Written Statement

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Spending on direct-to-consumer (DTC) advertising of prescription drugs in the United States totaled $3.2 billion in 2003[1]. Much of this spending is for drugs used to treat conditions that affect the elderly, including high blood cholesterol; stomach ulcers and heartburn; degenerative arthritis; stroke; and depression.[2] Critics charge that DTC advertisements lead to over-prescribing of unnecessary, expensive, and potentially harmful medications, while proponents counter that they can serve a useful educational function and help avert under-use of effective treatments for conditions that may be poorly recognized, highly stigmatized, or both.

How are older Americans responding to these ads? A survey conducted by *Prevention* Magazine in late 2003 concluded that 62.4 million consumers have talked to their doctors about advertised medicines, and of these, 16.2 million have asked for an advertised medicine. Older Americans (>=65 years) are somewhat less likely to talk with their doctors about advertised medicines than "Baby Boomers," but not by much (27% vs. 36%).[3] While some physicians welcome these discussions, many find them a distraction from the myriad of clinically critical tasks already packed into a typical office visit. Furthermore in study of 1431 visits in Sacramento (CA) and Vancouver (Canada), physicians were much more likely to register "therapeutic ambivalence" after prescribing an advertised drug that a patient had requested.[4] (Ambivalence was defined as answering "possibly" or "unlikely" to the question, "If you were treating another similar patient with the same condition, would you prescribe this drug?")

There is no disputing that DTC advertisements find their audience, motivate consumers, and result in requests for medication. The question for the health of America's seniors (and younger citizens as well) is whether those requests result in better and more appropriate care. The pharmaceutical industry has long claimed that DTC ads merely educate patients about potentially beneficial treatments and that it is up to the physician to decide whether medication is warranted. After all, neither patients nor drug companies have the power to prescribe. This position assumes that physicians are reliable "learned

[1] Prescription Drug Trends. Menlo Park, Calif: Kaiser Family Foundation; 2004. Fact sheet 3057-03.
[2] TNS Media Intelligence. In *MM&M* April 2005; p.38.
[3] Prevention Magazine's 7th Annual Survey: Consumer Reaction to DTC Advertising of Prescription Medicines, 2003-4, p. 50.
[4] Mintzes B, Barer ML, Kravitz RL et al. CMAJ. 2003 Sep 2;169(5):405-12.

intermediaries," welcoming their patients' requests for beneficial therapies but steering them away from those that are unnecessary or harmful.

To address these issues, our research group at the University of California and the University of Rochester devised an elaborate experiment focused on antidepressant medications. Antidepressant medications consistently rank among the top DTC advertising categories. Major depressive disorder carries stigma, is frequently under-diagnosed, and can be treated successfully in the majority of patients.[5] A thoughtful DTC advertising campaign could encourage patients to seek effective care. However, DTC advertising could also promote prescribing of antidepressants for patients with minor symptoms in the absence of clearly defined indications. Although some short-term studies have shown benefit from antidepressants in minor depression, there is no professional consensus about the need for immediate treatment as opposed to watchful waiting. Patients with minor symptoms of short duration who are prescribed antidepressants at initial presentation would be subject to short-term side effects (e.g., sexual dysfunction) and potential hazards (including suicidality) that would have to be weighed against marginal gains.

In an ideal world, patients presenting to primary care doctors with symptoms of major depression would almost always receive antidepressant medication (or psychotherapy), if not at the first visit then soon thereafter. Patients with adjustment disorder (transient problems in living), on the other hand, would be spared drug treatment, at least until the picture further clarified itself. With these qualifications in mind, failure to prescribe antidepressants (or to arrange for mental health consultation or follow-up) for patients with major depression constitutes "underuse" of effective care, while prescribing antidepressants at the first visit to patients with adjustment disorder is at the margins of clinical appropriateness.

Our trial used Standardized Patients (SPs) to determine how practicing physicians actually respond to patients' requests for antidepressant medicines. SPs are actors trained to portray the clinical and psychological features of a patient role. We enrolled 152 physicians in 3 US cities; each physician consented in advance to participate in 2 unannounced SP visits. (The doctors knew they would see the actor-patients but did not know when.)[6] Eighteen SPs were trained to portray 6 roles, created by crossing 2 clinical conditions (symptoms consistent with major depression or adjustment disorder) with 3 request types (brand-specific, general, or none). The overall design is depicted in the table below.

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[5] Simon GE. Gen Hops Psychiatry 2002;24:213-224.

[6] Participating physicians were told that they would see two SPs presenting with a combination of common physical and mental health symptoms but were not told specifically that some of the SPs would be making requests for medication. They also knew the visits would be audiorecorded. Project staff worked assiduously with medical office staff and insurers to arrange the visits under a veil of secrecy. Post-visit surveys suggested that 13% of physicians were "suspicious" that they had seen an SP. Practices were reimbursed for their participation in the study.

	Brand-Specific Request	General Request	No Request
Major Depression	Role A (N=51)	Role B (N=50)	Role C (N=48)
Adjustment Disorder	Role D (N=49)	Role E (N=49)	Role F (N=51)

All SPs were middle aged white women.[7] Those playing the major depression role ("Louise Parker") complained of depressed mood for a month, worse during the past two weeks, accompanied by fatigue, low energy, and early morning awakening, but no suicidality. Those playing the adjustment disorder role ("Susan Fairly") complained of much milder symptoms whose onset followed a minor upheaval at work.

To understand the effect of requests on physician behavior, actors portraying major depression were further assigned to experimental conditions A, B, or C; those portraying adjustment disorder were assigned to conditions D, E, or F (Table). Sub-roles A and D were to make a brand-specific request within the first 10 minutes of the visit or before the physical examination (whichever came first). They began: "I saw this ad on TV the other night. It was about Paxil®. Some things about the ad really struck me. I was wondering if you thought Paxil® might help." Paxil® was chosen because at the time of the study it was widely promoted, priced higher than generic fluoxetine, and available on the formularies of participating health care organizations in all three cities. Paxil® did not become available as generic paroxetine until midway through the study (September, 2003). Sub-roles B and E were to make a general request for medication. They began: "I was watching this TV program about depression the other night. It really got me thinking. I was wondering if you thought a medicine might help me." Sub-roles C and F were to make no explicit request.

Major findings from the study were as follows:

- Among SPs portraying **major depression**, antidepressant prescribing was highest when a general request was made (76% of visits), middling when a brand-specific request was made (53%), and lowest when no request was made (31%).
- Among SPs portraying **adjustment disorder**, antidepressant prescribing rates were 55% among SPs making a brand-specific request, 39% among those making a general request, and 10% among those making no request.
- The results were confirmed in statistical models that adjusted for city, specialty, physician gender, and whether the doctor was "suspicious" of seeing an SP. These same models showed that brand-specific "DTC" requests had significantly greater relative potency in adjustment disorder than in major depression. In other words, brand-specific requests promoted prescribing in both depression and adjustment disorder, but they were *particularly* effective in adjustment disorder.
- "Minimally acceptable initial care" (any combination of an antidepressant, mental health referral, or follow-up within two weeks) in the major depression role was

[7] Cost constraints precluded a more diverse sample, and in any case depression is somewhat more prevalent among women than men.

offered to 98% of SPs making a general request, 90% of those making a brand-specific request, and 56% of those making no request ($p<0.001$).

What can be learned from these results? First, patients' antidepressant requests (whether brand-specific or general) are a powerful influence on physicians' prescribing decisions. Second, such requests can improve care for patients with major depression. Third, physicians are not always be the stalwart intermediaries the pharmaceutical industry claims and the law assumes – a DTC-driven-request by "Susan Fairly" increased the probability of marginally appropriate prescribing for adjustment disorder from 10% to 55%.

The net social value of DTC advertising and the requests they engender may depend upon the specific context. The benefits of advertising will tend to dominate when the target condition is serious and the treatment is very safe, effective, and inexpensive. Harms are most likely when the target condition is trivial and the treatment is relatively perilous, ineffective, or costly. If one accepts this perspective, an outright ban on DTC advertising *could* do more harm than good. A more judicious approach would:

- Place a moratorium on DTC advertising of new drugs, allowing a reasonable period of time for important side effects to emerge;
- Raise the bar for DTC advertising in terms of public health importance, safety, and effectiveness;
- Encourage DTC advertising or joint public-private partnerships to raise public awareness of effective treatments for important public health conditions.

An ample moratorium period would allow information on potential adverse effects to accumulate. If such a moratorium had been in place during the launch of the Cox-II inhibitors, many lives would have been saved.

Raising the bar for DTC advertising means that not every FDA-approved drug could be advertised directly to the public. Under this concept, advertising would be restricted to drugs or classes of drugs that are known to treat important conditions (ie those causing significant morbidity or mortality in the population), are extremely safe and effective, or are notably under-used. The FDA would be well-positioned to make such determinations.

DTC advertising, or variations on it, should be supported and even encouraged in special cases. For example, a campaign to increase the proportion of patients with previous myocardial infarction (heart attack) who take beta-blockers and aspirin could save thousands of lives annually.