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Combating corruption in the pharmaceutical arena

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Abstract

Corruption in healthcare generally and specifically in the pharmaceutical arena has recently been highlighted in reports by Transparency International. This article focuses on four areas of corruption: legislative/regulatory, financial, ideological/ethical, and communications. The problems identified and the solutions considered focus on structural considerations affecting how pharmaceuticals are discovered, developed, distributed, and ultimately used in clinical settings. These include recourse to user fees in the regulatory sphere, application of intellectual property rights to medical contexts (patents and access to research data), commercial sponsorship of ghost writing and guest authors, linkage/delinkage of the funding of research and overall health objectives to/from drug pricing and sales, transparency of payments to healthcare professionals and institutions, and credible regulatory sanctions. In general, financial and other incentives for all actors in the system should be structured to align with the desired social outcomes — and to minimise conflicts of interest among researchers and clinicians.

Introduction

The governance of public healthcare and medical research is strategically important for public policy; however, its technical complexity creates the potential for corruption that can undermine public health objectives. The issue of corruption has been highlighted in recent articles (1) and especially in two 2016 reports from Transparency International that document how "corruption is part of doing business in the healthcare sector all over the world" (2) and defend the view that "combatting policy and structural issues that increase corruption vulnerabilities in the pharmaceutical sector will help prevent unnecessary medicine expenditure costs and ideally improve health outcomes for all" (3).

Many types of corruption in the pharmaceutical sector are equally rampant in high-income countries and low-income ones; for example, conflicts of interest, misrepresentation, lack of transparency, and corporate influence over prescribing habits (4). Of equal import to documenting instances of corruption is identifying strategies and tactics to reduce corruption. This undertaking is particularly meaningful given the inclusion of reduction of corruption (and bribery) in the

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Sustainable Development Goals as one of the necessary target actions needed to achieve Goal 16: "[to] promote peaceful and inclusive societies for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at all levels" (5).

Following on from the Transparency International reports, we focus specifically on corruption in the pharmaceutical sector. We identify some core weaknesses in this sector's governance practices that incentivise corruption and illustrate these weaknesses with examples from the United States (US) and Canada, and also from India, to emphasise the global nature of the problem and its relevance to both developed and developing countries.

Corruption and unethical practices in the pharmaceutical sector have been well documented (6, 7), including corruption in clinical trials (6), pharmaceutical companies (8), the medical profession (9), and drug regulatory systems, such as the US Food and Drug Administration (FDA) (1). Here we broaden the scope of previous scholarship and take a thematic approach, focusing our discussion on four types of corruption—legislative/regulatory, financial, ideological/ethical, and communications — with a final discussion of possible structural solutions. These categories are by no means mutually exclusive; in fact, they often occur in combination. We use a wide definition of corruption that includes not just illegal activities but also an impairment of integrity or moral principle that, among other outcomes, hides the true effectiveness and safety of products and/or makes them unavailable to the populations that need them by virtue of their cost. By understanding the weaknesses within the sector, we can seek solutions to best address them, as we do in the final section of our article.

Types of corruption

Legislative/regulatory corruption

Legislative/regulatory corruption happens when legislators — yielding to pressure —enact laws or regulations that benefit a particular sector or weaken the government's ability to regulate and advance public interest. For example, user fees create government dependence on industry, favour Big Pharma by making it more difficult for smaller players to enter the market, and — more seriously — increase the ease with which new, potentially harmful products are approved for use. This is evidenced by the fact that, soon after the initiation of user fees in the US, a survey found almost one in five FDA scientists felt pressured to approve drugs despite safety concerns (10). A wealth of research demonstrates a link between shorter drug approval times and a subsequent increase in safety problems in the post-market phase, as well as a greater need for drugs to be removed from the market (11-15).

As another example of legislative corruption, the act that established Medicare Part D, providing coverage of outpatient medicines for people aged 65 and over in the US, specifically forbade the government from negotiating prices (16). This prohibition occurred despite prescription drug prices for seven top-selling drugs in the US being significantly higher than those in multiple other countries, even after taking discounts into consideration (17). Overall, the price of patented drugs in the United States is, on average, 138% more than the median of Organisation for Economic Co-operation and Development (OECD) countries (18). Figures from the OECD put per capita US spending on pharmaceuticals in 2013 at $1026 versus the OECD mean of $515 for all 29 industrialised countries included in the survey (19). In such a context, a legislated impediment to market competition through negotiation of prices is clearly unethical and inefficient. The fact that this impediment could have been instituted at all is a symptom of underlying corruption, plausibly attributable to the undue influence of interested parties over the legislative process and to the predominance of the desire to be re-elected over the duty to serve the greater public good.

A third area where governments have adopted the interests of the pharmaceutical industry to advance the latter's objectives has been intellectual property rights (IPRs). IPRs came to the fore during the negotiations that led to the 1994 Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), one of the fundamental treaties of the World Trade Organization (WTO) (20). Prior to the WTO, governments—especially in low-and middle-income countries (LMICs)—often did not grant patents for pharmaceuticals. In the case of India, the country only allowed process patents—patents on how the product was made but not on the actual product itself. After sustained lobbying by the pharmaceutical, entertainment, and software industries, governments in the US and the European Union pressed for and were eventually successful in getting a 20-year patent term incorporated into the TRIPS Agreement (20). Longer patent terms delay the introduction of low-cost generics, the most effective way of lowering drug prices in LMICs (21).

The establishment of the global intellectual property regime under the WTO was the result of negotiations where not all relevant interests were represented, where few LMICs had full information about the consequences of the agreement, and where coercion was used in persuading importers of intellectual property rights to sign the agreement that significantly increased the costs of prescription drugs (22).

Since 2005, one of the conditions for Indian membership in the WTO has been allowing full product patenting. As a result, in 2016, India granted a patent to Pfizer for its pneumonia vaccine Prevnar 13, thereby ensuring a monopoly for the company until 2026 (23). Regulatory corruption in India contributes to why substantial numbers of unapproved formulations of non-steroidal anti-inflammatories, anti-depressant/benzodiazepine, and antipsychotic fixed-dose combination products remain on the market despite concerns about their effectiveness and safety (24).

Financial corruption

In the context of this paper, financial corruption is defined as the use by pharmaceutical companies of financial power to create undue influence over medical research and prescribing habits. Corrupt practices include illegal or lavish promotion, misrepresentation of harms and benefits, ghostwriting and guest-authoring, ghost management, payments to physicians, and outright fraud. Since 1991, drug companies have paid $35.7 billion in civil and criminal penalties in the US—more than any other industry (25). GlaxoSmithKline alone has paid $7.9 billion, of which $127 million was in criminal penalties for withholding data from the FDA (26,27). Unfortunately, profits generated through violations currently far outweigh penalties (28,29). Companies simply budget for expected penalties. What is far more concerning is that almost no major pharmaceutical company executive has ever gone to jail for criminal acts (29,30).

Ideological/ethical corruption

Ideological/ethical corruption speaks to the manipulation of public trust to benefit companies while harming or defrauding patients. Examples include funding patient advocacy groups to carry corporate messaging (31), normalising and downplaying financial conflicts of interest between industry and academic institutions and researchers (32), and using the World Health Organization (WHO) logo in advertisements for medicines to imply WHO endorsement of the messages carried in the ads (33). Incentives for corruption can result from a misalignment between financial benefits for drug companies and social good.

Profits depend on maximising drug sales, not optimising health outcomes, for which the public bears all the risk. Accumulating capital through product sales requires controlling public perceptions and shaping social narratives about health, illness, and medicines and is accompanied by strategies, including ghost management and ghostwriting, that shape both the demand for medicines and the research to support their development and use (34). We believe that ghostwriting is an example of ethical corruption in so far as it is an abuse of power by the companies that produce or sponsor the ghostwritten articles and the clinicians or scientists who are named as authors on the published articles. Guest authorship requires the guest authors to shirk their professional responsibilities and abandon their concern for the objectivity and integrity of research and the wellbeing of patients. Ethical concerns here surpass plagiarism and the misattribution of authorship. Misinterpreting and manipulating trial data often minimises or masks unwanted side-effects and exaggerates treatment effectiveness—both to the detriment of users. In ghostwritten studies, moreover, the raw data related to the trial are protected as intellectual property and typically remain under the control of the pharmaceutical company (35). Maintaining data control also means that companies control the way these data are published. For instance, most negative clinical trials examining the effectiveness of antidepressants are either not published or are published in a manner that makes them appear as positive (36).

Another concern relates to unethical behaviour in the production of clinical data. The clinical trial for two human papilloma virus (HPV) vaccines on tribal girls, a marginalised population, in Andhra Pradesh in 2009 is a good example. The HPV vaccines were administered to girls through "vaccination camps" held at schools and hostels. In one case, consent for vaccination was given by the teacher in charge of a hostel and in another probably by the hostel warden. In some cases, the parents of the girls were not told about the vaccinations. Many of the girls who received the vaccine were prepubescent although the consent form states that the vaccine would be administered to adolescent girls (37).

Communications corruption

The pharmaceutical communications industry is critical for developing and guiding spin-strategies by shaping the disease narrative through publication planning, which involves extracting "the maximum amount of scientific and commercial value out of data and analyses through carefully constructed and placed papers" (34: p 171). The entire process of undertaking clinical research, analysing and writing up its results, and submitting articles to journals is performed with a commercial motivation that is ultimately under the control of the company seeking to market a product (34). For the pharmaceutical industry, the real market value is no longer in producing drugs but in producing the right medical discourse.

A systematic review has demonstrated that when physicians receive their information directly from the pharmaceutical industry, prescribing—as measured by cost, frequency, and appropriateness—either does not change or deteriorates, barring very few exceptions (38). Another example, from the US, of the corruption in communication is the $5.8 billion spent on direct-to-consumer advertising of prescription medicines (39), when the evidence that this type of activity improves patient outcomes is, at best, extremely weak (40).

Although direct to consumer advertising of prescription drugs is not allowed in India, companies are able to get around this restriction by using social media. On the patient discussion forum Cancer Compass, a friendly medical representative gives the information that the anticancer drug Nexavar (sorafenib), marketed by Bayer, is available in India without stating the price (41).

Recommendations for reducing corrupt practices

To reduce current corrupt practices, we must delink profits from drug sales so that financial incentives for pharmaceutical companies are structured to align with desired social outcomes rather than to make unethical and corrupt practices possible and profitable. For example, payers should not be paying for the drugs in and of themselves but rather for the desired therapeutic effect they bring about. This type of "value-based pricing" not only reduces the incentive to oversell the benefits of drugs, but it also provides financial incentives for medical research that is focused less on me-too drugs and more on breakthrough drugs that could significantly improve health outcomes. While value-based pricing is attractive, it has

several obstacles to overcome. At present, value is based on industry-funded clinical trials, which are more likely to yield positive results and conclusions compared to trials with any other type of funding (42). This model would probably also not be feasible in LMICs because of affordability issues and the total cost of medicines. Even in high-income countries, it may need to be accompanied by other strategies such as tendering and price-volume agreements.

To deal with the problems of companies controlling clinical trials and the data that come out of them, Schafer has proposed what he calls the "sequestration thesis" or the separation of researchers from the process of commercialisation, which would involve the complete isolation of industry from clinical trial data (43). There are what we term "weak" and "strong" variations of this thesis. The weak model is exemplified by the proposal from Finkelstein and Temin (44). They suggest creating an independent, public, nonprofit Drug Development Corporation (DDC) that would act as an intermediary to acquire new drugs that emerge from private sector research and development. Rights to sell the drugs would then be transferred to a different set of firms that would then compete on price.

The stronger version of this model would see an institution such as the National Institutes of Health organise and manage clinical trials and the resulting data with funding from taxes collected from the pharmaceutical industry and/or general tax revenue (8, 45). "Drug companies would no longer directly compensate scientists for evaluating their own products; instead, scientists would work for the testing agency." (45)

In both cases, the authors argue that the companies should continue to fund a significant portion of the research agenda "in order to discourage the wholesale testing of marginal drugs with little therapeutic value, or candidate medicines with little chance of clinical adoption" (45). While companies would continue to develop and market their products they would be separated from the process of generating and interpreting the clinical data. Baker goes even further in arguing for a system whereby all clinical trials would be publicly financed with the cost of the trials in the US being covered through lower drug prices under the Medicare drug programme and other public healthcare programmes (46).

On the global front, there have also been proposals directed at increasing research and development in neglected diseases. One of the key recommendations of the Consultative Expert Working Group on Research and Development, established by the World Health Assembly (WHA) in 2010, was a legally binding research and development treaty to which all countries would allocate 0.01% of their GDP (47). However, when this proposal was put forward as a resolution at a subsequent meeting of the WHA, it was rejected by member states in favour of a voluntary mechanism (48).

Increased accountability and transparency can also counter corrupt practices. Citizens do not always understand or have full information about the drug regulatory process, or how and

why governments make decisions. Government transparency must thus be coupled with the appropriate accountability mechanisms, which ought to cut across financial, performance, and political domains. In addition, sanctions for pharmaceutical companies that violate laws must be punitive enough to discourage such activity. This could involve an escalation pyramid of sanctions such as that which has been advocated by Ayres and Braithwaite, which recommends that as the number and severity of the violations increase, so do the penalties (49). This method should also be adapted for dealing with illegal promotion. Even fines in the range of billions of dollars have failed to control promotion since, as noted above, the profits to be made from this type of activity run into several magnitudes of order more than the value of the fines imposed.

The Physician Payments Sunshine Act (PPSA) in the US is part of the Affordable Care Act and has helped to drive transparency and the possibility for greater accountability by health practitioners and pharmaceutical and medical device companies in the United States. By mandating the public reporting of all payments of $10 or more to doctors and healthcare institutions, the PPSA helps address financial conflicts of interest (FCOI)—an endemic problem in medicine. These private dollars work to fund physician-researchers, who are also subsidised through public research funding mechanisms such as the National Institutes of Health in the United States. These physician-researchers often also have FCOI relationships with drug companies (50), and relationships have been linked with skewed research results in favour of the product being tested (51). Moreover, FDA safety panels and National Academy panels are stacked with physicians who have FCOI relationships with drug companies whose products are under review (52-54). Companies also funnel significant amounts of money into "continuing medical education" for physicians (55), raising questions about whether marketing has replaced education. While only a minor first step, the PPSA allows for researchers and journalists to examine the correlation between industry money and prescriptions and temporal changes in this relationship. In short, transparency creates the possibility of greater accountability, and these rules can help in other areas of science that lack such transparency measures (56).

While FCOI disclosure is necessary, it is not sufficient. The ultimate goal should be to exclude people with FCOI from decision-making capacity. As much as possible, payment for medical research should come from public funds and go to researchers who do not have direct conflicts of interest. More public funding for clinical research will help to prevent researchers from engaging in trials that are being conducted for marketing purposes.

Finally, the medical profession at large must reform itself to focus on best treatments, instead of intentionally organising itself based on the best ways to obtain external corporate funding including, but not limited to, for continuing education. One of the key ways for the medical profession to move towards this goal is to develop more effective methods of

education and communication to clinicians about drug benefits and harms to improve the way that drugs are prescribed and to decrease reliance on biased medical literature and promotion.

Conclusions

We have seen that corruption occurs in the pharmaceutical sector when actors ostensibly responsible for promoting the health and well-being of the population allow themselves to be distracted from this duty by other considerations. The end result of that corruption has meant that instead of medicines primarily being a means to advance healthcare, they have become a means to primarily increase corporate profits. Exploring ways of combating corruption stimulates new discussions about the potential for systemic change. This type of change is necessary to realise societal governance goals and transform ideas of corporate social responsibility to ensure that consumers and their favourable outcomes remain the ultimate goal of pharmaceutical companies in the international market.

Competing interests

Between 2015 and 2017, Joel Lexchin received payment from two non-profit organisations for being a consultant on a project looking at indication-based prescribing and on a second looking at which drugs should be distributed free of charge by general practitioners. In 2015, he received payment from a for-profit organisation for being on a panel that discussed expanding drug insurance in Canada. He is on the Foundation Board of Health Action International. Jillian Clare Kohler is the Director of the WHO Collaborating Centre for Governance, Accountability and Transparency for the Pharmaceutical Sector at the Leslie Dan Faculty of Pharmacy. Paul Thacker reports receiving travel funding from universities to give talks about conflicts of interest. Marc-André Gagnon reports grants from Canadian Institutes for Health Research (CIHR) during the conduct of the study; personal fees from Prescrire International, personal fees from Canadian Association of Pharmacy in Oncology, grants from Canadian Federation of Nurses' Unions, outside the submitted work. James Crombie and Adrienne Shnier report no conflicts.

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