PERSPECTIVE

Direct-to-Consumer Drug Advertisement and Prescribing Practices: Evidence Review and Practical Guidance for Clinicians

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Direct to consumer advertising (DTCA) of prescription drugs has increased dramatically in the past two decades. The effect of this increase in advertising on the frequency of inappropriate prescribing is poorly understood, as are the factors that may underly inappropriate prescribing. A review of existing observational and experimental studies that address advertising-related prescription requests and contain some measure of prescription appropriateness demonstrate that DTCA increases prescription requests, increases the likelihood of prescription, and increases both appropriate and inappropriate prescribing. Patient expectations, insufficient information sharing, and patient satisfaction surveys are proposed contributors to potentially inappropriate prescribing in response to DTCA.

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INTRODUCTION

Spending on drug product advertising increased from $17.7 billion in 1997 to $29.9 billion in 2016, with an estimated 32% of this (~$10B) spent on Direct to Consumer Advertisement (DTCA).[1] While a larger total amount of ad spending is directed at healthcare professionals, the rapidity with which DTCA spending has increased (460% from 1997 to 2016) indicates that providing information about drug products directly to consumers, rather than medical professionals, has recently become a key priority of drug manufacturers. The ability to reach consumers directly has occurred previously in the history of medicine, but with the advent of television, radio, and other forms of media, the scale with which consumers can be reached is unprecedented.

Although DTCA may result in benefit or harm to patients it must be understood that all drug advertisements represent a conflict of interest in which a commercial entity stands to benefit financially from the dissemination of product-related information. It has been suggested that DTCA increases access to care, improves timely diagnosis, helps to destigmatize certain diseases, and empowers patients to assume greater responsibility for their own care.[2] Alternatively, DTCA may result in inappropriate prescribing, create undue economic strain on an already overburdened healthcare system, and undermine the patient-physician relationship.[3–5] Studies that have explored the impact of DTCA on prescribing practices suggest that DTCA can potentially result in inappropriate prescribing, although conflicting data exist. Due to the inherent difficulty of measuring inappropriate prescribing, and the wide-ranging impact of this potential problem, we propose 3 contributing factors that could lead to inappropriate prescribing and associated mitigating strategies for clinicians.

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THE IMPACT OF DTCA ON PRESCRIBING PRACTICES

We reviewed studies of DTCA-related patient-clinician interactions which included assessment of the clinical appropriateness of prescriptions resulting from such encounters. Either published clinical criteria of appropriateness or clinician judgment of appropriateness were allowed. Clinician judgment of appropriateness was included as this is the most feasible way of capturing all patient and agent-related variables which impact prescribing in observational studies. MEDLINE (Ovid) was queried using the search terms “advertising” and “prescribing” with the limits: year 2000–current, English language, human studies. This yielded 114 studies, whose abstracts were reviewed manually, ultimately yielding 6 studies (Table 1). These search criteria yielded many survey-based studies that did not include assessment of prescribing and clinical appropriateness. On manual review, if the methodology section of an abstract did not explicitly mention assessment of the clinical appropriateness of DTCA prescriptions, the study was excluded. This resulted in a large number of studies being excluded relative to the amount yielded by our query.

Three survey studies of 1678 physicians conducted between 2000 and 2002[6–8] suggest that DTCA inquiry is responsible for 4.5–5.2% of sampled outpatient visits, such inquiry results in the prescription of a DTCA-drug 39–77% of the time, and 48–49% of such prescriptions may be potentially clinically inappropriate. In one study, 48% of surveyed physicians responded that they disagreed with a DTCA-drug request but complied with it in order to accommodate the patient,

Table 1 Summary of Results from Studies of DTCA Associated Prescribing which Report Appropriateness Measures

Ref	Methods	N	Exp to DTCA	DTCA-patient-MD interaction	Requestfulfilled	Appropriateness	Other outcomes	LOE
[6]	Physician survey	535	-	56% of 395 surveyed "last-recalled" DTCA conversations resulted in a request for DTCA-drug	77%	49% of fulfilled requests deemed inappropriate	Inaccurate advertisement, poor patient understanding of advertisement independently associated with inappropriate requests	III
[7]	Physician survey	643	-	643 "last-recalled" DTCA-drug conversations, request rate NR	39%	48% felt other drugs were equally effective but wanted to accommodate patient	Most common reasons for denial were cost and clinical considerations	III
[8]	Patient and physician survey	500	81%	4.5% of 944 surveyed visits for any reason were DTCA-drug-related, 51% recalled DTCA-drug requests	76%	NR, 46% reported no benefit of DTCA on patient interaction, 18% reported a negative effect	Most common reasons for not prescribing were clinical and cost considerations, followed by insufficient information from the advertisement	III
[9]	Case-control; outpatient DTCA visits compared with non-DTCA visits, patients and physicians surveyed	1431	94%	5.2% of 1431 surveyed visits for any reason were DTCA-drug-related	71% vs. 26% if no DTCA request (OR 16.9)	50% surveyed reported ambivalence about DTCA associated prescription	Strong dose-response relationship between the number of ads viewed and likelihood to request DTCA drug	II
[10]	Claims study; assessed appropriateness of COX-2 inhibitors prescription with clinical criteria	2929	80%	20% who viewed COX-2 advertising asked for a prescription	78% vs. 43% if no DTCA request	Fourfold, and sevenfold increase in inappropriate, and appropriate prescribing of COX-2 inhibitors, respectively	Specialist setting and increased age-associated with more appropriate prescription, female sex associated with inappropriate prescription	II
[11]	Randomized trial; SP's portraying MDD or AD with or without DTCA-drug request, clinical appropriateness assessed	298	-	MDD: 101 DTCA-drug requests, 51 no request. AD: 98 DTCA-drug requests, 51 no request	MDD: 64% vs. 31% (OR: 8.0) AD: 47% vs. 10% (OR: 13.3)	"Minimal acceptable care" met more frequently (90–98% vs. 56%) in DTCA-request group for MDD, 34% inappropriate prescription rate in AD	Multivariate analysis: impact of DTCA-request on increasing prescription in AD much greater than that in MDD	I

Ref reference number, n total units of analysis, Exp to DTCA patient exposure to DTCA, DTCA direct to consumer advertising, LOE level of evidence, NR not reported, OR odds ratio, SP standardized patient, MDD major depressive disorder, AD adjustment disorder

suggesting that they prescribed it even though they did not think it was clinically appropriate.[7] Another survey of 535 physicians reported that physicians complied with DTCA requests for prescription or referral 77% of the time, despite physicians deeming 49% of them clinically inappropriate, based solely on the physician's own judgment of what constituted clinically inappropriate prescribing.[6] In a physician survey conducted by the FDA, physicians complied with DTCA requests 76% of the time, despite 64% of those surveyed reporting no benefit or a negative effect of DTCA-inquiry on patient visits.[8]

A more rigorously designed case-control study in which 1,431 patients presenting to primary care providers were surveyed along with their physicians compared DTCA-drug request visits to visits not involving DTCA, finding that 5.2% of all visits were for DTCA-drug requests.[9] Those making drug requests were 16.9 times more likely to receive a prescription (71% vs. 26%), despite physicians communicating ambivalence about 50% of these prescriptions. This study also demonstrated a strong dose-response relationship between the amount of advertising viewed and the likelihood of a DTCA-inquiry. Another study, which examined claims data for COX-2 inhibitor prescriptions, also found a high degree of advertising exposure, which prompted COX-2 inhibitor prescriptions at a much higher rate than non-DTCA-inquiry visits (78% vs. 43%). This study applied published definitions of clinical appropriateness to analyze DTCA-prompted COX-2 inhibitor prescriptions and found a fourfold and sevenfold increase in both appropriate and inappropriate prescribing, respectively.[10]

Finally, the most robust evidence assessing the impact of DTCA on prescribing comes from a randomized controlled trial of 298 encounters in which standardized patients trained to portray major depressive disorder (MDD) or adjustment

disorder (AD) either made or did not make DTCA-drug requests.[11] Although standardized patient encounters may be suspected by providers and thus bias study results, only 12.4% of participating physicians reported that they suspected a standardized patient encounter had occurred during the study period. In addition, the development of the MDD and AD roles was evidence-based, strictly adhering to published diagnostic criteria. The authors found greater prescribing for those who made DTCA requests, in both the MDD (64% vs. 31%, $p < 0.001$) and AD cohorts (47% vs. 10%, $p < 0.001$). This translated to an increase in clinical guideline-defined appropriate care for MDD, driven by increased prescribing prompted by DTCA-drug requests. It also resulted in increased inappropriate prescriptions in AD, which is not treated pharmacologically.

CONTRIBUTORS TO INAPPROPRIATE PRESCRIBING AND MITIGATING STRATEGIES

As demonstrated in the data presented above, physicians frequently fulfill DTCA-drug requests despite reporting concerns about clinical appropriateness, and several studies demonstrate the potential for DTCA to cause inappropriate prescribing. However, none of these studies addresses the factors that contribute to potentially inappropriate prescribing in response to DTCA. We describe 3 important contributors and offer mitigating strategies for clinicians to consider when faced with DTCA-drug requests from patients. This is not intended to be an exhaustive list of the contributors to DTCA-influenced prescribing practices, but rather a description of consistently identified themes that we found in our literature review.

Assess the Appropriateness of a Medication Request and Address Patient Expectations

Advertising begets demand, an axiom that is borne out time and again in studies of the impact of DTCA on prescribing practice.[6–11] One can logically conclude that parties with vested interests would not spend tens of billions on advertising otherwise. Because of this, DTCA is transforming the patient-physician relationship from a professional model requiring reliance on a learned intermediary with a fiducial responsibility to a consumer model, where patients enter with a preconceived notion of the service they would like to be rendered. Regardless of this dynamic, physicians must fulfill their fiduciary obligation to protect the best interests of patients. Patients have negative rights, including the ability to decline interventions based on their goals of care. They do not have positive rights or the ability claim that their health care provider must act in a certain way that is aligned with their priorities. How should clinicians evaluate the appropriateness of DTCA-drug requests and address patient expectations? Several studies indicate that providers often feel underequipped to assess DTCA drug requests.[12, 13] We propose a memory device: "ABCD" (adverse effects, benefits, cost, diagnosis) to aid in this process.

The guiding principles of greatest urgency are derived from consideration of potential clinical benefits and the likelihood of adverse effects. Ensuring efficacy and minimizing toxicity remain the most important considerations when deciding whether to prescribe a requested drug. This consideration is complicated by the fact that newly marketed drugs often have insufficient safety information available. Physicians should rely on information from randomized controlled trials to decide when a DTCA request is reasonable and to help correct misconceptions imparted by DTCA.

The United States Government Accountability Office (GAO) has repeatedly reported that newly marketed drugs (which are more heavily advertised) incur more costs to individuals and the healthcare system than generic drugs.[1, 14–16] Indeed, of all the literature reviewed, this variable is the most frequently cited by clinicians when explaining their reasons to not fulfill a DTCA-related request.[6–8] At the point of prescription, physicians should consider and discuss with the patient whether a drug presents a financial barrier that could result in the patient going untreated, or if there is a comparable but more cost-effective alternative. HMOs and formularies which incentivize cost-effective prescribing can help serve to minimize the burden of this consideration on the prescribing physician. Social workers and case managers are also exceptionally helpful in navigating cost concerns.

Finally, the patient's diagnosis must be considered, as physicians have a fiduciary obligation to choose the most appropriate therapeutic agent that is clinically indicated. The gravity of the patient's condition likely impacts the benefit that the patient receives relative to cost and adverse effects (e.g., prescribing Diclegis® for pregnancy nausea vs. switching warfarin to apixaban for atrial fibrillation). Physicians are generally already able to differentiate between indication priorities, but published guidance on this topic also exists.[17, 18] Inappropriate prescribing has been shown to be more frequent for indications with fewer potential clinical consequences in the DTCA literature.[11] What is critical in responding to DTCA-drug requests is that physicians are able to explain to patients whether the requested drug is clinically indicated in their case, and if not, why not.

Incomplete Information

In most instances, the decision to prescribe a new medication requires simple consent, involving an explanation of the change, and the patient's implied or stated agreement after discussing risks, benefits, and alternatives.[19] Multiple content analyses,[20–23] as well as physician surveys, indicate that drug advertisements provide insufficient information to patients regarding alternative therapies, efficacy, and potential adverse effects. Incompletely informed requests coupled with physicians' time constraints may drive inappropriate prescribing. Complicating this dynamic further is physician familiarity

with newly marketed medications, which is frequently poor.[24] Policy intervention is often cited as having the greatest potential to improve the educational value of drug advertisements, either in the form of more stringent guidance from the FDA or by creating tax-funded public-private partnerships to produce advertisements, which may reduce the influence of profit motive on DTCA.[25] A slightly more impassioned remedy to this issue has been circulated in the patient safety literature, termed "strategic prescribing," in which physicians who only utilize a limited number of medications with great frequency.[26] Finally, if physicians feel that there is insufficient information exchange to produce simple consent in the case of a DTCA-drug request, referral to a specialist who is more familiar with its use is a viable option.

The Advent of Patient Satisfaction Metrics

Emphasis on improving healthcare quality by the Institute of Medicine created value-based reimbursement schemes for institutions, which employ measurement of patients' satisfaction with their care.[17] Several studies indicate that receipt of a prescription opioid for non-cancer-related chronic pain (an indication where opioids have no demonstrated benefit) is associated with higher patient satisfaction scores.[27, 28] Other studies have demonstrated a strong positive correlation between patient satisfaction and an antibiotic prescription for upper respiratory tract infections (which are typically viral).[29, 30] Examples like these demonstrate that financial pressures placed on physicians stemming from the interaction of their patient satisfaction evaluations and prescribing practices have the potential to contribute to grave public health crises such as the opioid epidemic and widespread antibiotic resistance. Strangely, physicians who oppose satisfaction-incentivized prescribing by practicing evidence-based medicine may be damaging their own interests. Combatting the negative impact of patient satisfaction surveys on appropriate prescribing begins with a better understanding of the problem, and more emphasis on researching this issue is necessary. This would permit the engagement of policymakers in efforts to improve the surveys themselves or alter their impact on reimbursement.

CONCLUSION

DTC drug advertisement prompts patient requests for newly marketed medications, and studies suggest that many physicians comply with these requests. This has been shown to increase inappropriate prescribing in some studies. Addressing patients' expectations adequately, incomplete comprehension of benefits and harms, and the recent introduction of patient satisfaction surveys likely all contribute to inappropriate prescribing. There are numerous resources available to clinicians that can aid them in responding to advertising-related prescription requests,[31–35] although there is still a great need for more data regarding this controversial topic.

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