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Potential Effects of Introducing Behind the Counter Drugs

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Contents

Abbreviations

BTC	behind the counter
CUSTOM	Consumer User Study of OTC Mevacor
DD	difference-in-differences
FDA	U.S. Food and Drug Administration
GERD	Gastro Esophageal Reflux Disease
GI	Gastro Intestinal
H_2RA	H_2-receptor antagonist
HMO	health maintenance organization
NAMCS	National Ambulatory Medical Care Survey
NDA	new drug application
NRT	nicotine-replacement therapy
OTC	over the counter
PPI	proton-pump inhibitor
UTI	urinary tract infection

Introduction

In the United States, drugs can be divided into two categories: prescription drugs, which are only available with a physician's prescription, and over-the-counter (OTC) drugs, which can be freely purchased from many outlets, such as pharmacies and grocery stores. Both classes of drugs are regulated by the U.S. Food and Drug Administration (FDA). OTC drugs can be introduced to the market in one of two ways. First, particularly for older drugs, the FDA has established drug monographs that detail acceptable ingredients, dosages, and formulations. Products conforming to these monographs can be marketed without premarket FDA approval. If a monograph does not exist for a particular drug, then the drug must be approved via the new drug application (NDA) process, which is similar to the process used to approve new prescription drugs. As with new prescription drugs, approval requires evidence demonstrating that the drug is safe and effective. In addition, the drug manufacturer or interested party must also establish that (1) the benefits of OTC approval outweigh the risks, (2) the potential for misuse and abuse is low, (3) consumers can understand the product label and accurately diagnose themselves for the indicated condition, and (4) health practitioners are not required for the safe and effective use of the product.

The requirement for a physician's prescription imposes a regulatory barrier to access which has advantages and disadvantages. The main advantage of this barrier is that it prevents misuse of prescription drugs, which may have serious consequences in many cases. Moreover, this requirement places the use of the drug under a physician's supervision, making it easier for him or her to encourage adherence to instructions, monitor any adverse effects, and identify any potential contraindications. However, requiring a prescription also imposes additional time and monetary costs on the patient; these may reduce access to potentially beneficial therapies. Although it is clear that the advantages of physician supervision may outweigh these increased costs in the case of drugs with high toxicity profiles, it is less clear in the case of many drugs with low toxicity. Therefore, in an effort to increase access to select low-toxicity drugs by eliminating the costs associated with obtaining a physician's prescription, the FDA is considering a third classification, called *behind-the-counter* (BTC) drugs. These drugs would be available without a physician's prescription but, unlike OTC drugs, would not be freely available

to patients. Rather, they would be available only in pharmacies and upon consultation with a pharmacist.

By removing the requirement for a physician's prescription, BTC drugs may increase access to beneficial therapies by lowering the time requirements and monetary costs associated with obtaining a physician's prescription, thereby improving patient health and wellbeing. Moreover, BTC drugs could reduce medical spending directly (by reducing the amount of money spent on physician-office visits) and indirectly (to the degree that increased access to these drugs becomes a substitute for more-expensive forms of care). However, BTC drugs are not without potential pitfalls. First, it is not clear that patient access to these drugs would actually increase after the switch. Although BTC drugs reduce the costs associated with physician-office visits, many insurers do not cover OTC drugs; indeed, in countries that have introduced the BTC classification, BTC drugs are not typically covered by private or public payers. Thus, out-of-pocket payments for patients may actually increase, which could reduce access as well as the potential health and spending benefits outlined above. Moreover, even if BTC drugs do increase access, it is not clear that this would increase patient health and decrease medical spending. Because BTC drug use would occur under the supervision of a pharmacist, and to the degree that this supervision would be a poor substitute for physician supervision, patient health could decrease and medical spending could increase due to increases in inappropriate use and adverse events.

Given these ambiguities, it is important to find ways to forecast the potential net benefits and costs of introducing BTC drugs. Although the United States has limited experience with BTC drugs, other countries have introduced the BTC class, and their experiences can provide insight into the potential effects of this new class of drugs. Moreover, although the United States has had limited experience with BTC drugs, it has a great deal of experience with OTC drugs. Indeed, according to the FDA's Office of Nonprescription Products, more than 100,000 OTC products are marketed in the United States, and these products comprise roughly 800 distinct active ingredients. Because OTC drugs are similar to BTC drugs in that they do not require a physician's prescription, analyzing the U.S. experience with these drugs may provide useful insights as well.

As a first step toward examining the potential effects of introducing BTC drugs, we performed an extensive literature review to identify papers that examine the effects of BTC/OTC drugs on utilization, medical spending, and patient health. Overall, we found that the introduction of OTC/BTC drugs generally causes patients to substitute BTC/OTC versions for prescription versions. The effect on overall utilization, however, is more ambiguous, and depends to some degree on the structure of private and public health insurance and on whether the BTC/OTC versions are covered by insurers. In addition, there is a general consensus that BTC/OTC drugs reduce spending on prescription versions of the same drugs for payers, such as private and public health insurers. However, no studies have examined to what degree this decrease in spending on prescription forms of the drugs is outweighed by increases in spending on BTC/OTC versions. In addition, while a few studies examined whether BTC/OTC drugs might reduce spending through indirect means, such as spending on physician-office visits, there was no general consensus on this point among these studies. In addition, few studies examined the effect of BTC/OTC drugs on patient health.

In addition to the general lack of consensus about how BTC/OTC drugs affect spending and patient health, we found that many of the studies of BTC/OTC drugs are plagued by methodological problems that suggest caution when interpreting the results. For example, many studies simply examined changes in outcome variables after the introduction of BTC/OTC drugs, failing to consider to what degree those changes were attributable to other factors. In addition, several studies used decision-analytic or demand curve–based methods, which are highly sensitive to assumptions about the parameters of the economic and decision models that the authors chose to use. In many cases, we found that these assumptions were insufficiently supported or justified.

Given that one of the main purported benefits of BTC and OTC drugs is to reduce costs by reducing the number of physician-office visits, we examined whether the introduction of OTC drugs aimed at treating allergic rhinitis, vaginal candidiasis, peptic ulcer disease, and nicotine dependence actually reduced the number of physician-office visits for these conditions. Our analysis used the National Ambulatory Medical Care Survey (NAMCS), a nationally representative sample of physician-office visits conducted since 1979. Using the NAMCS, we examined how the number of physician-office visits for each of these conditions changed after

the introduction of OTC drugs aimed at treating the condition. We used trend-break analysis to control for other, time-related factors as well as preexisting trends in the number of physician-office visits that might confound the results. Overall, we found evidence that, even when prior trends are taken into account, the introduction of an OTC drug reduces the number of physician-office visits for the conditions it is intended to treat by 33 percent. However, this average effect masks a large degree of heterogeneity across diseases: We found large, significant effects for vaginal candidiasis and allergic rhinitis; a large, statistically insignificant effect for nicotine dependence; and no effect at all for peptic ulcer disease. It is intriguing to speculate about the causes of this heterogeneity. Patients may be less inclined to see a physician for vaginal candidiasis (a disorder related to genital organs) and allergic rhinitis (a disease with relatively minor symptoms), so the introduction of an OTC drug may reduce physician-office visits related to these conditions. For peptic ulcer disease, whose symptoms can be more severe, the number of physician-office visits may be less sensitive to the introduction of OTC drugs.

Our data also suggest that OTC drug effects are two-fold: OTC drugs cause decreases in both the *number* and *growth rate* of physician-office visits. We speculate that the decrease in the number of visits is due to an initial surge of patients who use the OTC drug and choose not to see a physician. Over time, as more about the OTC drug's safety and efficacy becomes known, more patients may choose to use the drug, thereby leading to a decrease in the growth rate of physician-office visits. Further work could more clearly elucidate the mechanisms by which OTC drugs affect both the number and growth rate of physician-office visits. However, since neither BTC nor OTC drugs require a physician's prescription, our results suggest that BTC drugs also have the potential to reduce costs by lowering the incidence of physician-office visits.

Our final analysis examined the effect of BTC/OTC drugs on drug utilization, prices, and spending using sales data on BTC/OTC drugs in the United States and abroad. We specifically examined changes in these three outcomes for four classes of drugs—emergency contraception, statins, anti-ulcer drugs (proton-pump inhibitors [PPIs] and H_2-receptor antagonists [H_2RAs]), and vaginal antifungals—in the United States, the United Kingdom, Australia, New Zealand, and Canada. Between 1997 and 2006, five drugs in these classes were switched to OTC status and three were switched to BTC status. Using a difference-in-differences approach to control for potentially confounding factors, we examined changes in utilization, prices, and spending after a

given drug was reclassified to BTC or OTC status. Overall, we found that BTC and OTC switches had substantial effects on sales, prices, and expenditures, but that the direction and magnitude of the effects varied significantly across the cases analyzed. We found weak evidence that BTC and OTC switches reduce prices. Of the eight switches analyzed in our study, prices declined significantly in five cases, increased significantly in one case, and remained unchanged in two cases.

We found weak evidence that BTC switches increase utilization of a drug: Of the three drugs that were switched to BTC status, sales increased for one and remained unchanged for the other two. We also found that OTC switches had mixed effects on utilization: Sales increased in one case (omeprazole), decreased in another (loratadine), and remained unchanged in the remaining three. Similarly, we also found that BTC/OTC switches had mixed effects on expenditures, which is unsurprising, given the heterogeneity in price and sales effects.

Overall, the results of our analyses suggest that the introduction of BTC drugs in the United States could have varied effects in practice, and it is unclear whether such a policy would increase access to drugs, reduce medical costs, or increase health. Our literature review revealed general consensus that BTC drugs may reduce spending on prescription drugs, but it is unclear whether this decrease could be outweighed by increases in spending on BTC drugs. Furthermore, there is little consensus about how BTC/OTC switches might affect medical spending or health. Our own analyses suggest that BTC drugs could significantly reduce the number of physician-office visits and might have significant effects on access, prices, and spending. However, our analyses generally found significant effects in the case of only a few drugs, as opposed to large effects across all drugs. Accordingly, it seems likely that the potential effects of BTC/OTC switches would vary on a drug-by-drug basis. Therefore, efforts to classify drugs as BTC should proceed on a case-by-case basis after examination of the potential costs and benefits. Furthermore, after classifying the drug, efforts should be made to monitor whether the reclassification is actually lowering costs and improving health and access.

Chapter One: Review of the Literature

Introduction

In the United States, drugs are currently classified into two categories: prescription and over-the-counter (OTC). While prescription drugs can only be purchased with a physician's permission, patients can freely purchase OTC drugs at pharmacies and grocery stores. In the United States, the Food and Drug Administration (FDA) has oversight over both prescription and OTC drugs. To obtain permission to market a drug OTC, the manufacturer (or another interested party) must establish that the drug meets the following characteristics:

- The benefits outweigh the risks
- The potential for misuse and abuse is low
- Consumers can understand the product label and accurately diagnose themselves for the indicated condition
- Health practitioners are not required for the safe and effective use of the product.

The FDA is considering the introduction of a new class of *behind-the-counter* (BTC) drugs that are neither prescription nor OTC. This new class of drugs would only be available from pharmacies and would require at least some clinical oversight by a pharmacist. Overall, it is unclear how this new class of drugs might affect utilization, patient health, and medical costs. For example, utilization could rise, since patients would no longer need a physician's prescription. To the degree that this use is appropriate, BTC drugs could improve patient health and reduce medical costs by reducing the number of physician-office visits. However, if the increase in utilization leads to a large increase in inappropriate use, patient health could fall and medical costs could increase.

As a first step toward examining the potential effects of introducing BTC drugs in the United States, this paper summarizes and synthesizes the current medical and economic literature on the experience of these drugs in the United States and abroad. Although the United States has

some limited experience with this drug class, BTC drugs are more prevalent in other countries, such as the United Kingdom, Canada, and Australia.[1] Analyzing the effects of BTC drugs in other countries can provide useful insight into what the U.S. experience might be. In addition, although the U.S. experience with BTC drugs is limited, the United States has a great deal of experience with OTC drugs. Indeed, according to the FDA's Office of Nonprescription Products, more than 100,000 OTC products are marketed in the United States, and these products comprise roughly 800 distinct active ingredients. In general, OTC drugs are either low-dose versions of prescription drugs that have been converted from prescription to OTC status, or in some cases, are new doses that are only available OTC. Therefore, analyzing changes in use, patient health, and medical costs after the introduction of OTC variants of prescription drugs can provide useful insights into the potential effects of introducing BTC drugs.

It is important to note, however, that there are limitations to using the experience of OTC drugs to forecast the potential effects of BTC drugs. First, whereas patients are free to purchase OTC drugs without oversight or restrictions, patients who purchase BTC drugs must receive at least some oversight from a pharmacist. In addition, in the United States, OTC drugs are typically not covered under health insurance, while it is unclear whether BTC drugs would be covered. As a result, there may be substantial differences in patients' out-of-pocket costs for BTC and OTC drugs.

We begin this chapter with a brief discussion of the methodology used in our literature review. The next three sections describe the primary literature that discusses how BTC/OTC drugs have affected utilization, patient health, and medical costs. For each topic, we separately discuss the effects of BTC and OTC drugs, given the potential limitations of using the experience of OTC drugs to forecast the effect of BTC drugs.

Methods

We began our literature search with an initial scan that yielded 15 papers related to evaluations of the experience of BTC/OTC drugs in the United States and abroad. These papers provided

[1] Analogues to BTC drugs include pharmacy-only medications in the United Kingdom and schedule-3 drugs in Australia and Canada.

citations to roughly 200 unique papers, reports, and newspaper articles. We reviewed this initial set of documents and identified the keywords with which they were tagged in Medline, Cinahl, EMBASE, and Econlit. We then searched each of these databases using these keywords. Any relevant articles obtained through the subsequent searches were reference-mined for additional articles, and these articles were reviewed for additional search terms. After obtaining a final series of keywords, we used these keywords to search additional databases, including the New York Academy of Medicine Grey Literature Collection, the Conference Papers Index, Worldcat, Thomson ISI Web of Science, and the Internet (using the search engine Google).

The Effect of BTC/OTC Drugs on Utilization

The effect of BTC/OTC drugs on utilization is theoretically ambiguous. On the one hand, eliminating the need for a physician's prescription, and thereby eliminating the monetary costs and time requirements associated with a physician-office visit, may lead more patients to use the BTC version of the drug. However, to the degree that patients simply substitute BTC versions of a given drug for prescriptions, overall use of the drug may not change. Investigators have used a wide variety of methods to estimate the effects of BTC/OTC drugs on utilization. The two most common methods are using (1) insurance claims and (2) retail sales data to examine changes in prescription drug and overall (prescription plus BTC/OTC version) drug use after the introduction of BTC/OTC versions of a drug. In addition, in the case of drugs used for emergency contraception, several randomized, controlled trials have been performed to examine how BTC/OTC versions might affect use.

The Effect of BTC Drugs on Utilization

Several studies have examined the effect of BTC drugs on utilization in the United Kingdom, where BTC versions of H_2-receptor antagonists (H_2RAs) were introduced in 1994. BTC versions of emergency contraception arrived in 2001 and BTC versions of simvastatin and omeprazole arrived in 2004. Furler et al. (2002) find that, after their introduction, BTC H_2RAs accounted for 0.9 percent to 1.35 percent of all H_2RA sales and for 0.42 percent to 0.56 percent of all gastro intestinal (GI) therapy sales between 1992 and 1997. This suggests that the introduction of BTC H_2RAs did not have a large effect on utilization of this class of drugs.

Filion et al. (2007) used data from the General Practice Research Database, which contains prescription drug usage data for 3.5 million patients, to examine trends in simvastatin use before and after the drug was switched to BTC status. Beginning in 2001, the number of prescriptions for 10-mg simvastatin increased by 437 per 100,000 persons per quarter. However, after a BTC version of the10-mg dose was introduced, the number of simvastatin prescriptions for 10-mg simvastatin *fell* by 281 per 100,000 persons per quarter. Thus, the introduction of BTC simvastatin seems to have reduced the use of the prescription version. Further analyses suggested that younger patients, females, patients with no cholesterol testing, and patients with high total serum cholesterol were more likely to discontinue prescription statin therapy. Two points should be noted about this study. First, the authors did not measure the use of BTC simvastatin, so it is unclear whether the drop in simvastatin prescriptions was made up for by increased use of BTC simvastatin. Second, utilization of the 20-mg dosage followed similar trends, even though no BTC version was introduced. Thus, it is unclear whether the observed declines in prescriptions for 10-mg simvastatin were caused by the introduction of the BTC version, or whether the declines were driven by unobserved factors that affected prescriptions of statins more generally.

Dhippayom and Walker (2006) used pharmacy sales data and prescription sales data from 22 local health boards in Wales to examine trends in omeprazole (a proton-pump inhibitor [PPI]) and other anti-ulcer drugs, including H_2RAs, between 2002 and 2005. From 2002 to 2004, the number of prescriptions for H_2RAs fell by roughly 6.1 percent, while the number of prescriptions for PPIs overall and omeprazole in particular increased by 12.4 percent and 1.3 percent, respectively. In addition, sales of the BTC version of H_2RAs increased by 34.3 percent over this period. Between 2004 and 2005 (after the introduction of BTC PPIs), sales of prescription H_2RAs fell by 5.7 percent; sales of prescription PPIs and omeprazole increased by 14 percent and 24 percent, respectively; and sales of BTC H_2RAs fell by 8.6 percent. Thus, it appears that the introduction of BTC omeprazole may have caused patients to substitute away from BTC versions of H_2RAs without having a large effect on the use of prescription H_2RAs or PPIs.

Several studies examined the experience of introducing BTC emergency contraception in the United Kingdom. Using survey data, Marston et al. (2005) found that the use of emergency contraception did not change, but that women substituted away from physicians and toward pharmacists in order to obtain emergency contraception. Along these lines, Mawhinney and Dornan (2004) found that hospital emergency departments received fewer requests for

emergency contraception after the switch to BTC status. Girma and Paton (2006) used a propensity-score matching approach to examine the effect of BTC emergency contraception on pregnancy rates in England by comparing (1) pregnancy rates in the local authorities that offered OTC emergency contraception to teenagers with (2) pregnancy rates in local authorities that did not. They found no significant difference in teenage pregnancy rates between the two groups.

Efforts to examine the effect of BTC drugs in countries besides the United Kingdom have mostly focused on emergency contraception. Several studies have attempted to examine the effects increased access to emergency contraception by randomizing patients to either (1) being able to receive it directly from a pharmacist or (2) receiving small quantities of emergency contraception in advance. In the United States, Raine et al. (2005) randomly assigned 2,117 women, ages 15 to 24, to one of three groups. The first group received an advance (3-pack) supply of emergency contraception, the second group was allowed to access emergency contraception directly from a pharmacist, and the last (control) group could obtain emergency contraception only through a physician. Six months after the study began, women who received an advance supply of emergency contraception were nearly twice as likely to use emergency contraception as women in the control group, while women who could access emergency contraception via a pharmacist were no more likely to use emergency contraception than the control group. Similar studies performed in the United States (Glasier, 1998; Raine et al., 2000; Pentel et al., 2004; Raymond et al., 2006; Walsh and Frezieres, 2006), (Glasier et al., 2004), China (Lo et al., 2004; Hu et al., 2005), Ghana (Lovvorn et al., 2000), and India (Ellertson et al., 2001) showed similar results.

In Canada, using health claims data, Soon et al. (2005) found that the number of emergency contraception prescriptions nearly doubled following emergency contraception's 2001 conversion to BTC status in British Columbia. Moreau et al. (2006a; 2006b) used survey data to find a 72-percent increase in the use of emergency contraception after emergency contraception was converted to BTC status in France; its use was doubled among women ages 15 to 24. In Sweden, Larsson et al. (2006) found that emergency contraception use among women requesting abortions at a family-planning clinic increased by 12 percent after its conversion to BTC status.

The Effect of OTC Drugs on Utilization

In addition to examining changes in H_2RAs sales in the United Kingdom before and after H_2RAs were converted to BTC status (see above), Furler et al. (2002) examined changes in U.S. sales of these drugs before and after they were converted to OTC status in 1995. In contrast to the United Kingdom, where the market share of BTC H_2RAs was relatively small and did not grow significantly, in the United States, the market share of nonprescription H_2RAs as a percentage of all H_2RAs and as a percentage of all GI therapies grew from 5 percent to 17 percent and 3 percent to 7 percent, respectively. Andrade et al. (1999) examined patterns of H_2RA use among members of the Fallon Community Health Plan, a mixed-model health maintenance organization (HMO) in Massachusetts that enrolls roughly 172,000 people, in the one-year periods before and after the introduction of OTC H_2RAs. Using administrative claims data, they identified 2,028 patients who were chronic H_2RA users prior to the introduction of OTC H_2RAs. After OTC H_2RAs were introduced, the mean number of annual per-patient prescriptions for H_2RAs and for GI therapies more generally among these patients fell by 1.5 and 1.3, respectively.

Sullivan et al. (2005) used insurance claims data to examine changes in the utilization of prescription versions of loratadine following the introduction of OTC versions of the drug in December 2002. The authors began by identifying allergic rhinitis patients who filled at least two prescriptions for intranasal corticosteroids or second-generation antihistamines in 2002. They then examined these patients' utilization of prescription second-generation antihistamines following the introduction of OTC loratadine. Patients were divided into one of three groups based on their health plan's classification of prescription second-generation antihistamines following the introduction of OTC loratadine: those whose plans did not change the formulary status of second-generation antihistamines (this was the "no-change" group), those whose plans shifted second-generation antihistamines to a nonpreferred brand status (this was the "third-tier" group), and those whose plans enacted prior authorization requirements for prescription second-generation antihistamines (this was the "restricted" group). After the introduction of OTC loratadine, utilization of prescription second-generation antihistamines fell by 66 percent among the "no-change" group, by 65 percent among the "third-tier" group, and by 88 percent among the "restricted" group.

Several studies have examined how the use of nicotine gums and patches, as well as nicotine replacement therapy (NRT) more generally, changed following the introduction of OTC nicotine gum in the United States in April 1996 and of OTC nicotine patches in the United States in July 1996. Keeler et al. (2002) performed a particularly detailed and thorough study using retail sales data of the nicotine patch and nicotine gum. The authors devised simultaneous supply-and-demand equations for these drugs, using the price of tobacco, proxies for the cost of capital, and proxies for the number of retailers as instruments to identify and estimate the demand curve. The authors found that the conversion of these products to OTC status increased the use of nicotine gum by 180 percent and the use of the patch by 78 percent to 92 percent.

Similarly, Pierce and Gilpin (2002) used data from the 1992, 1996, and 1999 versions of the California Tobacco survey to examine the effect of OTC availability on the use of NRT more generally. They found that the use of NRT in quitting attempts increased from 9.3 percent to 14.0 percent between 1992 and 1999, and that the percentage of smokers who made attempts to quit increased from 38.1 percent to 61.5 percent. Smokers who used nicotine-replacement therapy were more likely than those who did not to remain abstinent in 1992, 1996, and 1999. However, in 1999, the effect was mainly short term (3 months); after this period, both NRT users and nonusers relapsed to smoking at a similar rate. In addition, in 1999, the benefits of NRT were confined to moderate and heavy smokers.

Although the study by Pierce and Gilpin (2002) is potentially useful for looking at long-term trends in the use of NRT, it did not explicitly control for factors, such as cigarette prices and taxes, that changed over time and that might have affected smoking behavior and the use of therapy products. To deal with this issue, Reed et al. (2005) used the California Tobacco Survey to examine trends in NRT use and smoking abstinence within a short timeframe (November 1995 to November 1996) before and after the introduction of OTC nicotine gums and patches. The rationale behind the short timeframe was that other factors, such as cigarette prices, were unlikely to drastically change during that period. Overall, their results confirmed the 2002 findings of Pierce and Gilpin that OTC availability increased the usage of nicotine gums and patches.

In contrast to these results, Thorndike et al. (2002) used data from the Massachusetts Tobacco Surveys to examine how OTC availability of NRT affected use of the therapy and

attempts to quit smoking. They found that the proportion of smokers who attempted to quit, quit successfully, or used NRT in an attempt to quit did not change significantly after the introduction of OTC NRT. Intriguingly, the authors found that older smokers (ages 46 and above) and nonwhite smokers were *less* likely to use NRT after its OTC introduction. The difference between these results and the previous results from Pierce and Gilpin (2002) and Reed (2005) likely stems from differences in confounding factors between the states of California and Massachusetts. For example, although both states enacted large-scale tobacco-control programs funded by excise taxes on tobacco, California's program was established in 1988, while Massachusetts' was established in 1992. Moreover, in 1996, Massachusetts enacted an additional increase in cigarette taxes, as well as a new tax on cigars, while California enacted a cigarette tax increase in 1999.

Antifungal drugs such as clotrimazole and tioconazole are used to treat vaginal yeast infections. In the United States, OTC versions of clotrimazole were introduced in 1991; OTC versions of tioconazole were introduced in 1997. Gurwitz et al. (1995) used administrative claims data from the Fallon Community Health Plan in central Massachusetts to examine usage of vaginal antifungal drugs before and after the switch to OTC status. The authors compared the number of prescriptions for these drugs, as well as the number of physician-office visits for vaginitis, in the one-year period before and after the switch to OTC status. Overall, they found that after the switch to OTC status, the number of annual prescriptions for vaginal antifungals fell by 6.42 per 100 women ages 11 and older; the number of annual physician-office visits for vaginitis fell by 0.66 per 100 members.

Studies have also examined the effect of OTC drugs on utilization in countries besides the United States. In Sweden, nasal sprays containing the decongestants oxymetazoline and xylometazoline were converted to OTC status in 1989. Lundberg and Isaacson (1999) used data from a research registry to examine changes in the use of these sprays in Tierp, Sweden, between 1988 and 1995. Their results show that use of nasal drops fell from 408 packages to 30 packages per 1,000 inhabitants during this period, while the use of sprays increased from 152 packages to 669 packages per 1,000 inhabitants. In addition, the proportion of physician-office visits for sinusitis and rhinitis fell from 10 percent to 8 percent. Similarly, between 1988 and 1992, the number of prescriptions for nasal sprays fell from 143 prescriptions to 37 prescriptions per 1,000 inhabitants. In another study, Carlsten et al. (1996) examined sales of 16 drugs that were

converted to OTC status in Sweden between 1980 and 1994. They found that sales of 14 of these drugs increased an average of 36 percent two years after their conversion to OTC status, and that prescriptions for these drugs fell an average of 26 percent.

Conclusions

Overall, there appears to be a general consensus that the introduction of BTC/OTC drugs reduces the number of prescriptions issued for these drugs.[2] One potential exception is the United Kingdom, where the introduction of OTC H_2RAs and PPIs did not have an appreciable effect on sales of prescription versions (Furler et al., 2002; Dhippayom and Walker, 2006). The discrepancy between the United Kingdom and other countries may come from idiosyncrasies in the UK national health system. In the United Kingdom, OTC versions of a drug are often more expensive than the prescription versions, particularly for patients with special exemptions that allow them to obtain prescription drugs for free (Thomas and Noyce, 1996; Baines and Whynes, 1997). Thus, UK patients may experience reduced financial incentives to switch to OTC versions of a drug.

Although BTC/OTC drugs appear to have reduced the use of prescription drugs, their effects on total (prescription plus BTC/OTC version) drug use are unclear because none of the studies discussed above explicitly measured BTC/OTC use. Put differently, the degree to which the drop in prescription drug use was offset by BTC/OTC drug use is unknown. Because total (prescription plus BTC/OTC) sales generally increase, it appears that the fall in prescriptions is accompanied by a substitution toward BTC/OTC versions of the drug. However, since the studies examining sales data typically do not examine changes in quantities, it is unclear how the increase in BTC/OTC use compares with the fall in prescription drug use.

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[2] See Andrade et al. (1999) and Furler et al. (2002) (H_2 receptor antagonists); Sullivan et al. (2005) (second-generation antihistamines); Filion et al. (2007) (statins); Pierce and Gilpin (2002), Reed et al. (2005) and Thorndike et al. (2002) (NRT); Dhippayom and Walker (2006) (proton-pump inhibitors); Gurwitz et al. (1995) (vaginal antifungals), Glasier (1998), Raine (2000), Raymond et al. (2006), Pentel et al. (2004), Walsh (2006), Glasier (2004), Hu (2004), Lo (2004), Lovvorn (2000) and Ellertson (2001) (emergency contraception); Lundberg and Isaacson (1999) (nasal decongestants); Carlsten et al, (1996) (several OTC drugs).

The Effect of BTC/OTC Drugs on Health

The varying effects of BTC/OTC drugs on patient health are primarily mediated through their effects on utilization. To the degree that these drugs increase use among patients who would otherwise not use the drug due to monetary costs and time requirements, patient health may improve. However, if these costs and requirements cause patients to inappropriately substitute BTC/OTC drugs for prescription versions, or to substitute these drugs for appropriate physician consultation, patient health could suffer. Studies examining the effect of BTC/OTC drugs have used several approaches. For emergency contraception drugs and mevastatin, randomized control trials were used to simulate the effect of BTC/OTC drugs. In addition, investigators have also used decision-analytic methods to model the potential health effects of BTC/OTC drugs.

The Effect of BTC Drugs on Patient Health

The vast majority of studies that examine the effects of BTC drugs on health have focused on emergency contraception. As described in the previous section, several randomized controlled trials in the United States (Raine et al., 2005; Glasier, 1998; Raine et al., 2000; Pentel et al., 2004; Raymond et al., 2006; Walsh and Frezieres, 2006), Scotland (Glasier, et al. 2004), China (Lo et al., 2004; Hu et al. 2005), Ghana (Lovvorn et al., 2000), and India (Ellertson et al., 2001) suggest that BTC provision of emergency contraception increases its use. However, these studies also unanimously found that BTC provision of emergency contraception has no effect on pregnancy rates. These results are corroborated by Girma and Paton (2006), who used a propensity-score matching approach to examine the effect of BTC emergency contraception on pregnancy rates in England by comparing (1) pregnancy rates in local authorities that offered OTC emergency contraception to teenagers with (2) pregnancy rates in local authorities that did not. They found no significant difference in teenage pregnancy rates between the two groups. Further research is needed to understand the possible reasons why these studies found that BTC status has increased use of emergency contraception without having an effect on pregnancy rates (Raymond et al., 2006).

The only other study to have examined the effect of BTC drugs on health examined selective β_2-agonist inhalers, which have been available BTC in Australia since 1985. Gibson et al. (1993) surveyed 403 patients ages 13 to 55 who purchased albuterol inhalers with and without

a prescription. Their results suggest that, compared to prescription users, BTC users are 2.9 times more likely to undertreat their asthma, although this difference disappears when controlling for the frequency of consultation with a physician. Thus, the primary reason why BTC users are more likely to undertreat their asthma is due to the fact that they are less likely to consult with their physician about asthma care.

The Effect of OTC Drugs on Patient Health

Using data from the U.S. National Health Interview Survey, Oster et al. (1990) estimated that in any given quarter, 5.7 million persons experience dyspepsia, of which 3.5 million self-medicate for the condition with antacids. Note that at the time of the study, H_2RAs had not yet switched to OTC status. Under the assumption that 30 percent of antacid users and 15 percent of non–self-medicating patients would opt to use OTC H_2RAs, they found that switching H_2RAs to OTC status would increase the percentage of self-medicating patients to 64.1 percent. The percentage of self-medicating dyspepsia patients experiencing side effects would fall from 12.2 percent to 11.8 percent, and the number of patients seeking professional care would fall from 58.2 percent to 53.1 percent. Thus, the authors concluded that switching H_2RAs to OTC status would, on the whole, be beneficial to patients.

Sullivan et al. (2003) used decision-analytic methods to simulate the cost-effectiveness of introducing OTC second-generation antihistamines. Overall, the authors calculated that such a policy would yield a total gain of 135,061 quality-adjusted life years as a result of reductions in the number of injuries and increases in the number of allergic-rhinitis patients who experienced symptom relief. These results were primarily driven by the assumption that first-generation antihistamines have a sedation rate of 17 percent, while second-generation antihistamines are nonsedating. The authors also assumed that OTC second-generation antihistamines would reduce the percentage of patients who did not seek treatment for allergic rhinitis from 14 percent to 7 percent.

In the United States, there have been efforts to switch low-dose statins to OTC status, although these efforts have not been successful—in 2005, a FDA panel recommended against switching lovastatin to OTC status. However, the Consumer User Study of OTC Mevacor (CUSTOM) examined patient usage of Mevacor (lovastatin) under simulated OTC conditions

(Brass, 2004; Melin et al., 2004). Out of 3,316 persons who were given an opportunity to purchase lovastatin under simulated OTC settings, 1,061 chose to purchase the drug. Over 98 percent of nonpurchasers were ineligible for the drug, as determined by the labeling criteria, while 66 percent of purchasers were eligible for the drug. After 26 weeks, only 2 percent of purchasers exhibited behaviors that were contraindicated by the label. In a follow-on study, Brass et al. (2006) used the results of CUSTOM to analyze the cost-effectiveness of moving lovastatin to OTC status. Given the risk profile of the CUSTOM patients, Brass et al. estimated that the use of 20-mg lovastatin for 10 years could reduce the number of coronary heart-disease events by up to 33,100 per 1 million users. However, taking into account the fact that some patients would inappropriately use OTC lovastatin instead of higher-dose prescription forms of the drug, the authors calculated that OTC lovastatin mightreduce coronary heart-disease events by up to 23,300 per 1 million users. Overall, then, these two studies suggest that introducing OTC statins may have net health benefits, even if some patients inappropriately use OTC statins in lieu of higher-strength forms.

The concern over inappropriate use was corroborated in a brief survey of 200 physicians, 273 pharmacists, and 600 consumers conducted by McKenney et al. (2004), who found that a large majority of physicians and pharmacists (75 percent and 79 percent, respectively) were concerned that patients would inappropriately replace their prescription statins with OTC versions. In addition to these studies, Gemmell et al. (2007) used decision analysis to show that the introduction of OTC statins for low- and moderate-risk patients could prevent as many coronary heart-disease events as providing prescription statins to high risk-patients. A weakness of this latter study, however, is that it does not consider the problems associated with inappropriate use of OTC statins.

As noted in the previous section, a substantial literature has examined how the introduction of OTC nicotine gums and patches affected the use of NRT. Much of this literature has also examined the effect of these OTC drugs on the frequency of attempts to quit and the probability of successful smoking-cessation attempts. Using data from the 1992, 1996, and 1999 California Tobacco Surveys, Pierce and Gilpin (2002) found that the use of NRT in quitting attempts increased from 9.3 percent to 14.0 percent between 1992 and 1999, and that the percentage of smokers who made attempts to quit increased from 38.1 percent to 61.5 percent. Smokers who used NRT were more likely than those who did not to remain abstinent in 1992,

1996, and 1999. However, in 1999, the effect was mainly short term (3 months); after this period, both NRT users and non-users relapsed to smoking at a similar rate. In addition, in 1999, the benefits of NRT were confined to moderate and heavy smokers. Using the same data, but focusing on a shorter period to avoid bias from any uncontrolled factors that might affect smoking quit rates over time, Reed et al. (2005) found similar results. In contrast, using data from the Massachusetts Tobacco Surveys, Thorndike et al. (2002) found that the proportion of smokers who attempted to quit, quit successfully, or used NRT in an attempt to quit did not change significantly after the introduction of OTC NRT. Intriguingly, the authors found that older smokers (ages 46 and above) and non-white smokers were *less* likely to use NRT after its OTC introduction. As stated in the previous section, the difference between this study and the studies by Pierce and Gilpin (2002) and Reed (2005) likely stems from differences in confounding factors between the states of California and Massachusetts.

Shiffman et al. (2002) compared the efficacy of prescription and OTC NRTs under real-world conditions. The study examined 6-week and 6-month abstinence rates among 2,981 OTC-gum and 2,367 OTC-patch users to rates among 324 prescription-gum and 669 prescription-patch users. Overall, abstinence rates with OTC NRTs were as high or higher than with prescription NRTs. On average, 16.1 percent of OTC gum users were abstinent at six weeks, and 8.4 percent were abstinent at six months. In contrast, 7.7 percent of prescription gum users were abstinent at six weeks and at six months. Similarly, 19.0 percent of OTC patch users were abstinent at six weeks and 9.2 percent were abstinent at six months, while 16.0 percent of prescription patch users were abstinent at six weeks and 3.0 percent were abstinent at six months. It is useful to note that patients were not randomized to receive either OTC or prescription NRT therapy; therefore, the study could rule out the possibility that inherent differences between OTC and prescription NRT users may explain the results.

Finally, Rubin and Foxman (1996) used decision analysis to examine the cost-effectiveness of switching oral antibiotics used to treat urinary tract infections (UTIs) to OTC status. Their study suggests that OTC antibiotics would reduce patient health because of the assumed large percentage (43 percent) of patients with urinary symptoms who misdiagnose themselves as having a UTI. This misdiagnosis would likely lead to inappropriate treatment of non-UTIs with OTC antibiotics.

Conclusions

In general, most of the studies that have examined the effects of BTC/OTC drugs on patient health are simulations that use decision-analytic methods. Using such methods, BTC/OTC status is forecasted to *improve* patient health—as in the case of H_2RAs (Oster et al., 1990), second-generation antihistamines (Sullivan et al., 2003), and statins (Brass, 2004; Melin, et al. 2004; Gemmell, et al. 2007)—*decrease* patient health—as in the case of UTI antibiotics (Rubin and Foxman, 1996)—or to have *no impact* on patient health—as in the case of emergency contraception and pregnancy rates in the United States (Raine et al., 2005; Glasier, 1998; Raine et al., 2000; Pentel et al., 2004; Raymond et al., 2006; Walsh and Frezieres, 2006; Glasier et al., 2004; Lo et al., 2004; Hu et al., 2005; Lovvorn et al., 2000; Ellertson et al., 2001; Girma and Patton, 2006). Thus, the quality of these studies is highly dependent on the underlying parameters driving the simulation model. Although many of these parameters, such as drug efficacy, are taken from the literature, it is not clear whether they will remain constant when patients use the drugs with less supervision. Moreover, the decision analyses generally fail to explicitly model the possibility of inappropriate use.

The only studies that empirically examined the potential health effects of BTC/OTC status focus on NRT, where two studies (Pierce and Gilpin, 2002; Reed et al., 2005) found that the switch to OTC status improved the probability and frequency of successful attempts to quit smoking, and one study (Thorndike et al., 2002) did not. As discussed above, discrepancies between the two studies may stem from the fact that the first two studies examined the effects in California, while the last study focused on Massachusetts; differences in other state policies may explain the disparate outcomes.

The Effect of BTC/OTC Drugs on Costs

In examining how BTC/OTC drugs might affect medical costs, it is useful to consider two types of costs: (1) the logistical costs patients face in acquiring prescription medications, particularly the time requirements and monetary costs of physician-office visits as well as the cost of the drug itself; and (2) medical costs associated with appropriate and inappropriate use of a drug. Since BTC/OTC drugs eliminate the need for a prescription, they will likely lower the first type of cost, particularly by reducing the number of physician-office visits and associated expenses. However,

their effects on medical costs are more ambiguous and, similar to their effects on patient health, depend on the degree to which the benefits of increased appropriate use are outweighed by the costs of inappropriate use. In addition to their effects on overall costs, it is important to note that BTC/OTC drugs may also shift the burden of costs toward the patient. Currently, prescription drugs are covered under insurance, so the costs of these drugs are split between patients and insurers. Because OTC drugs are not covered by insurance, patients bear the full cost of these drugs. It is unclear whether insurers will cover BTC drugs, and therefore it is unclear how the costs of these drugs will be split between patients and insurers.

The vast majority of studies have examined the effect of OTC drugs on costs; indeed, we could find only two studies that examined the use of BTC drugs on costs. These studies have typically followed one of two approaches. The first approach uses insurance claims data to compare spending by insurance plans before and after BTC/OTC versions of a drug are introduced. The second approach uses decision-analytic methods to forecast the potential effects of the introduction of BTC/OTC drugs. Both methods have their advantages and limitations. Studies using claims data are useful because they provide empirical evidence of the effects of BTC/OTC drugs on costs. However, many of the studies we reviewed do not explicitly examine the costs of inappropriate use. Moreover, by design, these studies only consider the insurer, and do not consider the societal perspective. For example, the claims-data studies do not take into account the amounts that patients spend on OTC versions of a drug. Decision-analytic methods are more useful because they often focus on the societal perspective, although some of the studies we review focus only on the insurer perspective. The main limitation of these decision-analytic studies is the quality of the underlying assumptions driving the simulation model.

The Effect of BTC Drugs on Medical Costs

Bojke et al. (2004) analyzed the effect of moving drugs to BTC status in the United Kingdom on physician workload. Their approach simulated the movement of drugs to BTC status by giving patients who called their physician with complaints of minor ailments an opportunity to consult with a pharmacist first. The pharmacist could then recommend a BTC drug to the patient, or could refer the patient to a physician if necessary. The simulated switch to BTC/OTC status did not have any effect on the total number of physician-office visits, but reduced by roughly one-

fifth (from 7.8 percent to 6.3 percent) the number of visits for minor ailments, providing some evidence that BTC drugs may lower the costs of physician-office visits associated with minor ailments.

Marciante et al. (2001) used decision-analytic methods to examine the cost-effectiveness of moving emergency contraception to BTC status in the United States. They estimated that doing so would reduce the incidence of pregnancy by 3.8 percent (from 4.9 percent to 1.8 percent), and that this reduction in pregnancies would reduce total medical costs by $158 per person per year for patients covered by private insurance and $48 per person per year for patients covered under public plans. Using similar methods, Zhu (2001) found that introducing OTC emergency contraception would save $13 billion annually in the U.S., and Trussell et al. (1997a and 1997b) estimated that advance provision of emergency contraception could save roughly $180 to $356 per female patient in managed care settings and $62 to $141 per female patient in public payer settings due to reductions in the number of pregnancies. However, it is important to note that all of these studies assume that emergency contraception will reduce pregnancy rates. Given the substantial literature discussed above that suggests that emergency contraception has little effect on the pregnancy rate in real-world settings, these studies may overestimate the savings from public provision of emergency contraception.

The Effect of OTC Drugs on Medical Costs

Several studies have examined the cost effects of introducing OTC H_2RAs in the United States. Kalish et al. (1997) developed a model that assumes that one-third of antacid users and one-eighth of patients using no medicine would switch to OTC H_2RAs. Overall, they found that introducing OTC H_2RAs is not likely to have an effect on medical costs, for three reasons. First, OTC H_2RAs and antacids were assumed to have roughly the same efficacy at relieving dyspeptic symptoms. Second, the authors assumed that the vast majority of people who would use OTC H_2RAs are persons who would otherwise have self-medicated with antacids. Therefore, OTC H_2RAs would be unlikely to reduce the number of patients seeking formal care. In addition, the authors assumed that physicians would be more likely to order expensive diagnostic tests, such as endoscopies, for patients who use OTC H_2RAs and did not find symptom relief, compared to patients who used antacids without effect.

Along these lines, Kunz et al. (1996) developed a model to forecast how the OTC introduction of a particular H_2RA, famotidine, would change costs for a 260,000-member managed-care organization. Data from the plan itself were used to calculate the incidence of dyspepsia and heartburn, as well as the costs of physician visits and laboratory examinations; data from existing literature were used to determine the efficacy of OTC famotidine. Overall, Kunz et al. estimated that in a five-year period, the plan would incur costs of $24 million to treat dyspepsia and heartburn, and that the introduction of OTC famotidine would save the plan $6 million, or 25 percent.

Andrade et al. (1999) examined patterns of H_2RA use among members of the Fallon Community Health Plan, a mixed-model HMO in Massachusetts that enrolls roughly 172,000 people, in the one-year periods before and after the introduction of OTC H_2RAs. Using administrative claims data, they identified 2,028 patients who were chronic users of these drugs prior to the introduction of the OTC version. After the OTC versions were introduced, the mean number of prescriptions for H_2RAs and for GI therapies more generally among these patients fell by 1.5 and 1.3 per person respectively. Although the mean number of physician visits and the incidence of gastro esophageal reflux disease (GERD)-related conditions did not change, health-plan costs for H_2RAs and GI therapies fell by $130.02 and $92.56 per patient, respectively, leading to overall savings of $187,712. Thus, the introduction of OTC H_2RAs appears to have reduced costs for the health plan. However, the study does not provide information on costs from the patient or societal perspectives, as it does not examine usage of OTC drugs. Nor does it mention whether co-pays for prescription H_2RAs s changed when OTC versions were introduced.

Shaw et al. (2001) performed community surveys in 1993 and 1997 to examine the effect of OTC H_2RAs on physician-office visits. In 1993, they surveyed 800 men and 800 women ages 20 to 80; in 1997, they surveyed 900 men and 900 women in the same age range. In 1993, 22.0 percent of patients who visited a physician presented with symptoms of dyspepsia and 23.6 percent presented with heartburn symptoms; in 1997, the percentages were 23.5 percent and 21.9 percent, respectively. Thus, the introduction of OTC H_2RAs does not appear to have reduced the number of physician-office visits with these two complaints.

In addition to analyzing the cost effects of OTC H_2RAs, several studies have examined the cost effects of introducing OTC second-generation antihistamines in the U.S.. We previously described a study by Sullivan et al. (2003) that used decision-analytic methods to estimate that introducing OTC second-generation antihistamines would yield a total gain of 135,061 quality-adjusted life years due to a reduction in accident-related injuries and an increase in the number of allergic rhinitis patients who found relief of their symptoms. The authors also found that introducing OTC second-generation antihistamines would yield cost savings per allergic rhinitis patient of $100 per year, for a total annual savings of $4 billion. In a related study, Cohen and DiMasi (2001) used decision analysis to examine the effect of an OTC loratadine, a second-generation antihistamine, on costs to health plans and patients. They found that health plans will benefit the most from the switch as patients shift to OTC versions of the drug, which are typically not covered by insurers. Cohan and DiMasi also found that uninsured patients could save as much as 80 percent, since OTC loratadine is likely to be cheaper than the prescription version. However, their results are ambiguous with respect to insured patients, since it is not clear whether these patients' existing co-payments for the prescription drug are likely to cost less than the OTC version.

In follow-on work, Sullivan and Nichol (2004) examine the cost-effectiveness, from a payer perspective, of covering OTC and prescription second-generation antihistamines under four scenarios:

1. Coverage of both OTC and prescription second-generation antihistamines as preferred branded drugs (tier 2), with coverage of OTC second-generation antihistamines requiring a physician's prescription

2. Coverage of prescription second-generation antihistamines as tier-2 drugs, with no coverage of OTC second-generation antihistamines

3. Coverage of prescription second-generation antihistamines as tier-3 drugs, with no coverage of OTC second-generation antihistamines

4. No coverage for either prescription or OTC second-generation antihistamines.

From the perspective of a managed care organization, the authors found scenario (1) highly preferable to scenarios (2) and (3) because costs are lower and patient health is higher

under scenario (1). Therefore, the main choice is between scenarios (1) and (4). Sullivan and Nichol found that managed care organizations should choose scenario (1) over scenario (4) as long as they are willing to pay at least $26,226 per quality-adjusted life year. Thus, the authors concluded that providing coverage for OTC second-generation antihistamines can be cost-effective for payers.

The above studies represent efforts to use decision-analytic methods to forecast the cost effects of OTC second-generation antihistamines. We previously described a study by Sullivan et al. (2005), who used insurance claims data to empirically examine changes in loratadine utilization following the introduction of OTC versions in December 2002. This study also examined the cost savings to insurers from the introduction of OTC loratadine, and found per-member, per-month savings ranging from $17.56 to $20.21 (i.e., 136 percent to 147 percent of baseline spending), depending on the restrictions placed on prescription versions of the drug.

With regards to NRT, we previously described a study by Keeler et al. (2002), which found that that the introduction of OTC nicotine gums and patches increased their use by 180 percent and 78 percent to 92 percent, respectively. The authors also used the literature on the effectiveness and use of these aids, as well as the literature on the value (in quality-adjusted life year terms) of smoking cessation, to calculate the social value of these increases in utilization. Overall, they estimated that the increase in use of smoking-cessation aids generated annual net social benefits of $1.8 billion to $2 billion.

Antifungal drugs such as clotrimazole and tioconazole are used to treat vaginal yeast infections. In the United States, OTC versions of clotrimazole were introduced in 1991 and OTC versions of tioconazole in 1997. Gurwitz et al. (1995) used administrative claims data from the Fallon Community Health Plan in central Massachusetts to examine use of vaginal antifungal drugs before and after the switch to OTC status. The authors compared the number of prescriptions for these drugs, as well as the number of physician-office visits for vaginitis, in the one-year periods before and after the switch to OTC status. Overall, they found that after the switch to OTC status, the number of prescriptions for vaginal antifungals fell by 6.42 per 100 women ages 11 and older, and the number of physician visits for vaginitis fell by 0.66 per 100 members. The authors estimated that OTC availability of antifungal drugs saved the plan

$42,528 in medicine costs and $12,768 to $25,729 in physician visits per year, depending on assumptions about the use of laboratory testing for vaginitis patients.[3]

Similarly, McCaig and McNeil (2005) used data from the National Ambulatory Medical Care Surveys (NAMCS), a nationally representative survey of physician-office visits, to examine how the introduction of OTC antifungals affected physician-office visits for vaginitis and prescriptions for antifungal drugs. They found that the rate of physician-office visits for vaginitis and for vulvovaginal candidiasis fell by 55 percent and 72 percent, respectively, from 1985 to 2001. The prescribing rate for intravaginal antifungals fell by 41 percent over this period, although the prescribing rate for all antifungals remained constant. However, it is important to note that all of these variables were already trending downwards *prior to the introduction of OTC antifungals*. Therefore, the degree to which the observed declines over this period are due to the introduction of OTC antifungals is not clear. The declines may have been, in part or wholly, due to other factors that reduced the incidence of candidal infections more generally. Lipsky et al. (2000) correct for this possibility using the NAMCS by showing that between 1985 to 1990, vaginitis visits fell by roughly 2 percent per year, while between 1990 to 1994 (after the introduction of OTC antifungals), vaginitis visits fell by 23 percent. Assuming that the pre-OTC decline of 2 percent per year represents a baseline trend due to other factors, their analysis suggests that the introduction of OTC antifungals reduced the frequency of vaginitis visits by 15 percent. The authors estimated that this reduction in physician-office visits resulted in savings of $45 million per year.

Gianfrancesco et al. (2002) also used administrative claims data to examine how the introduction of OTC tioconazole affected medical costs. However, in contrast to the studies described above, they found that medical costs *rose* by 21 percent after the introduction of OTC tioconazole. They identified 55 patients who used prescription versions of these drugs in the six months before the OTC approval date, and compared these patients' medical costs, measured as the total amounts billed for claims under the medical benefit, in the six months before and after the approval date. To control for unobserved factors that might have affected medical costs, they

[3] In the year following the introduction of OTC antifungal drugs, the health plan covered 67,365 women ages 11 and over.

compared the change in medical costs for these patients against 56 patients who were diagnosed with a vaginitis but who did not use the drugs. There are several possible reasons why these findings might differ from the studies cited above. First, the sample size means that the estimate may be very imprecise, and indeed, the authors do not report confidence intervals for their estimates. Second, unlike the previous studies, the authors use a control group to control for unobserved effects that may have influence medical costs. Thus, the decreases in medical costs reported by the previous studies may simply represent the effect of underlying trends, as opposed to switches to OTC status. Indeed, medical costs fell among the control group in this study, suggesting the presence of underlying trends in medical costs.

Ryan and Yule (1990) examined the economic benefits of introducing OTC versions of loperamide, an antidiarrheal drug, and 1-percent topical hydrocortisone in the United Kingdom. Using a demand-curve framework, as well as data on the sales of prescription and OTC versions of each drug, they estimated the social benefit of OTC availability of loperamide to be worth a total of £9.9 million between 1985 and 1987. For 1-percent topical hydrocortisone cream, the value of OTC availability was £2.0 million in 1987. One potential flaw with their analysis is that it in effect calculates the economic value of increased consumption due to the OTC availability of both drugs. However, against this economic value must be weighed the costs of any (non-price–related) consequences from increased consumption, such as increases in side effects or adverse reactions, which the authors do not consider.

Gianfrancesco et al. (2002) use administrative claims data to examine how the introduction of OTC cromolyn, ketoconazole, and terbinafine affected medical costs. They identified patients who used prescription versions of these drugs in the six months before the OTC approval date, and compared these patients' medical costs, measured as the total amounts billed for claims under the medical benefit, in the six months before and after the approval date. To control for unobserved factors that might have affected medical costs, they compared the change in medical costs for these patients against patients who were diagnosed with conditions for which these drugs are prescribed. They found that medical costs *increased* after the introduction of OTC version of each of the drug. Costs increased by 21.7 percent for cromolyn patients, 35.9 percent for ketoconazole patients, and 36.5 percent for terbinafine patients. It is important to note, however, that the authors do not report confidence intervals for their estimates, so it is unclear whether these results have statistical significance.

Temin (1992) calculated the effects of the introduction of OTC cold medications on consumer welfare in the United States. He found that this introduction reduced the number of physician visits for colds by 110,000 per year, although his approach toward this estimate is mostly descriptive, and it does not account for the possibility of underlying trends. This reduction in physician-office visits saved consumers $70 million in 1989. In addition, Temin estimated a rudimentary demand curve for cold medications and used this curve to calculate the increase in consumer surplus from the switch to OTC. His results suggest that the introduction of OTC cold medications increased consumer surplus by $700 million in 1989.

Rubin and Foxman (1996) used decision analysis to examine the cost-effectiveness of switching oral antibiotics used to treat UTIs to OTC status. Surprisingly, they found that the switch would *not* be cost-effective. For example, their estimates suggest that, over a 20-year horizon, such a switch would also lead to a $301 million increase in costs for treatment and physician-office visits. The main factor driving these results is the large percentage (43 percent) of patients with urinary symptoms who misdiagnose themselves as having a UTI. This misdiagnosis would likely lead to inappropriate treatment of non-UTIs with OTC antibiotics.

Lundberg and Isaacson (1999) used data from a research registry to examine changes in the sales in the number of physician visits for rhinitis and sinusitis in Tierp, Sweden, between 1988 and 1995, following the introduction of OTC decongestant nasal sprays in 1989. Their results show that the proportion of physician-office visits for sinusitis and rhinitis fell from 10 percent to 8 percent, and that the number of prescriptions for nasal sprays fell from 143 to 37 prescriptions per 1,000 inhabitants. Overall, the authors estimated that the decrease in the number of physician-office visits for rhinitis and sinusitis reduced public expenditures due to physician visits for these diseases by 24 percent. In another study, Carlsten et al. (1996) examined sales for 16 drugs that were converted to OTC status in Sweden between 1980 and 1994. They found that sales increased an average of 36 percent for 14 out of the 16 drugs two years after their conversion to OTC status, and that prescriptions for these drugs fell an average of 26 percent. Overall, they estimated that the conversion to OTC status saved the government $400 million.

Conclusions

Given that BTC/OTC status reduces the use of prescription forms of the drug, it is not surprising that it also reduces the amount that private and public health insurers pay for the drug. However, the OTC version of the drug is typically not covered by insurance, and little is known about the degree to which reduced spending by the health plan is made up for by increased consumer spending. While it is true that net sales increase, few of the studies above decomposed the change in sales into the portion due to increases in price versus increases in quantity, making it difficult to assess whether the degree to which the increase in sales is due to increases in utilization versus increases in drug costs.

One of the main ways in which the introduction of BTC/OTC drugs is thought to affect medical costs is by reducing physician-office visits for prescription versions of these drugs. Here, the evidence is mixed. The number of physician-office visits fell after the introduction of OTC vaginal antifungals in the United States (Gurwitz et al., 1995; Lipsky et al., 2000; McCaig and McNeil, 2005) but did not change in the case of H_2RAs (Andrade et al., 1999; Shaw et al., 2001). Given this ambiguity over the effect of BTC/OTC drugs on physician-office visits, it is not surprising that there is similar ambiguity over whether these drugs reduce medical costs. Using administrative claims data to compare how much insurers spent, in total, on patients who used a given drug before and after it switched to BTC/OTC status, it appears that medical costs fell in the case of H_2RAs (Andrade et al., 1999) and vaginal antifungals (Gurwitz et al., 1995; McCaig and McNeil, 2005) and rose in the case of some other drugs (Gianfrancesco et al., 2002), although the latter study did not report whether the increase was statistically significant. However, the H_2RA and vaginal antifungal studies are limited by the fact that they only examined costs directly related to the disease under consideration (i.e., the cost of the drug itself, physician-office visits for the disease, and any related expenses) and did not consider other costs, such as costs due to adverse reactions and inappropriate treatment.

In addition to these empirical studies, several decision-analytic studies suggest that BTC/OTC status reduces medical costs in the case of second-generation antihistamines (Cohen and DiMasi, 2001; Sullivan et al., 2003), emergency contraception (Trussell et al., 1997a; Trussell et al., 1997b; Marciante et al., 2001; Zhu et al., 2001), and nasal decongestants (Lundberg and Isacson, 1999), and would have no effect on costs in the case of H_2RAs (Kalish et

al., 1997) and antibiotics used to treat UTIs (Rubin and Foxman, 1996). However, these studies are typically based on parameters obtained from the literature, such as clinical trials, and may not hold in actual practice. Accordingly, these results need to be viewed with caution. For example, several decision analyses suggest that providing BTC/OTC versions of emergency contraception may save costs by reducing the number of pregnancies and abortions. However, all of these studies assume that emergency contraception use is efficacious at reducing pregnancy rates, when in fact nearly all empirical studies suggest the opposite. Ultimately, then, while the literature is clear that changes to BTC/OTC status reduce the amount of medical costs borne by public and private insurers, it is less clear whether they reduce costs more generally. Indeed, it may be the case that medical costs rise for some drugs and fall for others, depending on the likelihood and consequences of inappropriate use.

Conclusions

Overall, our review of the literature suggests the following:

- The introduction of OTC/BTC drugs generally causes patients to substitute toward the BTC/OTC version and away from the prescription version, but the effect on overall use is more ambiguous, and depends to some degree on the structure of private and public health insurance.
- Although many studies have examined the effect of BTC/OTC status on use, far fewer studies have examined the effect on medical costs. There is a general consensus that BTC/OTC status reduces the cost of prescription drugs for payers, such as private and public health insurers. However, the degree to which this is countered by increases in consumer spending is unknown. There is also far less consensus over whether BTC/OTC status reduces medical spending through other means, such as reduced physician-office visits.
- Very few studies have examined how OTC/BTC status affects patient health.
- Many of the studies that we have examined exhibit methodological issues that suggest caution when interpreting the results.

The studies that we examined typically fall into one of three categories: (a) decision analysis–based evaluation of prescription-to-BTC/OTC changes, (b) demand curve–based evaluation of prescription-to-BTC/OTC changes, and (c) empirical comparisons of various outcomes (sales, prescription-drug claims, etc.) in the period before and after a drug switched to BTC/OTC status. It is important to understand the limitations of these studies more generally, as well as additional limitations based on the implementation of these approaches in the studies that we reviewed. Decision analyses are limited by the quality of the parameters. While these parameters, such as drug efficacy, are often estimated from the literature, it is not clear whether they will remain valid when patients use the drugs with less supervision. Moreover, the decision analyses used in the studies we reviewed generally fail to address the possibility of inappropriate use.

Demand-curve analyses typically calculate changes in consumer welfare by assuming that the demand curve takes a given functional form, and then calculating changes in welfare based in changes in the prices and quantities consumed before and after the switch to BTC/OTC status. The limitations here are threefold. First, the authors must assume a specific functional form for the demand curve. Second, at least in some cases, the authors do not always consider whether any other factors besides the change in BTC/OTC status may drive any changes in prices and quantities. Finally and perhaps most important, the underlying assumption of the demand curve–based analyses is that prescription and BTC/OTC forms of a drug are the same product. However, prescription drugs include the advice and supervision of a physician, while BTC/OTC drugs do not. The value (or cost) of the physician's advice (in terms of reduced probability of adverse events, as well as the costs of a physician visit) is not always fully accounted for in the demand-curve analyses.

For studies that examined the effects of BTC/OTC drugs on utilization, health, or costs by estimating how these outcomes changed after the introduction of BTC/OTC drugs, the main methodological issue is that most studies do not control for any other possibilities that may have affected the outcome variable, nor do they "net out" any underlying trends in the outcome variable that may have occurred prior to the BTC/OTC switch. The latter point is particularly troubling: Because the vast majority of switches that occur are from prescription to BTC/OTC and not the other way around, failure to control for underlying trends means that anything due to these trends will be erroneously attributed to the BTC/OTC switch itself. For example, a growing

population means that drug sales will "naturally" increase over time. If the investigator fails to account for this trend, then sales will naturally be higher in the period after the BTC/OTC switch compared to the period before, but at least some of this gain will be due to population growth, as well as the policy itself. This failure to net out trends is particularly troublesome for the vaginal antifungals, statins, PPIs, and H_2RAs, where, despite the fact that data provided by the authors clearly show that sales are trending either upwards or downwards before the switch to BTC/OTC status, there was no attempt to control for this trend.

Overall, our review of the literature suggests that the introduction of BTC/OTC drugs caused patients to substitute away from prescription drugs and toward OTC drugs, thereby reducing costs for insurers. In addition, the introduction of BTC/OTC drugs appears have increased total sales of the drug, but it is unclear whether this increase in sales reflects an increase in use. The literature about how introduction of BTC/OTC drugs has affected medical costs and patient health is much more ambiguous and sparse. We believe that some methodological issues urge caution in interpreting and applying the results of the extant literature.

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Chapter Two: The Effect of OTC Drugs on Physician-Office Visits

Introduction

In the United States, drugs can be divided into two categories: prescription drugs, which are only available with a physician's prescription, OTC drugs, which can be freely purchased from many outlets, such as pharmacies and grocery stores. Both classes of drugs are regulated by the FDA. OTC drugs can be introduced to the market in one of two ways. First, particularly for older drugs, the FDA has established drug monographs that detail acceptable ingredients, dosages, and formulations. Products conforming to these monographs can be marketed without premarket FDA approval. If a monograph does not exist for a particular drug, then it must be approved via the new drug application (NDA) process, which is similar to the process used to approve new prescription drugs. As with new prescription drugs, approval requires evidence demonstrating that the drug is safe and effective. In addition, the drug manufacturer or interested party must also establish that (1) the benefits of OTC approval outweigh the risks, (2) the potential for misuse and abuse is low (3) consumers can understand the product label and accurately diagnose themselves for the indicated condition, and (4) health practitioners are not required for the safe and effective use of the product.

Expanding the number of OTC drugs is often thought to provide the potential to increase efficiency by improving patient health and reducing health care costs. Proponents of OTC drugs argue that expanding the number of drugs (1) improves health by increasing access to beneficial therapies and (2) reduces costs both directly (by reducing the amount spent on physician-office visits) and indirectly (through improvements in health) (Gossel, 1991; Andersen and Schou, 1994; Newton, Popovich, and Pray, 1996; Reeves et al., 1999; Abrams, 2005; Gotto, 2005, Tfelt-Hansen 2007). On the other side, opponents argue that inappropriate use of these drugs may increase costs and reduce health (Ryan, 1994; Tonore, 2002; Choudry and Avorn, 2005; Strom, 2005). The debate over the merits of expanding the number of OTC drugs has received much attention from policymakers and the medical community, with special attention being paid to the introduction of high-profile OTC drugs. For example, in 2005, the FDA denied approval for an OTC version of lovastatin following a highly public debate, with proponents arguing that OTC

lovastatin would improve health by increasing access to cholesterol-lowering therapies, and opponents arguing that patient health would be harmed through inappropriate use. This debate is likely to resurface: In 2007 Merck, the manufacturer of lovastatin, made another attempt to gain FDA approval to market an OTC version of the drug. Yet, despite the debate over the merits of introducing more OTC drugs, there has been little effort to date to systematically and empirically determine whether the benefits of OTC drugs outweigh their costs (for a review, see Sun, Sood, and Blume-Kohut, 2008).

In this paper, we provide a first step toward estimating the benefits and costs of OTC drugs by using data from NAMCS, a nationally representative sample of physician-office visits, to analyze how the introduction of OTC drugs affects physician-office visits. In theory, OTC drugs should reduce physician-office visits for their indicated conditions, since patients no longer need to obtain a physician's prescription. However, OTC drugs may have little effect on physician-office visits if patients continue to consult their physicians for advice on whether to initiate a particular drug, or to discuss an OTC drug's inefficacy or adverse effects. Therefore, whether and to what degree OTC drugs reduce physician-office visits remains an empirical issue. Several studies have addressed this issue by examining how the frequency of physician-office visits for a particular medical condition changes after the introduction of an OTC drug aimed at that condition. The introduction of OTC H_2RAs appears to have had little effect on physician-office visits for peptic ulcer and gastroesophageal reflux disease (Andrade, Gurwitz, and Fish, 1999; Shaw et al., 2001), while the introduction of vaginal antifungals appears to have lowered physician-office visits for vaginal candidiasis (Gurwitz, McLaughlin, and Fish, 1995; McCaig and McNeil, 2005; Lipsky, Waters, and Sharp, 2000).

However, a major limitation of these studies is that they essentially compare the number of physician-office visits after the introduction of the OTC drug to the number of visits prior to its introduction, and do not make a sophisticated effort to net out any underlying trends in physician-office visits that may have occurred prior to the BTC/OTC switch. This omission may lead to misleading inferences. For example, suppose that the incidence of vaginal candidiasis is falling due to changes in demographics and patient behaviors. Since the incidence of the disease is falling, the number of physician-office visits for the disease will also display a downward trend. Given this downward trend, physician-office visits will naturally be lower in the period after the OTC is introduced compared to the period before, but at least some of this difference

will be due to the downward trend in disease incidence, *not* to the introduction of the drug itself. Thus, failing to account for the trend will tend to overestimate the effect of OTC drugs. Indeed, the data reported by McCaig and McNeil (2005) show that physician-office visits for vaginal candidiasis had already been trending downward prior to the introduction of OTC antifungals; thus, failing to account for this trend may explain a large part of the reported decrease in physician-office visits.

Our paper therefore improves upon previous work by incorporating controls for preexisting trends in physician-office visits for a particular disease in order to obtain more-accurate estimates of the effect of OTC drugs. In addition, we perform a comprehensive analysis of the effects of OTC drugs by analyzing the effects of common OTC drugs, such as second-generation antihistamines and NRTs, not previously considered in the literature. Finally, our analysis incorporates more-recent years of data in order to examine both the long-term effects of OTC drugs as well the effects of more-recently introduced OTC drugs. Overall, we find that OTC drugs do reduce the number of physician-office visits for the diseases they are intended to treat, although there is wide heterogeneity across diseases. For the four diseases or conditions that we consider (allergic rhinitis, vaginal candidiasis, peptic ulcer disease, and nicotine dependence), the effects of OTC drugs range from no effect (peptic ulcer disease) to a 21-percent decrease in physician-office visits (vaginal candidiasis). In addition, our results suggest that this decrease is due to both an immediate decrease in the number of physician-office visits as well as a long-term downward shift in the annual trend of physician-office visits. As a whole, these results suggest that OTC drugs do have the potential to reduce medical costs by reducing spending on physician-office visits.

Data

NAMCS is a nationally representative sample of physician-office visits. The survey was conducted annually from 1973 to 1981, in 1985, and annually since 1989, with 2005 being the latest year for which data is available. In each year, the sample of patients is randomly drawn through a three-stage process. First, 112 geographic areas known as *primary sampling units* are selected. Then, within each area, a random sample of non–federally employed, office-based

physicians are selected.[4] The final stage is the selection of patient visits during a randomly selected one-week reporting period throughout the survey year.

For each visit, NAMCS records (a) up to three patient-reported reasons for the visit (b) up to three diagnoses reported by the physician, and (c) any prescriptions written by the physician. To obtain (a), the survey asks the patient to describe up to three of the symptoms or diseases that prompted the physician-office visit. These symptoms and diseases are then coded by NAMCS into the standardized symptoms given in *A Reason for Visit Classification for Ambulatory Care*. Similarly, the physician is asked to list up to three diagnoses that were made during the visit; these diagnoses are then coded into standardized values in accordance with the *International Classification of Diseases, Ninth Revision, Clinical Modification*. Data on prescriptions are coded according to an internal classification scheme developed at the National Center for Health Statistics. Due to changes in the way patient-reported symptoms were coded starting in 1979, we have restricted our research to data from 1979 onward. Therefore, our final sample consists of survey years 1979–2005. (Recall that NAMCS was not conducted during six of the years in this timeframe;[5] thus, our final sample consists of a total of 21 years.)

Methods

We focused our analysis on physician-office visits for four diseases/conditions: allergic rhinitis, peptic ulcer disease, vaginal candidiasis, and nicotine dependence. We chose these diseases/conditions because all four are extremely common and because OTC drugs targeting each of these diseases were introduced during the years covered by our sample. Second-generation antihistamines such as loratadine are one class of drugs used to treat allergic rhinitis. Loratadine is the only member of this class that is available without a prescription; OTC versions of the drug were introduced in 2002. H_2RAs and PPIs are used to treat peptic ulcer disease. The OTC H_2-receptor antagonists cimetidine and famotidine were introduced in 1995, followed by

[4] Anesthesiologists, pathologists, and radiologists are excluded from the survey.

[5] NAMCS was conducted annually from 1973 to 1981, in 1985, and annually since 1989; therefore, there is no data for 1982–1984 and 1986–1988.

another two members (ranitidine and niaztidine) in 1996, and an OTC version of a PPI, omeprazole, in 2003.

Vaginal antifungals—such as clotrimazole, miconazole, and tioconazole—are used to treat vaginal candidiasis. OTC versions of these three drugs were introduced in 1991 (clotrimazole and miconazole) and 1997 (tioconazole). Finally, various forms of NRT are used to treat nicotine dependence. The patch and gum forms of nicotine were made available OTC in 1996, followed by the sublingual form in 2002. Table 2.1 provides a summary of these drug classes.

Table 2.1

Diseases/Conditions of Interest

Indications	Drug Class	OTC Drug (Release Date)
Peptic ulcer disease	H_2RAs, PPIs	Cimetidine (1995), ranitidine (1996), famotidine (1995), nizatidine (1996), omeprazole (2003)
Allergic rhinitis	Second-generation antihistamines	Loratadine (2002)
Vaginal candidiasis	Vaginal antifungals	Clotrimazole (1991), miconazole (1991), tioconazole (1997)
Nicotine dependence	NRT	Nicotine (gum or nicotine polacrilex, 1996), nicotine (patch,1996), nicotine (sublingual, 2002)

Our goal is to examine how the introduction of an OTC drug aimed at a particular disease/condition affects the number of physician-office visits for that disease/condition. Our data gives us three potential measures of the number of physician-office visits for a particular condition: the number of physician-office visits during which the patient reported a symptom consistent with the condition, the number of physician-office visits during which the physician actually diagnosed the condition, and the number of physician-office visits during which a physician prescribed a drug used to treat the condition. Our analysis focused on the first of these three measures because we are interested in how the introduction of OTC drugs affects patient

behavior and, in particular, in how that introduction affects the probability that a patient chooses to see a physician, given a particular set of symptoms. The number of visits during which the physician diagnosed the condition or prescribed a drug for the condition are less-perfect proxies of patient decisions, since they eliminate visits during which a patient suspected that he or she had a particular condition and chose to visit a physician but was not diagnosed with the disease. In addition, those visits include cases where a patient did not visit the physician for a particular condition but was diagnosed nonetheless. Therefore, we use the number of physician-office visits during which the patient reported symptoms consistent with the diseases associated with each drug. Table 2.2 lists the standardized symptoms from *A Reason for Visit Classification for Ambulatory Care* that we associated with each disease.

Table 2.2

Patient-Reported Symptoms Associated with Diseases/Conditions of Interest

Disease/ Condition	Patient-Reported Symptoms
Peptic ulcer disease	Chest pain and related symptoms; chest discomfort, pressure, tightness; burning sensation in the chest; heartburn and indigestion (dyspepsia); stomach and abdominal pain, cramps; gastrointestinal bleeding; decreased appetite; diseases of the esophagus, stomach
Allergic rhinitis	Discharge from eye; discharge from eye—tearing, watering; eye itching; eye burning; allergy problems referable to eye; swelling of eyes; itching of eyelids; nasal congestion; other symptoms of nose; sinus problems; sinus congestion; sneezing; cough
Vaginal candidiasis	Vaginal discharge; other vaginal symptoms; vaginal pain; vaginal infection; vaginal itching, burning; vulvar disorders; vulvar itching and irritation, swelling; vulvar mass, lump; vulvar growth, wart, cyst, ulcer, sore
Nicotine dependence	Smoking problem

Given the number of physician-office visits for a specific condition, our general approach was to use trend-break analysis to examine the effects of OTC drugs on physician-office visits. Specifically, for each of our drug classes/diseases of interest, we estimate regression models of the following form:

$$\ln(visit_{it}) = \alpha + \beta OTC_{it} + \lambda t_i + \gamma \ln(AllVisit_t) \qquad (2.1)$$

In this model, $\ln(visit_{it})$ is the natural log of the number of physician-office visits in year *t* for condition *i* and $\ln(AllVisit_t)$ is the natural log of the number of all physician-office visits in year t, which serves to control for any factors that may have affected physician visits more generally. t_i represents a linear time trend, and OTC_{it} is an indicator variable that equals 1 in the years after the introduction of the first OTC drug in a class and 0 for all other years. β is our parameter of interest and reflects the percentage increase in the number of visits for condition *i* following the introduction of the first OTC drug in a given class. In effect, equation (2.1) takes as given any preexisting linear time trend in the number of visits for a particular condition, after controlling for any factors that might have affected the total number of physician-office visits in a year more generally, and identifies the effects of OTC drugs by estimating the deviation from this preexisting trend following the OTC drugs' introduction.

Equation (2.1) represents our baseline specification, to which we add several related models. First, since we estimate equation (2.1) separately for each drug/class condition, we may not have sufficient statistical power to precisely estimate β, given only 21 years of data on physician-office visits. To conserve statistical power, we also pool the observations for each drug class and estimate models of the following form:

$$\ln(visit_{it}) = \alpha + f_i + \beta OTC_{it} + \lambda t_i + \gamma \ln(AllVisit_t) \quad (2.2)$$

In this model, f_i is now a fixed effect for each disease. Equation (2.2) imposes the restriction of a common OTC effect across all four diseases in exchange for greater statistical power—by pooling the data, we now have 84 observations (21 observations for four drug classes).[6] The small size of our sample is driven by the fact that, as outlined above, there were only four common indications/diseases for which OTC drugs were introduced during the period covered by our sample.

[6] Note that since $AllVisit_t$ is common to all drugs within a given year, it serves not only as a control for the total number of visits in a year, but also as a time-fixed effect more generally.

Equations (2.1) and (2.2) estimate an average effect of on physician-office visits over time. To more precisely identify the timing of this effect, we consider the following regression model:

$$\ln(visit_{it}) = \alpha + f_i + \beta OTC_{it} + \lambda_i t + \theta * (OTC_{it} * t) + \gamma \ln(AllVisit_t) \quad (2.3)$$

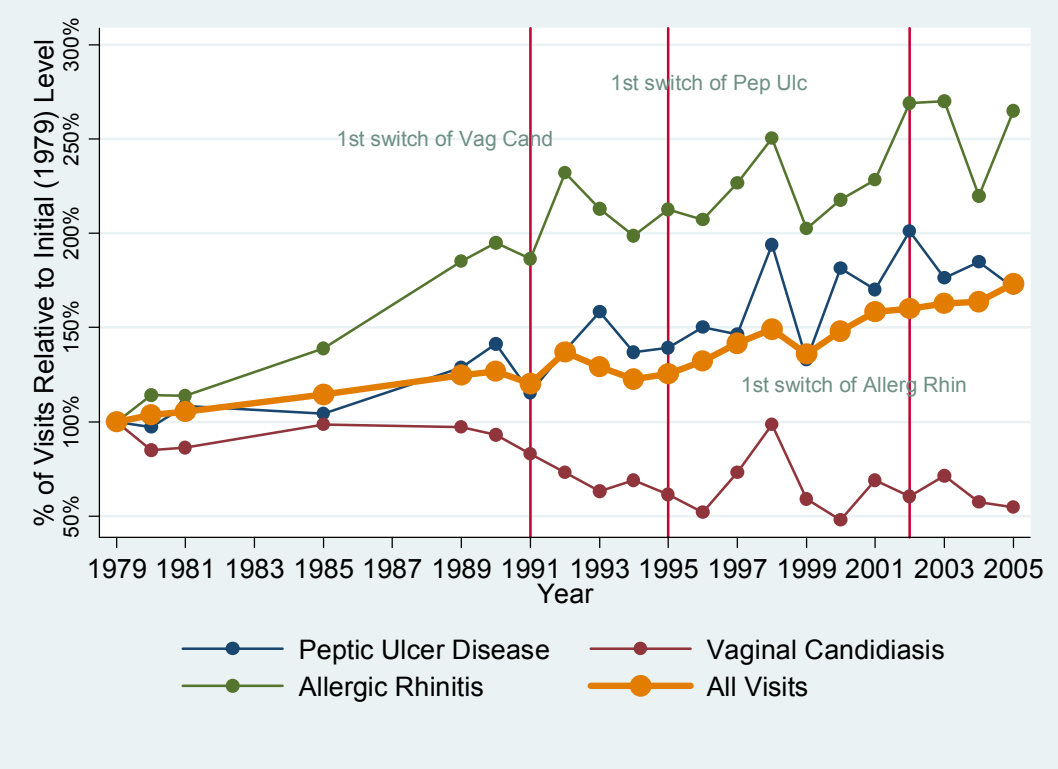
Equation (2.3) is similar to equation (2.2), except that we also interact the time trend with the OTC_{it} indicator variable to examine whether the introduction of OTC drugs has an effect on the time trend of physician-office visits. Thus, in equation (2.3), β estimates an immediate, one-time effect of OTC drugs on the level of physician-office visits, while θ estimates the effect of OTC drugs on the growth rate of physician-office visits over time. For equation (2.3), we pool observations from all the drugs together and assume a common effect because adding the interaction term further reduces statistical power.

Results

Between 1979 and 2005, the total number of physician-office visits increased from 550 million to just under 1 billion. Figure 2.1 shows the number of physician-office visits for each of the diseases of interest, as well as the overall number of physician-office visits between 1979 and 2005. Specifically, we show the number of visits for each condition and for the number of physician-office visits overall relative to the initial level in 1979. A key finding from Figure 2.1 is that there is a clear underlying trend in physician-office visits for each disease *prior* to the introduction of OTC drugs aimed at that disease. For example, Figure 2.1 shows that the number of physician-office visits for vaginal candidiasis had already been falling prior to the introduction of OTC antifungals in 1991, and that the number of physician-office visits for allergic rhinitis, nicotine dependence, and peptic ulcer disease had been increasing prior to the introduction of drugs aimed at these diseases. Therefore, failure to adjust for these underlying trends would lead an investigator to overestimate the effect of OTC drugs in the case of vaginal candidiasis, and to underestimate the effect of OTC drugs for the other diseases.

Figure 2.1

Number of Physician-Office Visits for Selected Conditions, 1979–2005



NOTES: This figure shows the total number of annual physician-office visits, and the number of visits for peptic ulcer disease, allergic rhinitis, and vaginal candidiasis, relative to their 1979 levels. The growth in visits for nicotine dependence was much more rapid than for these three diseases, and therefore is shown in Table A.1 in the appendix.

Table 2.3 presents our first set of regression results. For the first four columns, we regress the natural log of the number of physician-office visits for each disease/condition on a linear time trend and a dummy variable for the introduction of an OTC drug aimed at the disease/introduction, along with other controls, as described in equation (2.1). In the last column, we estimate a pooled model with disease-specific fixed effects and time trends, as outlined in equation (2.2). Our results suggest that the introduction of OTC drugs reduced the number of physician-office visits for vaginal candidiasis by 21.3 percent ($p<0.05$) and the number of physician-office visits for allergic rhinitis by 19.7 percent ($p<0.05$). The coefficient for peptic ulcer disease is precisely 0, with an extremely small standard error (0.005), suggesting that the

introduction of OTC NRTs had no effect on physician-office visits for peptic ulcer disease. Finally, the coefficient for nicotine dependence, -1.094, is large, and would reflect an extremely large effect; however, the large standard error indicates that this effect is imprecisely measured. Taken as a whole, the pooled model suggests that, on average across the four diseases, the introduction of an OTC drug reduced the number of physician-office visits by 33.8 percent ($p<0.05$).

Table 2.3

Effect of OTC Drug on Physician-Office Visits

	(1) Peptic Ulcer Disease	(2) Vaginal candidiasis	(3) Allergic Rhinitis	(4) Nicotine Dependence	(5) Pooled Model
OTC	0.000	-0.213[b]	-0.197[b]	-1.094	-0.338[b]
	(0.005)	(-2.277)	(-2.221)	(-1.598)	(-2.123)
Ln(All Visits)	1.189[c]	1.383[b]	2.156[c]	9.311[a]	3.415[b]
	(3.138)	(2.444)	(4.211)	(1.884)	(2.395)
Constant	-7.443	-12.246	-26.017[b]	-176.633[a]	-51.453[a]
	(-0.974)	(-1.072)	(-2.512)	(-1.769)	(-1.787)
Disease-specific time trend	Yes	Yes	Yes	Yes	Yes
Disease-specific fixed effects	No	No	No	No	Yes
R-squared	0.813	0.616	0.836	0.500	0.944
N	21	21	21	21	84

NOTES: See equation (2.1) for the regression model used to estimate the results in columns 1–4. See equation (2.2) for the regression model used to estimate the results shown in column 5. T-statistics (calculated using robust standard errors) are shown in parentheses.
[a] $p<0.1$
[b] $p<0.05$
[c] $p<0.01$

Given that the introduction of OTC drugs appears to reduce the number of physician-office visits, we examine the timing effect by estimating regression models that interact the linear time trend with the OTC indicator, as described in equation (2.3). Table 2.4 presents our results. Overall, our results suggest that the effect of OTC drugs is primarily mediated both through an instantaneous effect of the number of physician-office visits and by longer-term effects on the trends in physician-office visits. The coefficient on the OTC indicator is -0.263, suggesting that the introduction of an OTC drug causes a one-time 26.3-percent fall in physician-office visits, although this effect is not quite statistically significant ($p<0.1$). The coefficient on the interaction term suggests that OTC drugs also reduce long-term trends in physician-office visits by 10.6 percent ($p<0.05$). For example, if physician-office visits for a given disease had been increasing by 5 percent per year, our estimates suggest that the introduction of an OTC drug would lower this trend by 10.6 percent, so that physician-office visits would fall by 5.6 percent per year following the introduction of the drug.

Table 2.4

Effect of OTC Drug on Long-Term Trends in Physician-Office Visits

	Pooled Model
OTC	-0.263[a]
	(-1.766)
OTC[a] time trend	-0.106[b]
	(-2.879)
Ln(All Visits)	2.356[a]
	(1.697)
Disease-Specific Time Trend	Y
Disease-Specific Fixed Effects	Y
R-squared	0.947
N	84

NOTES: See equation (2.3) for the regression model

used to estimate the results. T-statistics (calculated using robust standard errors) are shown in parentheses.
[a] $p<0.1$
[b] $p<0.01$

Conclusions

Overall, we find evidence that, even when prior trends are taken into account, the introduction of an OTC drug appears to reduce the number of physician-office visits for the conditions it is intended to treat. Our pooled regression suggests that, on average, the number of physician-office visits falls by 33 percent following the introduction of an OTC drug. But this average masks a large degree of heterogeneity across diseases. We find large, significant effects for vaginal candidiasis and allergic rhinitis; a large, statistically insignificant effect for nicotine dependence; and no effect at all for peptic ulcer disease. It is intriguing to speculate about the causes for this heterogeneity. Patients may be less inclined to see a physician for vaginal candidiasis (a sexually transmitted disease) and allergic rhinitis (a disease with relatively minor symptoms), so the introduction of an OTC drug may reduce physician-office visits. In contrast, the symptoms of peptic ulcer disease can be more severe, and therefore, the number of physician-office visits may be less sensitive to the introduction of OTC drugs.

Our data also suggest that the effect of OTC drugs occurs because of decreases in both the number and growth rate of physician-office visits. We speculate that the decrease in the number of visits is due to an initial surge of patients who use the OTC drug and choose not to see a physician. Over time, as more about the OTC drug's safety and efficacy become known, more patients may choose to use the drug, thereby leading to a decrease in the growth rate of physician-office visits. Further work could more clearly elucidate the mechanisms by which OTC drugs affect both the number and growth rate of office visits.

In addition, recently in the United States, there has been interest in developing a new class of drugs, known as BTC drugs, whose use would not require a physician's prescription, but would require a pharmacist's approval. Few studies have examined empirical evidence about how BTC drugs affect costs and patient health. Because both BTC and OTC drugs do not require a physician's prescription, our results suggest that BTC drugs also have the potential to reduce costs by lowering physician-office visits.

It is useful to note several limitations to our study. First, we did not examine whether higher-order trends or other variables might be driving our observed results. However, it the limited sample size makes it difficult to estimate less-parsimonious models than ours. More generally, we are aware that in some cases, our small sample sizes make it difficult to precisely estimate results unless we use a pooled sample, particularly when we examine the effect of OTC drugs on the number and growth rate of physician-office visits. While a pooled sample increases the precision of our estimates, it does assume the restriction of a common effect across all four diseases we examine, which may be more difficult to justify given that we found some evidence of heterogeneity across diseases. Finally, it is important to note that we cannot rule out the possibility that OTC drugs increases physician-office visits for other causes, such as visits due to adverse reactions or inappropriate use.

In conclusion, our results provide an important first step toward analyzing the benefits and costs of OTC drugs by establishing that, in general, these drugs reduce the number of physician-office visits for the conditions that they are intended to treat. Therefore, OTC drugs have the potential to reduce costs by decreasing the number of physician-office visits. However, this analysis is simply one facet of the issue. Further research should build upon this work by estimating the degree to which OTC drugs increase access and inappropriate use in order to build a more comprehensive picture of the costs and benefits of OTC drugs.

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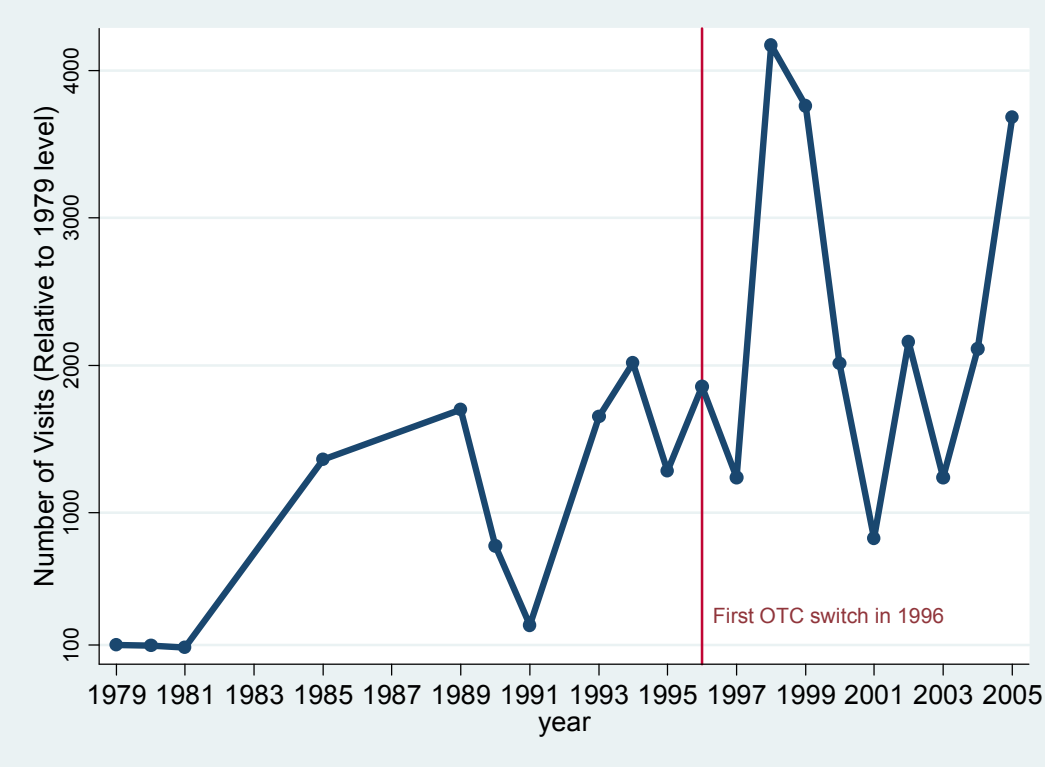
Appendix to Chapter Two

Figure A.1

Number of Physician-Office Visits for Nicotine Dependence, 1979–2005



NOTE: Figure A.1 shows the number of physician-office visits for nicotine dependence, relative to the number of visits in 1979.

Chapter Three: Effect of BTC/OTC Drugs on Utilization, Prices, and Expenditures

Introduction

Increasing access to prescription drugs has received much attention from policymakers and researchers, and significant effort has been devoted to examining how financial barriers, such as insurance status and cost-sharing, affect access, health, and medical costs (for a review, see Goldman, Joyce, and Zheng, 2007). However, in addition to these financial barriers, several other impediments to access exist, such as regulatory barriers. For example, in the United States, the vast majority of drugs are available only with a physician's prescription. In contrast, consumers may freely purchase the remaining OTC drugs from many outlets, such as pharmacies and grocery stores.

The requirement for a physician's prescription imposes a regulatory barrier to access which has advantages and disadvantages. The main advantage of this barrier is that it prevents misuse of prescription drugs, which may have potentially serious consequences in many cases. Moreover, this requirement places the use of the drug under a physician's supervision, making it easier for him or her to encourage adherence to instructions, monitor any adverse effects, and identify any potential contraindications. However, requiring a prescription also imposes additional time and monetary costs on the patient, which may reduce access to potentially beneficial therapies. Although it is clear that the advantages of physician supervision may outweigh these increased costs in the case of drugs with high toxicity profiles, it is less clear in the case of many drugs with low toxicity. Therefore, in an effort to increase access to select low-toxicity drugs by eliminating the costs associated with obtaining a physician's prescription, the FDA is considering the introduction of the BTC class of drugs. These drugs would be available without a physician's prescription but, unlike OTC drugs, would not be freely available to patients. Rather, they would be available only in pharmacies and upon consultation with a pharmacist.

At first glance, BTC drugs appear to allow for increased access and use of drugs while mitigating the risks of unsupervised use, since patients would now use these drugs under the supervision of a pharmacist. However, some of these benefits might not materialize in practice due to changes in patient, pharmaceutical industry, and insurer behavior. For example, pharmaceutical firms might respond by increasing prices or reducing advertising to physicians, thereby reducing use of BTC drugs. Similarly, insurers might decline to cover BTC drugs, consequently raising the cost of the drugs to consumers and thereby reducing their use. To the degree that a pharmacist's supervision serves as a poor substitute for physician supervision, patients could be worse off due to inappropriate use, noncompliance with therapy instructions, and poor surveillance of adverse effects. In summary, it is difficult to predict a priori how BTC drugs might affect utilization, prices, medical costs, and patient health.

Despite these ambiguities, there has been no systematic effort to assess the effect of BTC drugs on access, patient health, or drug expenditures. In this paper, we examine how switching a drug to BTC status affects access and expenditures by examining effects on drug sales (quantities sold), prices, and expenditures.[7] Because the United States has little experience with BTC drugs, we answer this question by examining the experience of BTC drugs in Australia, the United Kingdom, Canada, and New Zealand, where the use of this class is more prevalent. We also consider U.S. and international experience with OTC drugs. While there are differences between the two classes, the key similarity—that neither requires a physician's prescription—may make it possible to infer the potential effect of BTC drugs by extrapolating from the effects of OTC drugs. Our approach utilizes a difference-in-differences approach that compares the pre- and post-BTC/OTC switch outcomes (sales, prices, and expenditures) of a given drug against the outcomes of a control group of drugs over the same period. We consider the use of two sets of controls: (1) outcomes of the drug in countries where it did not switch status and (2) outcomes of other drugs in the same class as the switched drug.

We first present some background material and a review of the literature. We then describe our data, methods, results, and conclusions.

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[7] BTC/OTC drugs are either former prescription drugs that have been converted to BTC/OTC status, or new, low-dose versions of prescription drugs. We use the term *switch* to refer to either case.

Background

Compared with the United States, which does not classify any drugs as BTC, BTC drugs are more prevalent overseas. Patients can freely access BTC drugs in pharmacies upon consultation with a pharmacist. Thus, in theory, BTC drugs allow for freer access to drugs while ensuring some level of supervision over their use. In the United Kingdom, BTC drugs are known as *pharmacy-only* drugs, in contrast to *general sales list* (i.e., OTC) and *prescription-only* (i.e., prescription medications). In Australia, New Zealand, and Canada, BTC drugs are known as *schedule-3* drugs, in contrast to *schedule-2* (i.e., prescription) and *unscheduled* (i.e., OTC) drugs. The United States currently does not classify drugs as BTC, although restrictions for a few OTC drugs (such as pseudoephedrine) mirror BTC regulations.[8] However, the FDA is currently considering the introduction of this class and recently scheduled several public hearings on the matter.

Several prior studies have examined how switching a drug to BTC status affects its use. Most of these studies focus on the BTC experience in the United Kingdom, where BTC versions of H_2RAs were introduced in 1994; BTC versions of emergency contraception were introduced in 2001; and BTC versions of simvastatin, a statin, and omeprazole, a PPI, were introduced in 2004. The introduction of BTC drugs did not appear to affect utilization in the case of H_2RAs (Furler et al., 2002) or PPIs (Dhippayom and Walker, 2006). In the case of simvastatin, Filion et al. (2007) found evidence that use of prescription versions may have fallen after the introduction of BTC versions, but their study did not examine the use of BTC versions themselves. Although few studies examined the effects of switching emergency contraception to BTC status in the United Kingdom, a wide literature has found that switching emergency contraception to BTC status increased its use in the United States (Raine et al., 2005; Glasier, 1998; Raine et al., 2000; Pentel et al., 2004; Raymond et al., 2006; Walsh and Frezieres, 2006) and other countries (Glasier et al., 2004; Lo et al., 2004; Hu et al., 2005; Lovvorn et al., 2000; Ellertson et al., 2001; Soon et al., 2005; Moreau et al., 2006a and 2006b; Larsson et al., 2006).

[8] Due to concerns over its use in the manufacture of methamphetamine, several states require that pseudoephedrine be sold BTC. In addition, federal law imposes limits on the quantities that patients can buy at any given time.

A wide literature has also examined the effect of OTC switches on the use of prescription drugs in the United States and abroad. In the United States, OTC switches reduced the utilization of prescription drugs in the case of H_2RAs (Andrade et al., 1999), vaginal antifungals (Gurwitz et al., 1995) and second-generation antihistamines (Sullivan et al., 2005). In addition, OTC switches appear to have increased the use of OTC drugs in the case of H_2RAs (Furler et al., 2002) and NRTs (Keeler et al., 2002; Pierce and Gilpin, 2002), although one study found no effect for NRTs (Thorndike et al., 2002). Overseas, two studies found that OTC switches increased utilization and sales for a wide variety of drugs in Sweden (Lundberg and Isaacson, 1999; Carlsten et al., 1996).

This paper builds and improves upon this literature is several ways. First, particularly with regard to emergency contraception, many of these former studies are based on randomized trials with small groups of patients; we analyze the effects of BTC/OTC switches more broadly, at the population level. Second, we consider the effects of BTC/OTC switches on a broad variety of drugs and countries not previously examined. Third, a key shortcoming of these studies is that they typically compare sales after a BTC/OTC switch to sales before the switch, without taking into account underlying trends and other observable and unobservable factors that might affect sales. This omission may lead to misleading inferences. For example, suppose that the incidence of hyperlipidemia is rising due to changes in demographics and patient behaviors. Since the incidence of the disease is rising, statin sales will also show an upward trend, so sales will naturally be higher in the period after the switch. However, clearly some of this increase will be due to the upward trend in disease incidence, not to the introduction of the drug itself. Thus, failing to account for the trend will tend to overestimate the effect of BTC/OTC switches. Finally, several of the former studies examine how BTC/OTC switches affect expenditures but not quantities sold. Because a BTC/OTC switch may affect both quantities and prices, focusing on expenditures alone does not allow the investigator to examine the switch's effect on access. Suppose, for example, that BTC/OTC switches lead to a fall in prices and a concomitant increase in quantities sold. In this case, there may be no change in expenditures despite the fact that patients would be consuming more of the drug in question. In this paper, we explicitly examine the effect of BTC/OTC switches on prices, quantities, and expenditures separately to more clearly assess the effect of these switches on access and costs.

Data and Methods

Data

We examined the effects of BTC/OTC switches for four classes of drugs—emergency contraception, statins, anti-ulcer drugs (PPIs and H_2RAs), and vaginal antifungals—in the United States, the United Kingdom, Australia, New Zealand, and Canada. We chose these classes and countries because all experienced BTC/OTC switches between 1997 and 2006, the years for which we have data on sales and prices (see below). We obtained data on the BTC/OTC status for each drug in each country from a variety of sources, including each country's drug regulatory agency and the World Self Medication Industry (World Self Medication Industry, 2007). We obtained annual sales data between 1997 and 2007 for each of the drugs listed in Table 3.1 from IMS Health, Inc. These data come from the MIDAS database and cover revenues or expenditures and sales (quantities) through retail and hospital channels. Using this data, we calculated the price as revenue divided by quantity. Appendix Table B.1 lists the drugs in each class and shows whether and when each drug was switched to BTC/OTC status in each country under consideration.

Table 3.1

Effect of BTC/OTC Switches on Drug Sales, Prices, and Spending, Using International Sales and Prices as Controls

Drug	BTC or OTC?	N	Sales		Price		Spending	
			No Trends	Trends	No Trends	Trends	No Trends	Trends
Ketoconazole	OTC	55	0.116[a]	-0.066	-0.130	-0.194[a]	-0.014	-0.260[b]
			(0.048)	(0.042)	(0.088)	(0.075)	(0.098)	(0.081)
Loratadine	OTC	22	-1.643[b]	-1.586[b]	-0.233	-0.175	-1.876[b]	-1.761
			(0.118)	(0.312)	(0.187)	(0.583)	(0.272)	(0.774)
Omeprazole	OTC	55	-0.197	0.540	-0.596[b]	-0.766[b]	-0.793[b]	-0.225
			(0.218)	(0.270)	(0.132)	(0.264)	(0.205)	(0.235)
Levonorgestrel	OTC	55	-0.320[a]	-0.023	0.368[b]	0.135[b]	0.048	0.112[a]
			(0.140)	(0.040)	(0.122)	(0.039)	(0.040)	(0.041)
	BTC		-0.185[a]	0.093	0.091	0.106[a]	-0.094	0.199[a]
			(0.076)	(0.047)	(0.055)	(0.043)	(0.058)	(0.079)
Fluconazole	BTC	44	-0.406	-0.007	1.283[b]	0.587	0.877[a]	0.580
			(0.210)	(0.346)	(0.316)	(0.496)	(0.339)	(0.500)
Simvastatin	BTC	55	0.516[a]	0.349[a]	-1.436[b]	-1.518[b]	-0.921[b]	-1.169[b]
			(0.230)	(0.165)	(0.198)	(0.279)	(0.194)	(0.236)

NOTES: Table 3.1 shows the estimates of BTC or OTC switches ("BTC/OTC") on quantities sold ("Sales"), prices ("Price"), and expenditures ("Spending"), as described in equations (1) through (3). "No trends" and "Trends" refer to the use of models which omitted and included a linear time trend, respectively. Robust standard errors are shown in parentheses.

[a] $p<0.05$

[b] $p<0.01$

Methods

We use a difference-in-differences (DD) approach to estimate the effect of BTC/OTC conversions on the three outcomes of interest: sales, prices, and expenditures. The treatment group consists of drugs that switched to BTC/OTC status. The first difference is the change in outcomes among the treatment group before and after the BTC/OTC switch, while the second difference is the change in outcomes among a control group of similar drugs over the same period. The first difference controls for time-invariant, unobserved factors particular to the treatment group; the second controls for time-varying, unobserved factors that might affect outcomes of both the treatment and control groups. Therefore, the two identifying assumptions of the DD approach are (1) that any unobserved effects that might affect outcomes are fixed over time, and (2) that the control group is a useful prediction of the counterfactual change in outcomes for the treatment group in the absence of the BTC/OTC switch.

We consider the use of two separate DD models for each outcome variable. The first model uses outcomes of a given drug in countries where it remained prescription-only (our control group). For example, in the case of simvastatin, which was converted to BTC status in the United Kingdom in 2005, our control group consists of simvastatin outcomes in Canada, the United States, Australia, and New Zealand, where the drug remained available by prescription only. We implement this approach using the following regression models for each of the drugs that switched to BTC/OTC status:

$$\ln\left(Sales_{it}\right) = \alpha + f_i + \delta_t + \beta_1 OTC_{it} + \beta_2 BTC_{it} + \varepsilon_{it} \qquad (3.1)$$

$$\ln\left(Price_{it}\right) = \alpha + f_i + \delta_t + \beta_1 OTC_{it} + \beta_2 BTC_{it} + \varepsilon_{it} \qquad (3.2)$$

$$\ln\left(Expenditure_{it}\right) = \alpha + f_i + \delta_t + \beta_1 OTC_{it} + \beta_2 BTC_{it} + \varepsilon_{it} \qquad (3.3)$$

In these equations, $Sales_{it}$, $Price_{it}$, and $Expenditure_{it}$ represent the sales, prices, and expenditures for the drug in country *i* at time *t*; f_i is a country fixed effect, δ_t is a year effect, OTC_{it} is a dummy variable that equals 1 in each year after the drug was switched to OTC status and 0 otherwise, and BTC_{it} is a dummy variable that equals 1 in each year after the drug was switched to BTC status and 0 otherwise. f_i therefore controls for time-invariant, unobserved

factors for each country, while δ_t controls for time-varying, unobservables common to all countries. β_1 and β_2, our parameters of interest, represent the effect of OTC and BTC switches, respectively, on drug sales, prices, and expenditures. Although equations (3.1) through (3.3) allow for different effects if a particular drug switches to BTC in some countries and OTC in others, in practice, all of the drugs in our sample (except levonorgestrel) switched to either BTC *or* OTC status. Therefore, for each drug, we report in Table 3.1 (1) whether the switch was to BTC or OTC status and (2) the corresponding estimate.

This approach uses countries where a drug did not switch to BTC/OTC status as the control group. A crucial assumption of this approach is that outcome trends for the drug in these control countries provides a useful estimate of counterfactual outcome trends in treatment countries (i.e., where the drug did switch to BTC/OTC) in the absence of the switch. This assumption will be less likely to prove true if drug sales, prices, and expenditures across countries are generally uncorrelated over time. For example, suppose the incidence of hyperlipidemia in the United States and the United Kingdom follows different trends in each country. In this case, statin sales in the United States would be a poor control for their UK counterparts. To address this concern, we developed two alternative models. In the first model, we further control for unobservable, time-varying, country-specific factors by including linear time trends for each country. In the second model, we use as the control group within-country sales, prices, and expenditures for molecules in the same class as the drugs that switched to BTC/OTC status. For example, since simvastatin switched to BTC status in the United Kingdom in 2005, we used the sales, prices, and expenditures of other statins in the United Kingdom as a control. The assumption that underlies this approach is that sales, prices, and expenditures of the drugs that were not switched to BTC/OTC status serve as useful predictors of the counterfactual changes in sales, prices, and expenditures for drugs in the same class that were switched to BTC/OTC status. To implement this approach, we estimate the following regression models:

$$\ln\left(Sales_{it}\right) = \alpha + f_i + \delta_t + \beta_1 OTC_{it} + \beta_2 BTC_{it} + \varepsilon_{it} \qquad (3.4)$$

$$\ln\left(Price_{it}\right) = \alpha + f_i + \delta_t + \beta_1 OTC_{it} + \beta_2 BTC_{it} + \varepsilon_{it} \qquad (3.5)$$

$$\ln\left(Expenditure_{it}\right) = \alpha + f_i + \delta_t + \beta_1 OTC_{it} + \beta_2 BTC_{it} + \varepsilon_{it} \qquad (3.6)$$

In these regression models, f_i is a fixed effect for each drug in the class, δ_t is a year effect, and OTC_{it} / BTC_{it} are indicators for whether the drug switched to BTC/OTC status, as described above. β_1 and β_2, our parameters of interest, represent the effect of OTC and BTC switches, respectively, on drug sales, prices, and expenditures. The regression models shown in equations (3.4) through (3.6) identify β_1 and β_2 by comparing the change in drug sales, prices, and revenues for drugs that switched to BTC/OC status against the change in similar drugs within the class that did not switch status. To further control for time-varying, unobservable, drug-specific factors, we also estimate alternative specifications of equations (3.4) through (3.6) that include linear time trends for each drug in the class. We estimate equations (3.4) through (3.6) separately for each class of drugs in each country where at least one member of the class switched to BTC/OTC status. As Table B.1 shows, generally only one drug per class underwent a BTC/OTC switch in a given country. The lone exception occurred in the United Kingdom, where two vaginal antifungals (ketoconazole and fenticonazole) were converted to BTC status. In this case, note that the regression coefficient represents an average effect across these two drugs. Although equations (3.4) through (3.6) allow for different effects if a drug switched to BTC status and then later to OTC status, in practice, none of the drugs in our sample followed this pattern. For each class of drugs, therefore, we report in Table 3.1 (1) whether the switch was to BTC or OTC status and (2) the corresponding estimate.

It is important to note that our two DD models impose different requirements on our data. In the first DD model, given by equations (3.1) through (3.3), we require observations on outcomes of a given switched drug across several countries. While fenticonazole switched to OTC status in the United Kingdom in 2001, it was not available for sale in other countries during the period under consideration. Accordingly, we drop fenticonazole from the first DD analysis. Conversely, the second DD approach, given in equations (3.4) through (3.6), requires that for each switched drug, we have outcomes of other drugs in the same class and in the same country where the drug switched. Thus, we are able to include fenticonazole in the analysis using our second DD model. However, levonorgestrel is the only drug used for emergency contraception, so we do not include it in our second DD analysis.

There are advantages and drawbacks to each of these DD models. As stated above, for drugs that switched to BTC/OTC status, using within-country sales, prices, and expenditures of

drugs in the same class that did not switch status appears to be a more natural control than using sales, prices, and expenditures of these drugs in countries where the drug did not switch status. For example, if there are divergent trends across countries in the underlying diseases for which these drugs are indicated, using foreign sales of a drug will be a poor control, while using domestic sales of same-class drugs that did not switch will be more likely to control for these trends. However, to the degree that patients substitute between drugs within a class, using domestic sales of same-class drugs will tend to overstate the effects of a BTC/OTC switch. This effect occurs because our DD approach in effect compares the difference in sales, prices, and expenditures between the treatment and control groups over time, so that any substitution from the control group to the treatment group will be double-counted. For example, suppose that after a BTC/OTC switch, 10 percent of patients who use the non-switched drugs in one class substitute towards the switched drug. Even though utilization of the drug only increased by 10 percent, the DD approach will report a 20-percent increase, since utilization of the non-switched drugs fell by 10 percent.

To examine the degree to which this substitution occurs, we perform trend-break analyses using the following regression model:

$$\ln\left(sales_{it}\right) = \alpha + \beta_1 OTC_{it} + \beta_2 BTC_{it} + \gamma_1 t + \gamma_2 t^2 + \varepsilon_{it} \qquad (3.7)$$

In this equation, $sales_{it}$ represents total sales of non-switched drugs in class i. β_1 and β_2, our coefficients of interest, represent the effect of OTC and BTC switches, respectively, on sales of non-switched drugs. We estimate equation (3.7) separately for each class of drugs in the countries where at least one member of the class switched to BTC/OTC status. Equation (3.7) attempts to determine whether a BTC/OTC switch of a drug in a given class caused sales of other drugs in the class to deviate from their underlying, pre-switch quadratic time trend. If patients were to substitute from non-switched to switched drugs, we should see a drop in sales of non-switched drugs after the switch date. Thus, a test of whether substitution is an important factor is whether β_1 or β_2 equals zero. We also estimate similar versions of equation (3.7) in which we use the natural log of sales for *all* drugs in a given class to determine the effect of BTC/OTC switches on the overall utilization of a given class of drugs.

Results

Results Using International Sales/Prices as Controls

Table 3.1 presents our first set of results, which represent the effect of BTC/OTC switches on drug sales (quantities), prices, and expenditures, using as controls the international sales and prices of the drug in countries where it did not switch. Specifically, Table 3.1 presents our estimates of β_1 and β_2 in equations (3.1) through (3.3) from above. As shown in Table 3.1, during the period covered by our study, two drugs (fluconazole and simvastatin) switched to BTC status, and another three (ketoconazole, loratadine, and omeprazole) switched to OTC status. Levonorgestrel is unique in that it switched to OTC status in Canada and the United Kingdom, and switched to BTC status in Australia; we report the effects of the BTC and OTC switches separately. Also, recall that while fenticonazole switched to OTC status in the United Kingdom in 2001, it was sold only in the United Kingdom. Therefore, the drug is excluded from our analysis because there is no control group.

When linear time trends are included, we find that BTC switches had no effect on sales of fluconazole and levonorgestrel but increased sales of simvastatin by 31 percent ($p<0.01$). Consistent with the sales effects, the regression estimates indicate that prices of fluconazole and levonorgestrel remained unchanged or increased slightly after the switch to BTC status, and the price of simavastatin declined by 81 percent ($p<0.01$). The expenditure effects for BTC switches mimic the price effects: We find that expenditures on simvastatin decreased by 72 percent ($p<0.01$) and expenditures on fluconazole and levonorgestrel remained the same or increased slightly after the switch to BTC status.

We find that OTC switches for the most part had no effect on sales of drugs, except loratadine, whose sales decreased by 82 percent ($p<0.01$). OTC switches had mixed effects on prices. The prices of omeprazole and ketoconazole declined by 59 percent ($p<0.01$) and 21 percent ($p<0.05$) respectively; the price of levonorgestrel increased by 12 percent ($p<0.01$); and the price of loratadine remained unchanged. Again, the expenditure effects are similar to the price effects: Expenditures on ketoconazole declined by 26 percent ($p<0.01$); expenditures on levonorgestrel increased by 9.6 percent ($p<0.05$); and expenditures on loratadine and omeprazole remained unchanged.

Results Using Domestic Sales of Same-Class Drugs as Controls

In Table 3.2, we present the results from our second DD model, which uses as controls domestic sales and prices of drugs in the same class as a switched drug. Recall that in this second approach, we do not report estimates for levonorgestrel—because it is the only drug in its class (emergency contraception), there is no control group. Conversely, we do report results for fenticonazole, which was omitted in the previous analysis. Also, recall that our analysis examines the effects of all switched drugs within a class in a given country. Therefore, because two vaginal antifungals (fenticonazole and ketoconazole) switched to BTC/OTC status in the United Kingdom, our estimates represent an average effect across these two drugs. Table 3.2 shows our estimates of β_1 and β_2 and correspond to equations (3.4) through (3.6) above.

Our estimates for BTC switches are similar to those generated by the previous DD model. We find no effects on sales, prices, or expenditures for fluconazole. We find that the BTC switch lowered prices (by 72 percent, $p<0.01$) and increased sales (by 160 percent, $p<0.05$) of simvastatin. The sales, price, and expenditure effects for OTC switches are also largely similar to the previous DD model. We find that sales of omeprazole in the United Kingdom increased by 188 percent ($p<0.01$) and sales of loratadine declined by 69 percent ($p<0.01$). OTC switches had significant price effects for fenticonazole/ketoconazole (an 18-percent decrease, $p<0.05$) and omeprazole (a 57-percent decrease, $p<0.01$). We find that the OTC switch reduced expenditures on loratadine (by 88 percent, $p<0.05$), increased expenditures on omeprazole in the United Kingdom (by 99 percent, $p<0.01$), and reduced expenditures on omeprazole in the United States (by 77 percent, $p<0.05$).

Table 3.2

Effect of BTC/OTC Switches on Drug Sales, Prices, and Spending, Using Domestic Sales of Drugs in the Same Class as Controls

Drug	Country	BTC or OTC?	N	Sales		Price		Spending	
				No Trends	Trends	No Trends	Trends	No Trends	Trends
Fenticonazole, Ketoconazole	UK	OTC	101	-2.452	-0.782	-0.239[a]	-0.182[a]	-2.691	-0.963
				(1.462)	(1.040)	(0.104)	(0.078)	(1.479)	(1.068)
Loratadine	U.S.	OTC	39	-1.452[b]	-0.961[a]	-1.711[b]	-0.914	-3.163[b]	-1.875[b]
				(0.212)	(0.428)	(0.294)	(0.659)	(0.290)	(0.471)
Omeprazole	UK	OTC	117	0.536	1.232[b]	-0.569[b]	-0.409[a]	-0.034	0.823[b]
				(0.271)	(0.346)	(0.169)	(0.186)	(0.256)	(0.270)
Omeprazole	U.S.	OTC	108	0.387	-0.251	-0.874[b]	-0.998[b]	-0.488	-1.249[a]
				(0.465)	(0.604)	(0.218)	(0.370)	(0.462)	(0.507)
Fluconazole	AU	BTC	77	0.272	0.034	0.184	0.254	0.456[b]	0.288
				(0.210)	(0.117)	(0.160)	(0.133)	(0.152)	(0.197)
Simvastatin	UK	BTC	49	0.441	1.154[b]	-1.309[b]	-1.143[b]	-0.868[a]	0.011
				(0.336)	(0.399)	(0.240)	(0.280)	(0.384)	(0.345)

NOTES: Table 3.2 shows the estimates of BTC or OTC switches ("BTC/OTC") on quantities sold ("Sales"), prices ("Price"), and expenditures ("Spending"), as described in equations (3.4) through (3.6). "No trends" and "Trends" refer to the use of models that omitted and included a linear time trend, respectively. Robust standard errors are shown in parentheses. AU=Australia, UK=United Kingdom, U.S.=United States, CA=Canada, NZ=New Zealand.
[a] $p<0.05$
[b] $p<0.01$

Our second DD approach tends to estimate those sales effects for simvastatin and omeprazole that are of significantly larger magnitude than those that occur during our first approach. The difference between the estimates in the first and second DD approaches could

represent one of two possibilities. First, international sales of a drug may prove to be poor controls, causing the estimates from the second DD model to be more accurate. Alternatively, as stated in the methods section, our second DD approach may be overstating the effects of BTC/OTC switches, depending on the degree to which consumers substitute between drugs in a given class. To examine whether patients are substituting away from non-switched toward switched drugs, we conducted trend-break analyses in which the sales/prices of non-switched drugs were regressed on a quadratic time trend and a dummy variable for whether a drug in the class switched to BTC/OTC status, as described in equation (3.7). If consumers were substituting away from non-switched drugs, then we would expect sales of these drugs to fall after the BTC/OTC switch. However, we find no evidence of substitution, since none of the point estimates were statistically significant (these data are not shown).

Discussion

In this study we analyzed the effects of eight BTC/OTC switches on sales, prices, and expenditures. Overall, we find that BTC and OTC switches had substantial effects on sales, prices, and expenditures, but that the direction and magnitude of the effects varied significantly across the cases analyzed. We find weak evidence that BTC and OTC switches reduce prices: Of the eight switches analyzed in this study, prices declined significantly in five cases, increased significantly in one, and remained unchanged in two.

We find weak evidence that BTC switches increase sales; of the three cases analyzed, sales increased for simvastatin and remained unchanged for fluconazole and levonorgestrel. The evidence of OTC switches on sales were mixed: Of the five cases analyzed, sales increased in one (omeprazole), decreased in one (loratadine), and remained unchanged in the other three. It is interesting to note that in contrast to omeprazole and simvastatin, which experienced an increase in sales, loratadine experience a decrease in sales. In fact, the manufacturer of loratadine, Schering-Plough, actively opposed the switch to OTC status and, after the switch, made extensive efforts to convince consumers to buy desloratadine, a newer, prescription form of the drug. These efforts may explain why utilization fell after the drug switched to OTC status, while usage increased for omeprazole and simvastatin. In addition, it is also important to note that one reason why effects of a BTC switch differ from effects of an OTC switch is that older drugs tend

to switch to OTC status (often soon after patent expiry). Therefore, the OTC switch may be capturing the effects of patent expiry. In contrast, BTC switches tend to occur for younger drugs.

We also find mixed evidence of the effects of BTC/OTC switches on expenditures. We found that expenditures fell for ketoconazole, omeprazole in the United States, and simvastatin, but increased for levonorgestrel, omeprazole in the United Kingdom, and loratadine. The heterogeneity in these expenditure effects is not surprising given the heterogeneity in price and sales effects. In addition, the differences in the effects of BTC/OTC switches between drugs and across countries could reflect differences in elasticities of demand—for drugs with inelastic demand, expenditures will move in the same direction as prices; for drugs with elastic demand, expenditures will move in the opposite direction as prices.

In conclusion, our results show that the introduction of BTC drugs in the United States could have varied effects in practice and it is unclear whether such a policy would increase access to drugs. However, the results do suggest that at least in some cases, BTC drugs have the potential to simultaneously reduce expenditures and increase access.

The results of this study should be viewed in light of the study's limitations. First, it is important to note that our data on drug sales do not account for fact that rebates from manufacturers to insurers are common for prescription drugs but are unlikely to occur with BTC drugs. Therefore, our results may overstate the potential price effects. Nonetheless, recall that in most cases, BTC/OTC drugs are simply lower-dose versions of prescription drugs, with the higher-dose versions remaining available via prescription only. Since our estimates of price reflect the average of prescription and nonprescription versions for each drug, to the extent that prescription drugs still remain a large share of sales, this source of bias will be mitigated. In addition, our reported price decreases are still much larger than average rebates in the United States. For example, private insurers in the United States typically receive rebates of 8 percent, while the Medicaid program receives rebates of 26 percent (United States House of Representatives, 2007). Second, a full analysis of the costs and benefits of BTC drugs should also consider the potential health effects and effects on physician-office visits. These are potential subjects for further useful research.

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Appendix to Chapter Three

Table B.1

List of Drugs, Classes, and BTC/OTC Switches

Class	Members	OTC Switches	BTC Switches
Second-generation antihistamines			
	Cetirizine		AU (1997), CA (1995)
	Desloratadine	CA (2002)	
	Fexofenadine	CA (1997)	AU (1997)
	Levocetirizine		
	Loratadine	CA (1990), UK (1993), U.S. (2002)	AU (1994)
Vaginal antifungals			
	Bifonazole	AU (1997)	
	Butoconazole		AU (2006)
	Clotrimazole	CA (1994), U.S. (1991)	AU (1994), UK (1992)
	Econazole		AU (1997), UK (1992)
	Fenticonazole	UK (2001)	
	Fluconazole	UK (1995)	AU (2003)
	Isoconazole		AU (1999), UK (1992)
	Ketoconazole	UK (1998)	AU (1994), UK (1992)
	Miconazole	CA (1994), U.S. (1991)	
	Miconazole + hydrocortine		AU (1999)
	Nystatin		AU (1990)
	Oxiconazole		
	Tioconazole	CA (1995), U.S. (1997)	AU (1999)

Class	Members	OTC Switches	BTC Switches
Emergency contraception			
	Levonorgestrel	CA (2005), UK (2001)	AU (2004)
Anti-ulcer drugs (H_2RAs and PPIs)			
	Acrivastine	UK (1993)	
	Cimetidine	UK (1994), U.S. (1995)	AU (1995)
	Esomeprazole		
	Famotidine	CA (1996), UK (1994), U.S. (1995)	AU (1995)
	Lansoprazole		
	Nizatidine	UK (1996), U.S. (1996)	AU (1996)
	Omeprazole	UK (2004), U.S. (2003)	
	Pantoprazole		
	Rabeprazole		
	Ranitidine	CA (1997), UK (1994), U.S. (1996)	AU (1995)
	Ranitidine bismuth		
Statins			
	Atorvastatin		
	Fluvastatin		
	Lovastatin		
	Pravastatin		
	Rosuvastatin		
	Simvastatin		UK (2004)

NOTE: AU=Australia, UK=United Kingdom, U.S.=United States, CA=Canada, NZ=New Zealand.