EDITORIAL

Manufacturer Spending on Direct-to-Consumer Advertising for Pharmaceutical Products

Amanda Starc, PhD

The tension between physicians and drugmakers, especially over marketing, dates to the era of patent medicines.[1] Since 1997, pharmaceutical manufacturers have advertised directly to US consumers, amplifying controversy over the role of drug marketing in clinical care. Critics argue that direct-to-consumer advertising drives use of expensive medications of marginal or no benefit. In 2015, the American Medical Association called for it to be banned.[2] Proponents claim that direct-to-consumer advertising may provide important information to consumers, empowering them and reducing underdiagnosis. Economic analysis has shown that direct-to-consumer advertising does exactly what Paul Starr[1] in his classic 1982 analysis of US medicine suggested physicians fear: influences consumer behavior, affecting physician authority.

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In this issue of *JAMA*, DiStefano and colleagues[3] bring more descriptive evidence to the debate, documenting statistically significant differences in the proportion of promotional spending allocated to direct-to-consumer advertising for lower- rather than added-benefit drugs. They speculate that this pattern may "reflect a strategy to drive patient demand for drugs that clinicians would be less likely to prescribe." Although describing the promotional strategies manufacturers use, their findings raise 2 important questions. First, how does a manufacturer decide on the mix of direct-to-consumer advertising and other promotional activity, such as detailing (ie, marketing to physicians)? Second, does increased demand for advertised drugs improve patient care and outcomes? This editorial offers an economist's view of the questions.

Regarding the first question, from an economic theory perspective, a dollar spent on direct-to-consumer advertising has the same return on investment as a dollar spent on alternative promotions for the same or a different drug; otherwise, a manufacturer would alter its mix of direct-to-consumer advertising vs other promotional activity to increase profits. Profit-maximizing behavior may not be consistent with the argument made by DiStefano and colleagues. For example, high added value drugs may be prescribed by a larger range of specialties, and manufacturers may increase their detailing budget to reach the larger number of physicians. Direct-to-consumer advertising and detailing may be complements of or substitutes for each other, informing manufacturer decisions and their impact on physicians and patients. Of course, profit-maximizing choices by manufacturers may not be socially optimal, which is to say it may not balance costs and benefits among all parties, including patients, perhaps most importantly.

Existing studies conclude that direct-to-consumer advertising may increase patient requests for advertised products, driving demand, and Iizuka and Jin[4] showed that direct-to-consumer advertising increases physician visits. Advertising directly to consumers also appears to increase physician prescriptions, interestingly for both the advertised drug and the drug class as a whole.[5] The category-expansion effect is driven by cost-effective generic options, due in part to business stealing among brands.[6] Increased use of advertised drugs may also improve adherence[7,8] and reduce workplace absenteeism.[9]

Direct-to-consumer advertising may be an easy target for the ire of physicians or other reformers (who seem largely silent about the propriety and impact such advertising by their health systems and health insurance payers), but numerous economic forces align to affect the patient-physician relationship, and the possible harms of directly advertising to patients must be measured against other incentives influencing outcomes in US medicine. Pharmaceutical manufacturers often make cash or in-kind payments to physicians, which increases prescribing behavior.[10,11] Health insurance payers use both patient cost sharing and formularies to steer patients to lower-cost drugs or, alternatively, to those that reduce other health care expenditures[12] and may also require prior authorization or step therapies. Health insurance payers will also respond to patient preferences. As a result, the notion of clinical benefit highlighted in the study by DiStefano and colleagues—and added clinical benefit in particular—may be incomplete in describing benefits to patients. If patients have good information about drug value, their purchase behavior can provide information about the value these therapies generate. Indeed, this demand will guide manufacturer strategy. If patients are not fully informed, physicians have an opportunity to shape the decision-making process.

Embedded in objections to intervention in these markets, for example, by more strictly regulating or banning direct-to-consumer advertising is in part a belief that physicians simply maximize patient well-being, regardless of economic factors. Yet physicians also respond to economic incentives. Indeed, variations in prescribing patterns indicate that discretion is the rule rather than the exception. Physicians are not perfect agents for their patients. Drug manufacturers, hospitals, and health insurance payers all have a role to play in improving patient health.

The economics literature describes the impact of direct-to-consumer advertising and marketing to physicians on average. However, there is almost certainly important heterogeneity across drug classes, physicians, and patients. For example, Grennan et al[11] found that firms target highly responsive physicians with detailing. Similarly, this study found that advertising directly to consumers is not deployed equally for all drugs. The conceptual and empirical arguments herein suggest that the advertising strategy will be more common in drug classes for which it is likely to have a larger impact.

It is then perhaps disconcerting that direct-to-consumer advertising is more common for drugs with low added clinical benefit. However, it is also perhaps not surprising. Drugs with low added benefit may be more likely to face competition within a class. Advertising directly to consumers may be one tool manufacturers use to distinguish their products. Some of this advertising may be create spurious differentiation, but it may have important spillover benefits.

A natural question is, "What is the role physicians play in prescribing low value drugs?" If the clinical benefits of these drugs are low in absolute terms (rather than relative or added terms), discouraging use may be an important goal. Yet an alternative explanation is that competition within these drug classes is valuable to patients because different drugs may be ideal for different patients and additional competitors within a class may bring down prices for health insurance payers or patients.

This competition and associated pharmaceutical innovation may improve outcomes. For example, Buxbaum et al[13] argue that 35% of the increase in life expectancy between 1990 and 2015 was attributable to pharmaceuticals. Of course, the mix of promotional activity may not maximize average clinical efficacy, and clinical measures may not be the only important metric. Patients may prefer options that minimize out-of-pocket costs or adverse effects.

The overall level of promotion by drug manufacturers may be too high or too low. For example, Shapiro[5] found positive category spillovers within antidepressants. Advertising for paroxetine can increase prescriptions for escitalopram. As a result, firms have an incentive to rely on the advertising of competitors to expand awareness and overall demand. Shapiro[9] further found that coordination of advertising decisions would expand category demand by 20%. Subsequent work finds important positive downstream effects of the use of antidepressants. The case study reported by Shapiro provides evidence that direct-to-consumer advertising may be inefficiently low especially in categories with public health benefits, such as preexposure prophylaxis. The level of direct-to-consumer advertising might also be low for drug categories with uninsured or underinsured patients; Alpert et al[14] found that the expansion of insurance under Medicare Part D increased advertising. An expansion of direct-to-consumer advertising might mitigate existing disparities.

Of course, the level of direct-to-consumer advertising could also be too high. For example, advertisements in crowded drug classes are sometimes purchased to "blunt the impact of…competitors' ads," a former vice president for global health policy at Merck noted.[15] The result can be a dizzying array of advertisements creating spurious product differentiation. Sinkinson and Starc[6] found evidence of this phenomenon. Despite this, there is evidence that direct-to-consumer advertising increases use of a cost-effective drug; economic modeling suggests that the monetized clinical benefits of increased use of statins achieved through detailing are enough to pay for all ads during Sinkinson and Starc's study period. For similar reasons, Grennan et al[11] found that detailing to physicians increases use of statins with substantial clinical benefits to patients.

The US is an outlier in its use of markets to deliver health care. And markets can fail to deliver high-quality health care at affordable prices to its entire population. It is important to understand the incentives that all market actors face and explore the extent to which policy can improve outcomes. By describing manufacturer promotional activity, the study by DiStefano and colleagues takes a valuable first step. Their findings can be placed in the context of a large empirical literature attempting to measure the impact of drug promotion. Promotional activities—and direct-to-consumer advertising in particular—do not have universally negative effects on physicians and patients. On the contrary, the literature suggests it causally increases the patient-physician interaction, increases use of valuable drugs, improves adherence, and increases productivity. Future work should explore heterogeneity across drug classes, patients, and physicians.

ARTICLE INFORMATION

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Adverse Pregnancy Outcomes—Risk Enhancers Whose Time Has Finally Arrived

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Heart disease is the leading cause of death globally for both sexes, affecting 1 in 5 women in the United States.[1] Although women have a lower prevalence of obstructive epicardial coronary artery disease compared with men of a similar age, they have higher rates of myocardial ischemia and associated cardiovascular morbidity and mortality.[2] While both sex-based differences due to biological factors such as the timing of menarche and menopause and gender-related differences related to social constructs (eg, delays in time to evaluation of chest pain for women vs men) contribute to these disparities, there is a growing recognition that traditional cardiovascular risk calculators fail to account for sex-specific risk factors such as adverse pregnancy outcomes, which are unique to birthing people who predominantly identify as women. Adverse pregnancy outcomes, including pregnancy-induced hypertensive disorders (preeclampsia and gestational hypertension), preterm birth, and fetal growth restriction, are common manifestations of ischemic placental disease[3] and share a vascular pathophysiologic origin. Along with gestational diabetes, adverse pregnancy outcomes comprise a group of sex-specific cardiovascular risk enhancers associated with a 2- to 4-fold increased risk of future heart disease.[4] Unfortunately, due to a lack of detailed pregnancy history in most existing cohorts and clinical trials of coronary artery disease, to date it has been difficult to examine whether there is a difference in the pathophysiologic development of coronary artery disease in women with a history of adverse pregnancy outcomes compared with those with uncomplicated pregnancies.

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Coronary computed tomography (CT) angiography is a highly accurate, noninvasive diagnostic test that can be used to assess for presence of obstructive epicardial coronary arterial disease with high sensitivity and negative predictive value.[5] While prior strategies of reducing heart disease risk focused on obstructive coronary artery disease burden (defined as stenosis >70%), there is a growing understanding that not only obstructive plaque, but also the presence of any plaque, even noncalcified, is associated with higher risk of cardiovascular morbidity and mortality in a dose-dependent manner (more plaque burden equals greater risk), particularly for women. Similarly, a coronary artery calcium (CAC) score has been shown to be positively correlated with and add incremental value to the assessment of future cardiovascular risk. Compared with a score of 0, even minimal CAC scores are associated with an increased risk of major adverse cardiovascular events.[5,6]

In this issue of *JAMA*, Sederholm Lawesson and colleagues[7] advance knowledge and provide information about the heightened risk of asymptomatic coronary artery disease following individual adverse pregnancy outcomes. Their protocol in the present work from the Swedish Cardiopulmonary Bioimage Study used a single low-dose CT scan to quantify the presence, severity, and extent of atherosclerotic coronary arterial stenoses as well as the presence of noncalcified plaque, and a CAC score. This cross-sectional, population-based cohort study examined 10 528 women with a median age at the time of the scan of 57 years, and in whom imaging was conducted a median of 30 years after their first linked pregnancy in the Swedish National Medical Birth Register. Consistent with other studies, 19% of women had a history of an adverse pregnancy outcome and those individuals also had a higher burden of traditional cardiovascular risk factors, including higher systolic blood pressure and higher prevalence of diabetes, at the time of imaging. The study reported several key findings, including a 3.8% absolute increase in the prevalence of any coronary atherosclerosis in women with a history of adverse pregnancy outcomes compared with those without (32.1% vs 28.3%). The highest increases were seen following a pregnancy affected by preeclampsia (8.0% prevalence increase, 3.1% absolute increase in significant stenosis, 4.2% increase in noncalcified plaque, and 4.1% increase in CAC score >100), with similar findings for gestational hypertension. This translates into an accelerated vascular age, the hypothetical adjustment to chronological age that accounts for the observed severity of coronary artery disease, of 4 to 11 years for women with an exposure to pregnancy-induced hypertensive disorders compared with women without this