editorials

Oncology Drug Prescribing: The Influences of Greed and Fear

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Both economic and noneconomic decisions are often motivated by greed and fear. Although one would hope that drug prescribing would be evidence-based, greed and fear also factor into such decisions. Wright et al[1] have used the Open Payments database to analyze one source of greed, high payments (in 2018) by pharmaceutical companies to high-profile physicians, also known as key opinion leaders.[2] This study identified the 1% of oncologists who received more than $100,000 US dollars in general payments associated with specific marketed cancer drugs, in aggregate totaling $24 million US dollars, comprising 37% of total industry payments to US oncologists for that year. Although some may be shocked by this analysis, it is consistent with many studies of other specialties.[3]

A more blatant example that greed is motivating is evidence of payments to high prescribers, as exemplified by an analysis by Singh et al of the same Open Payments database (for 2013-2014) in regard to ophthalmologists' usage of antivascular endothelial growth factor drugs to treat various eye diseases. This analysis is of particular interest, given that many ophthalmologists administer miniscule doses of intravitreal bevacizumab, rather than intravitreal ranibizumab or aflibercept (a distinct product from intravenous aflibercept), since all three agents have similar efficacy and toxicity. However, the cost of the off-label approach (bevacizumab) is a small fraction (3%-5%) of the cost of the two US Food and Drug Administration (FDA)–approved agents.[4] Not surprisingly, those ophthalmologists who are high prescribers of one of the approved products have received high payments from the manufacturers of those agents, whereas off-label bevacizumab was the most commonly used agents among those ophthalmologists who received no payments at all. In other words, the least cost-effective prescribers received the greatest industry compensation.

Oncology is particularly complex, given the extraordinary cost of newer drugs and the opportunity for physicians, hospitals, and pharmacies to reap significant financial benefits on the differential between purchase price and reimbursement. In addition, payers generally receive confidential rebates from pharmaceutical manufacturers and thus may also be similarly motivated to encourage prescribing of expensive oncology drugs (eg, if they are processing claims on behalf of a self-insured corporation who is the ultimate payer).[5]

Meanwhile, fear of recurrence and death is common among patients with cancer, and high levels of anxiety and worry can interfere with appropriate decision making. Thus, a financially motivated physician interacting with a scared patient often leads to administration of an expensive drug, particularly since a discussion about less toxic or less expensive treatment options (or a watch and wait approach) is time-consuming, yields no revenue related to prescribing, and scores no key opinion leader prescribing points. Patients are also influenced by increasingly prevalent direct-to-consumer advertisements regarding niche oncology drugs, a concept that makes little sense other than to bias patients and interfere with objective physician prescribing.

I am not suggesting that oncologists should not interact with or consult for the pharmaceutical industry. In fact, that would be hypocritical, as evidenced by my own disclosure statement. However, there is a difference between true consulting regarding drug development and assistance with marketing. Participation in speakers' bureaus should be considered a pure marketing activity with no academic value since the physician is provided a set of slides developed by the company or its contractor for the sole purpose of persuading peers to prescribe a particular product.

In this context, it is important to take a closer look at the data analyzed by Wright et al.[1] Their analysis focused on general payments but did not separately analyze the payments by subcategories, such as consulting fees and speakers bureaus (ie, "compensation for services other than consulting, including serving as faculty or as a speaker at a venue other than a continuing education program"). Noting that 25% of those receiving high payments had 0-2 publications in 2018, only 24% had served on an editorial board in the preceding five years and only 56% practiced in academic institutions, many of those oncologists receiving high payments appear to have been rewarded for their nonacademic activities, potentially a large number of prescriptions for specific products. It would be of particular interest to see an analysis correlating prescribing data with pharmaceutical payments, as was

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performed for ophthalmologists administering antivascular endothelial growth factor therapies.[6]

Wright et al are also appropriately concerned regarding proindustry bias on guideline panels. However, recent pharmaceutical payments are likely an insensitive measure for detecting such bias. Rather, proindustry bias among those physicians involved in industry-funded clinical trials is prevalent, given that most clinical trials at most National Cancer Institute–designated cancer centers are funded by industry. Furthermore, physicians who participate in guideline panels that approve recommendations in favor of a particular drug may be specifically targeted by an industry to speak about such recommendations. In other words, the proindustry bias on a guideline panel may not be preceded by industry payments; rather, the industry payments may be a delayed reward for participating in a favorable review of the product.

Given the inexorable rise in both the unit cost and total cost of oncology drugs, there will eventually come a tipping point in how we fund oncology care.[7] Will patients be well served by a system in which 80%-90% or more of the total cost of oncology care is for the pharmaceutical products, rather than for services provided by physicians, nurses, therapists, social workers, pharmacists, and hospitals? In addition, will 90% of total cost be sufficient for industry, or will corporate greed drive this number as close as possible to 100%?

Although there has been extensive debate about drug pricing, a better strategy is to modify the demand for oncology drugs, which will affect the total cost, rather than the unit cost. In this context, the financial incentives for prescribing expensive drugs not only should be eliminated but also should be reversed. For example, those ophthalmologists who administered intravitreal bevacizumab rather than the two approved alternatives should receive a higher administration fee, given that the less expensive therapy is equivalent and much cheaper, and the physician is unlikely to receive industry payments.[6] A similar model could be used in oncology where physicians who prescribe less expensive alternatives that have been demonstrated to have comparable clinical benefit should receive a higher administrative fee, rather than a fee scaled to the cost of the prescribed agents. Similar incentives could apply to physicians who enroll patients on postmarketing clinical trials aiming to show near equivalence of lower doses of marketed agents.[8,9]

It is particularly notable that the FDA Oncology Center of Excellence (OCE) has recently instituted a requirement for dose optimization of all new oncology drugs, known as Project Optimus. Although this will not affect drug pricing, it should markedly reduce the risk that a drug will be approved at an excessive dose and thus reduce the costs of managing adverse events of oncology drugs. However, the basis for requiring such dose optimization also applies to many marketed oncology drugs, namely that less is more.[8,10]

In the absence of a change in FDA regulations, it is very unlikely that FDA OCE will require companies to conduct postmarketing dose optimization studies of the many potential candidate agents. However, the US Department of Health and Human Services could initiate a funded program of postmarketing dose optimization trials. Ideally, new funds would be appropriated by Congress for such a program so as to not take away from existing research priorities, perhaps administered by FDA OCE, with input from the Centers for Medicare and Medicaid Services and the National Cancer Institute. This would ensure that the studies would be impactful and that results demonstrating that less is more could be applied to reimbursement policies regarding specific drugs and diseases.

Professional societies such as ASCO could also play an important role, by setting forth stronger policies regarding speakers' bureaus. In April 2013, ASCO published a policy prohibiting inclusion in an SCO educational or scientific program if certain authors had participated in a speakers' bureau on behalf of the sponsoring company.[11] However, implementation of this restriction was stayed and rescinded in 2017.[12]

It is now time to again reconsider and strengthen ASCO's position on speakers' bureaus. ASCO's current policies prohibit certain individuals in leadership positions (Chief Executive Officer, President, President-Elect, Chair of the Board, and Immediate Past President), as well as the Editors-in-Chief of all ASCO journals from receiving any industry compensation (including but not limited to speakers' bureaus). Furthermore, individuals who participate in a speakers' bureau may not participate in an ASCO guideline panel, if the company would be affected by the guideline. And speakers' bureau compensation, if disclosed by the authors, is clearly demarked in all ASCO publications. These policies demonstrate ASCO's recognition that such activities represent commercial speech, rather than intellectual discourse.

However, ASCO could do a lot more. Specifically, individuals receiving such compensation within the past two years could be banned from speaking in Accreditation Council for Continuing Medical Education-accredited sessions at ASCO meetings. Instead, ASCO could create a special speaker's bureau area, perhaps a corner of the exhibit hall, for presentations and peer meetings, as organized by the exhibitors. ASCO could also maintain and publicize a list of all members who participate in speakers' bureaus as the Open Payments database has not sufficiently dissuaded our colleagues who participate in this marketing activity.

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AUTHOR'S DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

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