health outcomes. This problem must therefore be tackled by transforming the financial incentives. Three potential solutions can help reconcile pharmaceutical profits and public health: fines, taxes, and pricing.

### **Increasing Fines for Misconduct**

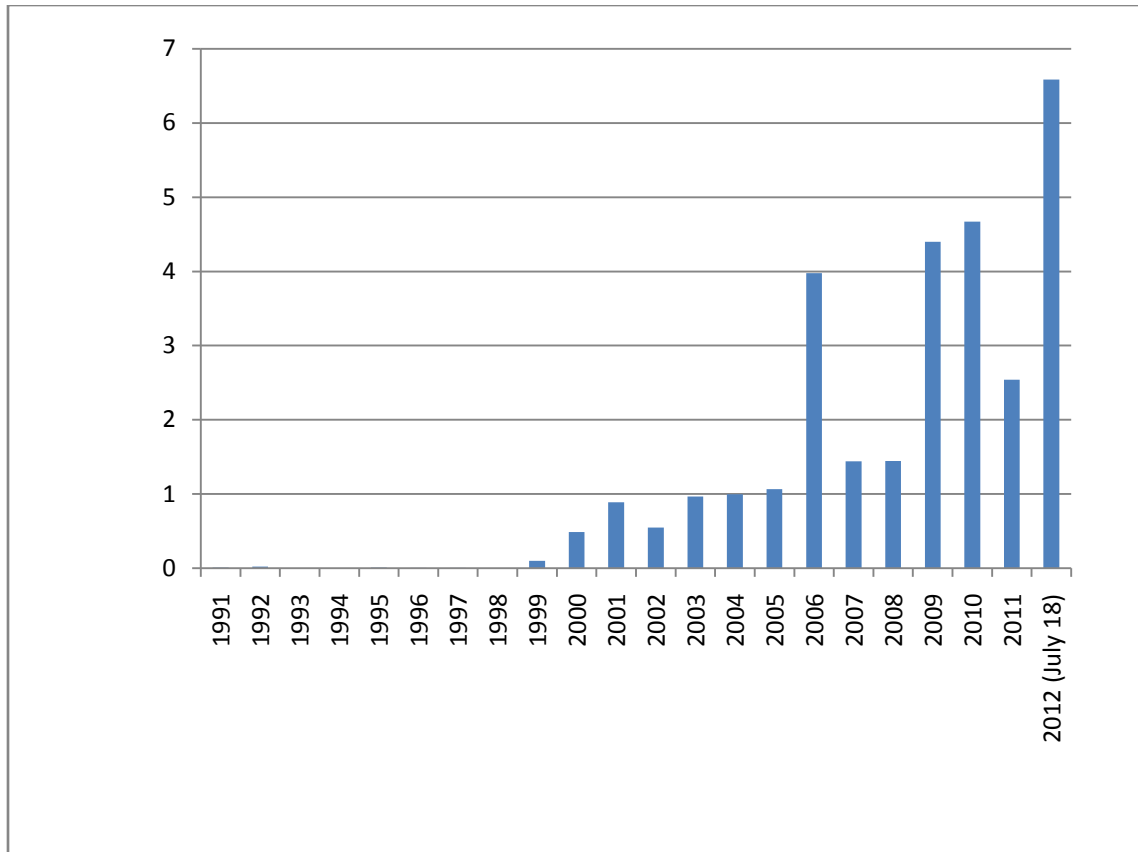
One reform seems self-evident: Increase fines and penalties for illegal behavior in order to transform the financial incentives at work.

### **Figure 2**

#### **Financial Penalties against Pharmaceutical Companies in the United States**

**(\$billion), 1991-2012**





Source: Public Citizen<sup>33</sup>

The importance of illegal practices can be observed in the mounting fines against drug companies in the last decade in the United States. Since 1991, drug companies have paid \$30 billion in financial penalties in the United States. These penalties arise mostly from out-of-court settlements for Medicare fraud, unlawful promotion, kickbacks, monopoly practices, and the concealment of study findings. In rare cases, there were fines for poor manufacturing practices, environmental violations, financial violations, and illegal distribution. While Medicare fraud is by far the most common reason for such settlements, unlawful promotion incurred the largest fines<sup>34</sup> and seems to be the norm, at

least for some categories of prescription drug. A case in point is atypical antipsychotics, one of the most prescribed drug categories: In 2007, Bristol Myers Squibb paid \$515 million in fines for unlawful promotion, kickbacks, and Medicare fraud in connection with the drug Abilify; in 2009, Eli Lilly settled for \$1.4 billion over charges of off-label promotion for Zyprexa and Pfizer settled for \$301 million on charges of off-label promotion and kickbacks for Geodon; in 2010, Astra-Zeneca settled for \$520 million on charges of ghostwriting, off-label promotion, and kickbacks for Seroquel; and in 2012, Johnson and Johnson settled for \$1.2 billion on charges of off-label promotion and concealing information about the adverse reactions to Risperdal. According to IMS Health data, these five drugs remain the five best-selling atypical antipsychotic drugs in the United States, accounting for more than 75 percent of sales in the \$18.2-billion market for antipsychotics in 2011.<sup>35</sup>

Fines for drug companies have recently set record highs. In 2009, Pfizer paid what, at the time, was the largest criminal fine ever imposed in the United States (\$2.3 billion) in an out-of-court settlement for the off-label promotion of Bextra and other drugs. GlaxoSmithKline surpassed this record in 2012 with a settlement for \$3 billion after pleading guilty to charges of unlawful promotion and failure to report safety data for drugs such as Avandia, Paxil, and Wellbutrin.

One might suppose that these fines would serve as a deterrent against socially harmful practices. However, given the profits and revenues of these companies, such fines have little financial impact. During the period for which GlaxoSmithKline settled for \$3 billion, sales for Avandia, Paxil, and Wellbutrin were \$10 billion, \$12 billion, and \$6 billion, respectively.<sup>36</sup> The \$30 billion paid for all criminal fines since 1991 is less

than half the profits made in 2009 alone by just the 10 largest U.S. drug companies appearing in the *Fortune* 500.

As long as the level of fines is not significantly higher, it will remain profitable for drug companies to engage in such practices that undermine public health. Higher fines for illegal practices, however, can have unintended consequences. Fines for such illegal activity are normally covered through insurance premiums paid by the companies. Higher fines thus mean increased risk-premiums, which, in turn, create an important barrier to entry for newcomers in the sector. What could function as an obstacle to business as usual can become a differential advantage for the dominant pharmaceutical firms, since they are better equipped than smaller firms to face the increased regulatory burden and higher insurance premiums.<sup>37</sup> Increasing the level of fines might reduce the incidence of some illegal practices, but might also reduce competition and consolidate even further the power of the major pharmaceutical companies.

Another option is to complement financial penalties with criminal prosecution of corporate officers, directors, and managers. Few pharmaceutical executives have served any jail time for unlawful practices that have sometimes caused the death of thousands of patients.<sup>38</sup> In his remarkable book on corporate crime in the pharmaceutical sector, John Braithwaite reminds us, however, that corporations can still resort to defensive strategies such as having pre-selected executives ready to take the blame in case of criminal prosecution.<sup>39</sup> Although higher fines and criminal prosecutions should be used to reduce the financial incentives for many harmful corporate practices, authorities need to proceed with caution and understand the sector's competitive dynamics and its ability to adapt to such penalties.

## **Using Taxes to Transform Financial Incentives**

In 1920, Arthur Cecil Pigou developed the concept of “negative externalities” to explain that the social cost of an activity might not be covered by the private cost of the producer.<sup>40</sup> In order to compensate for such negative externalities, he suggested imposing taxes to cover the costs associated with the externality. The cost of the externality thus becomes included in the private cost of production and the state gains the resources necessary to compensate the social cost generated by the manufacturer. In economics, the idea of taxing negative externalities is now referred to as a “Pigouvian tax.”<sup>41</sup>

Could a tax reduce those pharmaceutical company activities that generate profits at the social expense of unnecessary treatments, adverse effects, and treatments that cost more without doing more? Taxing only undesirable activities is difficult since, if we could easily identify them, they would not be taxed but eliminated. A possible solution is to tax all promotional activities directed towards health care professionals and use the revenues to promote more rational uses of medicines.

The idea of imposing a tax on promotional expenditures aimed at physicians is not far-fetched. In Italy, since 2005, the regulatory agency for prescription drugs, the Agenzia Italiana del Farmaco (AIFA), required all international and national pharmaceutical companies operating in Italy to contribute five percent of their yearly expenditure for promotional activities targeting Italian health professionals to a national fund for independent research.<sup>42</sup> Promotional activities included advertisements, supporting materials, meetings, trade fairs, freebies and gifts, but not the salaries of sales

representatives. In the first three years of the program, AIFA collected around \$60 million per year, half of which was used to support independent research and independent drug information<sup>43</sup> and half to pay for expensive orphan drugs—those developed to treat rare diseases.<sup>44</sup> In the United States, a tax like that could reduce returns on promotional spending and create public funding for independent drug information; for example, by funding public clinical trials to determine which drug should be used as a first-line treatment for a specific condition or by funding academic detailing or non-commercial-based educational outreach to promote the rational use of medicines.

Some issues need to be taken into account before implementing such taxes. First, if the funding of programs for public research or academic detailing is determined by how much tax can be levied from pharmaceutical promotion towards physicians, then those programs can become dependent on the activity that creates negative externalities. The agencies managing the programs could end up calling for *more* corporate spending on drug promotion.<sup>45</sup> This problem can be resolved by disconnecting program funding from the amount of taxes obtained. In that case, however, we end up not with a tax to recoup the negative externality, but simply a tax to reduce the financial returns on promotion.

The second problem is that such a tax would suggest that all promotional activity aimed at physicians induces a social cost. In theory, pharmaceutical promotion can be useful to disseminate knowledge and make health care professionals aware of new treatments, in which case a tax would be counterproductive. However, a systematic review published in *PLoS Medicine* in 2010 showed that the existing literature offered no support for the idea that pharmaceutical promotion improves physicians' prescribing

habits, while the bulk of the literature indicates that pharmaceutical promotion can undermine the rational use of medicines.<sup>46</sup> But then, if most promotion aimed at health care professionals undermines the goals of medicine, why not just prohibit promotion rather than taxing it? In spite of these problems, and because the outright elimination of pharmaceutical promotion might not be politically or legally feasible, a tax on promotion could help persuade companies to spend less on promotion and more on developing innovative therapeutics.

### **Pricing Based on Therapeutic Value**

Where fines or taxes focus on the fine-tuning of financial incentives, transforming the rationale behind drug pricing can lead to systemic reform of the financial incentives in place.<sup>47</sup> Two approaches to transforming pharmaceutical pricing are being explored in different countries: reference-based pricing (RBP) and value-based pricing (VBP).<sup>48</sup>

The rationale behind RBP is that, since most new drugs do not offer any greater therapeutic benefits than others already on the market, therapeutically interchangeable drugs should be competing on price to gain market share. With RBP, a standard price or reimbursement level is set, often based on the lowest-priced drug in the class, and manufacturers may then price their drugs above or below this reference price as they see fit. If patients choose a more expensive drug than the reference price, then they pay for the difference out-of-pocket. RBP has been used in Canada (British Columbia), Germany, Netherlands, New Zealand, Norway, and Spain and by the Veterans Health Administration and employer-sponsored drug plans in the United States,<sup>49</sup> where RBP is

often described as a “maximum allowable cost (MAC) program.”<sup>50</sup> By encouraging market competition between therapeutically interchangeable drugs, RBP significantly reduces prices, increases the use and adherence of targeted drugs, and promotes switching from expensive products to lower-cost alternatives.<sup>51</sup>

The advantage of RBP is that it establishes a reference price above which a budget constraint becomes central in determining which therapeutically equivalent product will be prescribed. Going back to the “dinner for three” metaphor, the third-party payer can now establish some pricing conditions to influence the physician’s choice of therapeutically equivalent products to prescribe. The growing influence of the third-party payer also curbs the waiter’s aggressive and sometimes unethical promotion of products. Pharmaceutical markets in which there is competition amongst therapeutically equivalent products will offer clear financial incentives for drug firms: New products offering a significant therapeutic advance will command a price premium, while new drugs therapeutically equivalent to existing ones will be put in competition with other products and earn much smaller revenues.

The limits of RBP, however, are also important. Therapeutic equivalence is not always obvious; for one thing, and we need to consider that different patients may react differently to “therapeutically equivalent” drugs especially in some therapeutic niches like anti-cancer drugs. RBP cannot apply to all therapeutic categories, but it certainly can be used for some popular categories such as proton pump inhibitors, statins, and calcium channel blockers. Another risk is that third-party payers might use RBP to reduce treatment costs to the detriment of patients’ health; caution would be required because the impact of RBP on patients’ health has not yet been carefully studied.<sup>52</sup>

A second type of pricing policy based on therapeutic value is called value-based pricing (VBP), whereby a price is negotiated on the basis of the new drug's therapeutic value, as determined through health technology assessment.<sup>53</sup> The idea is simple: getting value for money by paying for health outcomes. In order to do this, however, we need to measure therapeutic value and establish a price for each unit of incremental therapeutic value. Health technology assessment, by measuring the incremental therapeutic value of a drug through quality-adjusted life years (QALYs), can be used here as a way to bridge science and policy. Based on a sociopolitical decision reflecting societal values, authorities can fix the price they are ready to pay for each QALY (for example, \$50,000 per QALY). Such a threshold is important, as it functions as an opportunity cost. If the cost of a health technology is more than \$50,000 per QALY, then public health is better served by spending money on some other health technology for which the cost is at most \$50,000 per QALY.

Many countries already use health technology assessment to decide whether or not to reimburse a drug.<sup>54</sup> VBP goes one step further by determining how much manufacturers will be paid for a patent-protected brand-name drug, based on the incremental therapeutic value it provides. In our “dinner for three” metaphor, VBP means that the third-party payer will let the physician prescribe whatever he wants, but will pay the waiter only according to that treatment's incremental utility for the patient over other existing treatments. The advantages of VBP are that it makes evidence-based medicine (rather than marketing-based medicine) central to the architecture of the pharmaceutical market and it directly aligns financial incentives with improving health outcomes. The pharmaceutical market would be reconstructed so that the only way for drug companies



to increase their profits would be to increase their contribution to health outcomes. In order to rebuild the pharmaceutical market on evidence-based medicine through health technology assessment, VBP requires institutional capacity to independently assess clinical evidence and even to conduct independent clinical studies to obtain the best available evidence. Such institutional capacity could help tackle corporate practices that create bias in medical research. However, since health technology assessment depends mostly on published medical literature, a greater reliance on health technology assessment might also provide greater incentives for firms to multiply practices to create bias in medical literature. In order to avoid this pitfall, institutional capacity for health technology assessment should rely not only on published medical literature, but also on unpublished data. Greater transparency of unpublished clinical data would significantly improve the quality of health technology assessment.<sup>55</sup>

However, VBP has several limitations. The main problem is the use of QALYs as a metric for incremental therapeutic contribution. Measuring the number of “standardized” life years gained by a population by the introduction of a new health technology is no easy task. QALYs—based on weighted preferences between different states of health—are a very blunt standard. They may not capture well how individuals value certain aspects of health, especially as compared to other aspects of life: they don’t take equity, patient autonomy, and fairness into account because they do not make distinction in gained life years by age or disease severity.<sup>56</sup> Another problem is that an orphan drug treating a rare disease might offer a fantastic medical breakthrough, but its contribution in QALYs to the overall population would be slight. VBP should thus consider a system of exceptions for orphan drugs.

Another limit of VBP is that it can only be implemented at a national level and in countries in which the state acts as the major or only drug purchaser. It thus seems suitable for European countries with universal pharmacare systems, but would be much more difficult to implement in the fragmented drug coverage systems of the United States and Canada. Also, VBP can only realign financial incentives if enough countries adopt it in parallel. At present, only Sweden officially uses VBP<sup>57</sup> and the United Kingdom has announced that it will implement VBP in 2014.<sup>58</sup> VBP remains in theory the best way to realign financial incentives with public health, but the success of its implementation on a large scale remains uncertain. As they say in England, “the proof is in the pudding,” and the U.K. experience with VBP should be followed carefully.

## **Conclusion**

Imposing higher fines on unlawful promotion, taxing promotional activities, and using RBP or VBP could help reduce unlawful promotion. Higher fines for ghostwriting and for concealing research results and greater institutional capacity for health technology assessment could help deter unethical scientific practices that create bias in medical research. Such reforms, however, will have limited impact unless there is also greater transparency in drug-company-sponsored clinical trials. More radical solutions include (a) an outright ban on pharmaceutical promotion deemed to be harmful to prescribing habits and (b) publicly funded and conducted clinical trials. However, such radical reforms are probably politically unrealistic, while fines, taxes, and pricing reform could

go a long way towards transforming the financial incentives in the pharmaceutical sector and reducing its institutional corruption.

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35. IMS Health data about sales for each drug are available the following website:

<<http://www.drugs.com/stats/top100/2011/sales>> (last visited June 17, 2013). Data about total sales for antipsychotic drugs are available on the IMS Health website:

<<http://www.imshealth.com/portal/site/ims/menuitem.5ad1c081663fdf9b41d84b903208c>

22a/?vgnextoid=fbc65890d33ee210VgnVCM10000071812ca2RCRD&vgnextfmt=default  
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37. *The Economist*, “An Unhealthy Burden,” June 30, 2007.

38. For example, in his testimony for the US Senate Finance Committee, David J. Graham, Associate Director for Science and Medicine in FDA’s Office of Drug Safety, estimated that the drug Vioxx caused between 88,000 and 137,000 excess cases of heart attacks in the United States. Of these between 30% and 40% died. The drug was marketed by Merck between May 1999 and June 2004 in the United States. To promote the drug Merck organized a ghostwriting campaign involving around 96 scientific articles. Key ones omit mentioning the death of some patients during clinical trials. During a class action lawsuit against Vioxx in Australia in 2009, it was discovered that the company had created a fake medical journal for Merck—the *Australasian Journal of Joint and Bone Medicine*, published by Elsevier. Merck’s internal e-mails, revealed during the class lawsuit, exposed that the company drew up a hit list of “rogue” researchers who needed to be “discredited” or “neutralized.” Eight researchers at Stanford complained that they received threats from Merck after publishing unfavorable results. In the United States, the only charges against the company have been charges of unlawful promotion, for which the company agreed to pay \$950 M in an out-of-court settlement. Between 1999 and 2004, sales amounted to \$11 billion in the United States. See M.-A. Gagnon and S. Sismondo, “The Ghosts of Medical Research,” *Genetic Engineering and Biotechnology News* 30, no. 10 (May 15, 2010); P. Loftus and B.

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