Do Pharmaceutical Sales Respond to Scientific Evidence?

Pierre Azoulay
Columbia University, New York, NY 10027-6902
pierre.azoulay@columbia.edu

I investigate how different sources of information influence the diffusion of pharmaceutical innovations. In prescription-drug markets, both advertising and scientific information stemming from clinical trials can affect physicians' prescription choices. Using novel indices of clinical-research output, I find that both marketing and scientific evidence directly influence the diffusion process in the antiulcer-drug market, with marketing having a more pronounced influence. I also find evidence that clinical outputs are important drivers of firms' marketing efforts, affecting sales indirectly. Taken together, the direct and indirect effects of science on demand imply strong private incentives for clinical research. I conclude that product-market competition in the pharmaceutical industry is shaped by both advertising rivalries and scientific rivalries. Moreover, drug advertising may perform an important informative function.

1. Introduction

How do different types of information influence the diffusion of pharmaceutical innovation? The spread of technological advances is limited by the extent to which relevant information is available among potential adopters. Furthermore, the information necessary for the diffusion of pioneer products may be different from that required for the market penetration of subsequent innovations.

In most industries, one would expect underinvestment in the production of knowledge to limit the availability of objective sources of information about product characteristics, safety, and efficacy (Arrow, 1962). However, in prescription-drug markets, two features of the institutional environment—extensive, government-mandated

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testing requirements, and the structure of incentives in academic medicine—provide a context in which privately valuable information is made publicly available through the publication of clinical studies in medical journals. In addition, pharmaceutical companies promote their products extensively, though disagreements remain among economists and policy makers concerning the role of drug advertising. For some, marketing activities foster the rapid dissemination of product information about potentially life-saving products, while others emphasize its strategic use by sellers of incumbent brands to jam information channels that could be used by new entrants (Leffler, 1981; Hurwitz and Caves, 1988).

A finding that pharmaceutical sales do not respond to scientific information (holding advertising intensity constant) would be consistent with the jamming hypothesis. In contrast, a positive science elasticity of demand would imply that a more nuanced view of the relationships between advertising, scientific information, and demand is needed. Moreover, boundaries between science and advertising in pharmaceutical markets are blurry, since much advertising refers explicitly to clinical results. Thus, the pharmaceutical industry provides a unusual setting in which to compare the informative as well as persuasive functions of advertising: Are firms' promotion efforts sensitive to changes in the supply of objective, scientific information contained in published clinical studies?

I explore these questions using data pertaining to a particular subset of the antiulcer-drug market: the therapeutic class of histamine2-receptor antagonists, commonly referred to as H_2 antagonists or simply H_2 blockers. It enjoyed explosive growth from 1977, the year of the pioneer drug's introduction, until the early 1990s, when there were four related molecules in this class vying for market dominance.[1] Importantly, product-market competition in this therapeutic market was marked by the overthrow of an established monopolist (Tagamet) by a subsequent entrant (Zantac). As noted by Suslow (1997), this change in market dominance could be the result of intense price competition, advertising rivalry (both persuasive and informative), or a battle to offer the most attractive package of nonprice attributes. In this paper, I argue that among these nonprice attributes, published clinical results contributed significantly to this turnover in market leadership.

1. During the time spanned by the dataset, none of these drugs went off patent or moved to the over-the-counter (OTC) market. Therefore, I can safely ignore important

Using a brand-level, discrete-choice model of product differentiation, I examine the impact of scientific information embodied in randomized controlled trials (RCTs) on the sales of these four drugs. I attempt to use the fact that RCTs can use either a placebo or a competing drug as a control group to isolate the effects of these two types of scientific information on drug sales, contingent on market structure. The results show that both marketing and science directly influence the diffusion process, with marketing having a more pronounced influence. I also examine the possibility of an indirect influence of scientific information on demand by estimating advertising response functions, and I find some evidence that clinical-research outputs indeed drive firms' marketing expenditures. Plugging back the advertising equation into the demand system, the sum of the direct and indirect effects yields total demand elasticities of science of between 0.3 and 0.5 for the pioneer drug and its challenger.

Overall, these results are consistent with a view that sees product-market competition outcomes in the pharmaceutical industry as the result of firms' rivalrous efforts in marketing and applied science. They cast doubt on the validity of the belief, widespread in the medical community, that drug advertising totally jams other conduits of professionally sanctioned information, such as the results of RCTs (Wade et al., 1989). Finally, these findings help explain the growing involvement of industry in the conduct and funding of clinical research. Not only do clinical expenditures contribute to meet safety and efficacy requirements (thereby securing regulatory approval for entry), they also constitute investments marked by long-lived and direct economic payoffs on the product market.

The remainder of the paper proceeds as follows. Section 2 reviews the literature on drug advertising and the diffusion of pharmaceutical innovations. Section 3 provides a short background on the antiulcer-drug market, in addition to describing the dataset and constructing clinical-output variables. Section 4 presents the econometric results for the discrete-choice model, while Section 5 provides estimates of advertising response functions. I offer some concluding remarks and suggestions for future research in Section 6.

2. Literature Review

The diffusion of pharmaceutical innovations is a complex social process and is subject to multiple influences. Because drugs are experience goods, the impact of entry is limited by physicians' switching

diffusion is rooted in learning, word-of-mouth, and other dynamic phenomena occurring within the population of potential adopters. In their landmark study of tetracycline's diffusion, Coleman et al. (1966) emphasized these *demand-pull* forces by documenting the heterogeneity of the physician population with regard to patterns of information consumption, and highlighted the role of "medical opinion leaders" who were both among the early adopters of this novel antibiotic and closely tied with the academic medical community. On the other hand, diffusion paths are also influenced by *technology-push* forces, in particular the approval by the Food and Drug Administration of additional indications for existing drugs (or of additional therapies within a given therapeutic market). These decisions result in the fall of quality-adjusted prices over time, triggering the adoption of inframarginal consumers.

While there exists numerous sources of information that might influence the adoption of pharmaceutical innovations at the individual physician level, at a more aggregate level information regarding product quality is made available to potential adopters through two primary information channels: advertising by pharmaceutical firms and published clinical results regarding the safety and efficacy of drug therapies.[2]

Beginning with Bond and Lean's (1977) FTC study, economists have extensively studied the role of drug advertising. In experience-goods markets, the mere fact that a product is advertised can signal to customers that it is of high quality (Nelson, 1974; Milgrom and Roberts, 1986). In this perspective, advertising can be interpreted as performing mostly a persuasive role, since it conveys information only implicitly. The medical literature has further argued that advertising swamps the effect of professionally sanctioned sources of information (Avorn et al., 1982; Manning and Denson, 1980) and has deleterious effects on medical practice (Wade et al., 1989). Pharmaceutical firms promote their products heavily, with advertising expenditures typically amounting to between 12% and 15% of sales. The most heavily used form of promotion—known as *detailing*—consists of visits to physicians by the sales representatives of the producers of branded pharmaceuticals. Another instrument for bringing product information to the attention of prescribing physicians is medical-journal advertising. Relative to detailing, journal advertising expenditures are modest, although the mix of promotion methods varies substantially across products and firms (Berndt et al., 1997).

2. At least, this was the situation during the period examined in this paper. The lift-

Despite the intensity of promotion, the overall concern and distrust for commercial messages is surprising, since the advertising of ethical drugs is quite stringently regulated by the FDA.[3] Comanor (1986) observes that the hypothesis of wasteful or jamming advertising is insufficiently formalized, and that evidence on its behalf is largely impressionistic, relying on comments, letters and editorials of a self-appointed group of physicians and health professionals. Indeed, other scholars have claimed that drug advertising performs an eminently informative function. Peltzman (1975) proposes that advertising helps to achieve an efficient rate of diffusion—where the benefit from increasing the rate just pays the costs required to do so. Leffler (1981) shows that product promotion has a significant positive effect on the entry success of new drugs yielding important therapeutic gains. However, this evidence must be pitted against results demonstrating the role of advertising outlays in building up *brand-name recall* effects that favor established products facing new competition by generic entrants (Hurwitz and Caves, 1988). In a similar vein, Stern and Trajtenberg (1998) find that physicians who prescribe a narrow set of therapies for a given condition are more likely to prescribe highly advertised drugs.

In one of the most detailed studies of pharmaceutical advertising, Berndt et al. (1997) examine the effect of marketing investments on the growth and changing composition of the antiulcer-drug market.[4] The authors find that the effect of these investments was substantial and long-lived, although it partly spilled over to competing drugs. They also show that the second entrant's intense promotion efforts were instrumental in overthrowing the market-share leadership of the incumbent. Finally, they hint—but do not explicitly test empirically—that advertising was more effective when it interacted with a superior bundle of product-quality attributes, such as lower dosage or fewer side effects.

Market power in prescription-drug markets seems to rest as much upon habit persistence as upon fears that serious adverse consequences (such as a malpractice lawsuit) will follow an inappropriate

3. Any material distributed by pharmaceutical companies must carry the "full package insert," i.e., the complete product information reviewed by the agency as part of the drug approval process. Also, the advertising of drugs for nonapproved indications is prohibited, and comparative advertising must be supported by well-controlled clinical studies. Finally, comparison of side-effect profiles is not allowed, because most drug studies are not designed to assess the incidence of adverse interactions (Kessler and Pines, 1990).

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