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Technology, Information and Decision Making in Health Care

Abstract

In this dissertation, I investigate how patients and providers respond to changes in healthcare technology with information and resource constraints. The following chapters are three diverse approaches to this core inquiry.

Pharmaceutical innovations in the 20^{th} century were transformative in the prevention and treatment of cardiovascular disease. Yet, the efficacy of medication may be lower than clinical expectations due to adjustments in perceived risk that cause changes in behaviors, a phenomenon known as risk compensation. In Chapter 1, the 1973 FDA approval of new classes of drugs to treat high blood pressure and high cholesterol is used to identify the effect of medication availability on nonsmoking, adherence to a diet, and body mass index. Results show that medication approval significantly decreases the probability of engaging in healthy behaviors, evidence of risk compensation. Once a diagnosis of cardiovascular disease (CVD) is received, a patient has updated information about the state of her health which may induce the adoption of healthy behaviors. For smoking, a diagnosis of CVD does partially attenuate the risk-compensation effect of medication. After medication is approved, individuals at high risk of CVD have increased take-up – an indication that risk screening is implemented. Also, a CVD diagnosis prompts medication use as a complement to multiple healthy behaviors. The evidence demonstrates the importance of promoting healthy behaviors to a broad population and increasing risk-factor salience prior to diagnosis.

Chapter 2 provides new evidence on how technology affects healthcare markets by focusing on one area where adoption has been particularly rapid: surgery for prostate cancer. Over just six years, robotic surgery grew to become the dominant intensive prostate cancer treatment method. Changes in patient volume due to robot adoption are estimated using a difference-in-differences design. Results indicate that adopting a robot drives prostate can-

cer patients to the hospital. Estimating changes in patient volume at the market level tests whether this result reflects market expansion or business stealing. The findings here are significant but smaller, suggesting that adoption expands the market while also reallocating some patients across hospitals. Marginal patients are relatively young and healthy, inconsistent with the concern that adoption broadens the criteria for intervention to patients who would gain little from it. The chapter concludes by discussing implications for the social value of technology diffusion in healthcare markets.

Chapter 3 returns to the consideration of pharmaceutical drugs with a theoretical look at the way information, through advertising, impacts the decision of a generic pharmaceutical manufacturer to enter the market after patent expiration. Brand-name pharmaceutical firms with patent protection advertise in two ways: to physicians as detailing and direct-to-consumers through mass media. Prior research shows that each type of advertising uniquely influences markets. Physician advertising generates goodwill that the brand retains after patent expiration while direct-to-consumer advertising (DTCA) expands demand for the entire class of drugs. A potential generic competitor's entry decision is based on its evaluation of future market conditions, which are affected by brand loyalties created by detailing and market size, as determined in part by DTCA. A two-stage vertical differentiation model is used to develop testable hypotheses that physician advertising is necessary for entry to avoid Bertrand competition, but in high levels acts as an entry deterrent. Conversely, DTCA promotes entry through market expansion. During the period of patent protection, the brand firm optimally chooses levels of detailing and DTCA to maximize expected profits over the patent-protection period and the period after patent expiration, anticipating the effects of its actions on generic entry. The analysis concludes by considering the impacts of pharmaceutical advertising and generic entry on consumer welfare.

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Chapter 1

From Prevention to Treatment: Prescription Medication and Health Behaviors[1]

1.1 Introduction

Over 60% of adults in the United States (U.S.) have cardiovascular disease (CVD), which is the number one cause of death, and accounts for $216 billion in annual health care costs (CDC, 2018; AHA, 2021). Research over the past century has improved understanding of CVD risk factors; yet, the unhealthy behaviors that contribute to CVD remain prevalent (Saklayen and Deshpande, 2016; Virani et al., 2020). One possible explanation is risk compensation (Peltzman, 1975). Individuals compensate for changes in perceived levels of risk by adjusting their behavior. It is less "costly" to engage in risky behavior when new technology can prevent catastrophic outcomes.

[1]This Manuscript was prepared using FRAMCOHORT Research Materials obtained from the NHLBI Biologic Specimen and Data Repository Information Coordinating Center and does not necessarily reflect the opinions or views of the FRAMCOHORT or the NHLBI.

Invasive and non-invasive technologies have been introduced to address the prevention and treatment of CVD, notably medication. Healthy behaviors also decrease the risk of CVD. The efficacy of medication as a treatment for CVD would be reduced if medication causes risk compensation by decreasing the perceived risk of poor diet, obesity and sedentary lifestyle (Ha, 2014; Trap-Jensen, 1988). Conversely, a diagnosis of CVD provides updated information about the consequences of past behavior choices and may increase the take-up of healthy behaviors. This paper asks: Does the availability of new medication negatively impact health behaviors? In turn, does a diagnosis of CVD offset the risk-compensation effect of medication?

Risk compensation in health care is well established. There are numerous instances of health interventions having lower efficacy in the real world than in clinical trials (Prasad and Jena, 2014). A survey by Golub et al. (2010) on preexposure prophylaxis (PREP) for the prevention of human immunodeficiency virus (HIV) found that of men who would use PREP, 35% would also decrease condom use. Statins, used to treat high cholesterol, are associated with increased waist size and poor diet (Mancino and Kuchler, 2009), and increased BMI, obesity and alcohol-drinking behavior (Kaestner et al., 2014). Also, diabetes patients view medication as more important that lifestyle changes, even though patients that used medication in addition to healthy behaviors had better management of blood glucose levels (Broadbent et al., 2011). In contrast, receiving the human papillomavirus (HPV) vaccine is associated with less risky sexual behavior across a number of studies (Kasting et al., 2016). A key difference is that it is often a parent, rather than the child, who makes the decision for the child to receive the HPV vaccine.

With the exception of diabetes, the research cited above does not distinguish between preventative care and treatment. Risk compensation often points to behavioral offsets that occur before the "crash" (Peltzman, 1975; Mancino and Kuchler, 2009; Kaestner et al., 2014; Golub et al., 2010). Once a diagnosis occurs, preventative care becomes treatment and the

patient has updated information about the state of their health. Oster (2018) links the precise timing of a diabetes diagnosis to assess changes in food purchases. Results indicate that a diagnosis of diabetes causes a small but significant decrease in consumption of high-calorie and high-sugar foods. Other work confirms that the magnitude of dietary changes after a diagnosis is generally small but statistically significant (Zhao et al., 2013; Shimokawa and Shimokawa, 2015). A study by Kim et al. (2019) considered diabetes, hyperlipidemia and obesity in Korea and found significant changes after diabetes diagnosis for weight loss, taking diabetes medications and increased future health screenings. Despite mixed findings for personal health information, the health shock of a family member causes a spillover of information that induces individuals to increase personal take-up of healthy behaviors (Fadlon and Nielsen, 2019; Thomas and Mentzakis, 2020; Hoagland, 2021).

I add to the existing literature by considering that risk compensation may occur in response to having medication *available* regardless of take-up. In contrast to prior work, I find that the option of FDA-approved medication, even if not taken, offsets healthy behavior. I also link the risk-compensation literature to the literature on the impact of diagnoses on behavior by considering how behavior changes from the initial risk of disease to diagnosis in relation to new treatment modalities. I hypothesize that risk compensation explains the limited impact of diagnostic information on inducing healthy behavior.

I consider how medication availability and a diagnosis affect behavior using the original cohort of the Framingham Heart Study. This is a longitudinal study of individuals from Framingham, Massachusetts who were clinically examined biennially from 1945 through their lifespan to determine the epidemiology of heart disease. The advantage of these data is that they allow for a long-study-sample period, between 1960 and 1982. This time frame includes the FDA approval of the first beta blocker, propranolol, to treat high blood pressure (hypertension) in the same year that the first bile-acid sequestrant, cholestyramine, to treat high cholesterol (hyperlipidemia) was introduced. Both drugs were revolutionary at the

time. The seminal randomized-controlled trial (RCT) on beta blockers found a reduction in cardiovascular mortality of 26% for individuals treated with propranolol (Srinivasan, 2019). Also, clinical evidence finds that cholestyramine significantly reduces low-density lipoprotein (LDL) cholesterol and reduces cardiovascular mortality by 24% (NHLBI, 1984). There were no medication innovations in the 15 years prior to these new treatments and none for the subsequent eight years for these conditions, see Table A1. This allows me to isolate behavior and medication use in relation to new innovations that address the biggest risk factors for CVD. During this period, the health benefits of dieting, nonsmoking and reducing BMI were becoming widely known and promoted by clinicians (La Berge, 2007; CDC, 2014). The panel design of the data and rich measures of health and behavior provide the ideal setting to consider how medication and behavior interact before and after a diagnosis in a U.S. setting while controlling for unobserved, time-invariant-individual characteristics.

I use a quasi-experimental design adapted from Fadlon and Nielsen (2019) and Deshpande and Li (2019) to estimate how the availability of new medication impacts health behavior in total and after a diagnosis of CVD. The "treatment" group in my sample consists of individuals who experience an initial diagnosis of CVD at one of six biennial exams and are followed for the subsequent two exams (four years). They are matched with controls who will also be diagnosed with CVD three or four exams in the future (6 to 8 years).[2] The only differences between the treatment and control groups are idiosyncratic because the timing of a CVD diagnosis can be unpredictable as is assumed in Chandra and Staiger (2007) and Fadlon and Nielsen (2019). This is plausible given that the ten-year risk of a CVD diagnosis is not systematically different between the treatment and control groups at the time the treatment group is diagnosed, and ten-year risk is not significantly associated with the timing of a diagnosis within my sample.[3] Each sample individual is a candidate for

[2]The health economics literature has viewed the precise timing of an acute myocardial infarction (AMI) or stroke as random (Chandra and Staiger, 2007; Fadlon and Nielsen, 2019). The main analysis broadens the defined health shock to a diagnosis of CVD for which risk is assessed in a 10-year time frame. The diagnosis of CVD falls within 10 years for both treatment and control individuals. As a test of robustness, the sample is limited to people who gain the diagnosis through an AMI or stroke alone. See Appendix Table 1.5.

[3]Ten-year risk indicates the probability that an individual will be diagnosed with CVD within the next

taking medication to prevent and treat CVD given future diagnosis. The model begins with a basic difference-in-differences design that follows from this setup and is then expanded to a triple-differences model that includes the fully-saturated interaction of CVD diagnostic status with the exogenous introduction of newly FDA-approved medication in 1973.[4] There are two effects of interest. The first is the total impact of newly approved medication on behavior, and the second is the interaction of new medication with being in the treated group after diagnosis which demonstrates the marginal effect of receiving a diagnosis and FDA approval on behavior.

The FDA approval of beta blockers and bile-acid sequestrants causes an 11 percentage point (29.6%) increase in current smoking, a 4 percentage point (44.2%) decrease in following a low-salt diet, a 1 percentage point (18.7%) decrease in following a low-fat diet, and a 0.49 (1%) increase in BMI.[5] All estimates are statistically significant. These findings support the idea that risk compensation is present in response to having a medication available to prevent CVD, regardless of use. Once CVD diagnosis is received and patients gain information about the consequences of past-behavior choices, the risk compensation response for smoking is decreased - there is a positive probability of non-smoking after FDA approval and CVD diagnosis. However, there is no change in the risk-compensation effect for dieting and BMI after receiving a CVD diagnosis in response to medication availability.

I next investigate the use of medication in combination with healthy behaviors after FDA approval. After new medication is available, patients may choose to use medication as a substitute or complement to other healthy behaviors. The outcomes considered are combi-

ten years. The specific timing of a diagnosis cannot be determined within the ten-year-time frame without updating the risk score which is recommend at least every six years (Wilson, 2021a). The mean ten-year-risk score at the time the treatment group is diagnosed is not statistically different between the treatment and control groups for those diagnosed before 1976. The last treatment group diagnosed has a risk score that is 1.7 percentage points higher than their matched control group. Also, regressing ten-year-risk score prior to the treatment group's diagnosis does not systematically predict being diagnosed. See Appendix Tables and A2 and A3.

[4]The predicted probability of a CVD event is not significantly correlated with FDA approval of beta blockers to treat hypertension and bile-acid sequestrants to treat hyperlipidemia in 1973.

[5]The results presented in Table 1.2 report coefficients for the probability of being a nonsmoker and decrease in BMI to maintain the consistency of the direction of coefficients.

nations of medication and behavior choices modeled using the same difference-in-differences design (excluding the FDA-interaction terms) with additional controls for being at high or low risk of CVD. Results show that experiencing a diagnosis increases the probability of complementing medication use with healthy behaviors but does not increase take-up of medication when controlling for risk status. Persons at the highest level of ten-year risk for CVD ($\geq$ 20%) are associated with increased take-up of medication and use medication more often as a substitute than a complement to singular-healthy behaviors. This indicates that risk screening is actively implemented. Concernedly, individuals with low-risk of CVD (<10%), but who will eventually be diagnosed, are associated with a lower probability of medication use and are less likely to use medication as a complement with multiple healthy behaviors compared to individuals with intermediate risk. For this group, risk score may underestimate true risk by not accounting for marginal factors that may influence disease manifestation (Wilson, 2021b). If this is the case, individuals in the low-risk category may not know their true risk of CVD and use fewer preventative measures that would be optimal.

Access to a medication to prevent and treat CVD can induce unhealthy behavior. Yet if taken, medication is often used to complement healthy behaviors for those that have a diagnosis or are at high risk of CVD. If individuals value unhealthy behaviors (such as smoking and eating high-sodium or high-fat foods) and also value health, risk compensation may be a utility-maximization strategy because the FDA approval of medication decreases the cost of unhealthy behavior. The concern is that the risk of CVD may not be correctly assessed. As a result, it is not until the true cost of unhealthy behavior is realized, via a CVD diagnosis, that medication and healthy behaviors are more likely to be used as complements. For clinicians and public health advocates, the findings highlight the importance of helping all patients (not just those at high risk of CVD) understand the risk factors of CVD and the importance of healthy behaviors, even when medication is available, before prevention becomes treatment.

The chapter proceeds as follows: Section 1.2 provides background on CVD and related medications and risk factors. Section 1.3 discusses the data. Section 1.4 presents the primary estimation strategy. Section 1.5 assesses the results. Section 1.6 explores treatment choice after medication is available. Section 1.7 discusses the findings and concludes.

1.2 Background

1.2.1 Cardiovascular Disease

Cardiovascular disease is a broad term for diseases that primarily affect the heart and/or blood vessels. The majority of CVD diagnoses are for coronary artery disease which is commonly referred to heart disease. Heart disease occurs when there is decreased blood flow to the heart muscle due to a build up of plaque (deposits of cholesterol) in the artery walls. Over time, plaque causes arteries to narrow which leads to chest pain and shortness of breath. If a plaque ruptures, it can form a blood clot that blocks the artery and causes a portion of the heart muscle to die. This is known as a acute myocardial infarction (AMI or heart attack). Since the 1950s, CVD has been diagnosed by laboratory tests, non-invasive tests such as electrocardiogram and echocardiogram and/or invasive tests such as cardiac catheterization (Hajar, 2017).

The behavioral risk factors for developing heart disease include a diet high in fat and/or sodium, smoking, excessive alcohol use and a sedentary lifestyle. Over time, these behaviors can lead to conditions that increase the probability of developing heart disease, including: high blood pressure (hypertension), elevated cholesterol levels (hyperlipidemia), obesity and diabetes. While heart disease can be treated with intensive interventions such as cardiac catheterization and bypass surgery, treatment also involves addressing behavioral-risk factors through lifestyle changes (CDC, 2018).

1.2.2 Medication and Cardiovascular Disease

In the 1940s scientists began focusing on the causes of heart disease. Linking elevated blood pressure to heart disease was an early discovery of this time, but even after the connection was made, hypertension was considered untreatable (Saklayen and Deshpande, 2016). In 1953, the FDA approved the first medication to treat hypertension. Hydralazine is a vasodilator that works by relaxing blood vessels thereby allowing blood to flow more easily. Five years later, the first diuretic, chlorothiazide, was FDA approved. Chlorothiazide lowers blood pressure by inducing the kidneys to clear excess water and salt from the body. During the 1950s and 1960s there was additional debate about what constituted diagnosed hypertension that was considered a risk for heart disease. The familiar reading of 120 systolic over 80 diastolic blood pressure is a modern standard developed years after this early learning period. This means that even though medications were available, hypertension as it would be identified today was often untreated into the mid-century (Saklayen and Deshpande, 2016).

Vasodilators and diuretics were the only medications available to treat hypertension for the next 15 years (FDA, 2020). The first beta-adrenergic blocking agent, propranolol, was FDA approved in 1973. Beta blockers (as they are commonly referred to) work by decreasing stress hormones in the body which brings down the heart rate and results in decreased blood pressure. A landmark RCT for beta blockers demonstrated that they reduced cardiovascular mortality by 26% (Srinivasan, 2019). Since beta blockers affect blood pressure from a different avenue than vasodilators, they are often combined in treatment (Stevens et al., 1983). After the introduction of beta blockers, 15 medications in this class of drugs have been developed with the most recent reaching the market in 2007. After the introduction of beta blockers, medication use to treat hypertension among study participants increased from 8% to 24%.[6] Appendix Table A1 for a timeline of FDA approvals.

[6]The increase is among study participants who attended exam 12 which spanned 1973 when propranolol was approved by the FDA. The sample was not restricted to individuals with hypertension or who were at high risk of CVD. Medication use to treat hypertension was 8% at exam 11, at exam 12 medication use increased to 19% and increased again to 24% at exam 13 (the exam after approval).

Medications to treat high-cholesterol levels were slower to be developed. In 1973, cholestyramine, a bile-acid sequestrant, was the first FDA-approved medication for hyperlipidemia (FDA, 2020). This medication binds to bile acids in the intestine and prevents their absorption. To compensate for the loss of bile acids, the liver converts cholesterol into bile acids which reduces the level of cholesterol in the blood. Take-up of cholestyramine was much slower than for hypertension medications despite evidence that bile-acid sequestrants can reduce cardiovascular mortality by 24% (NHLBI, 1984). In the six years after approval, 79.3% of study participants were taking medication to treat hypertension compared to medication to treat hyperlipidemia.

At the time these drugs were developed, pharmaceutical advertising was limited to physicians. Yet, the clinical benefits of these medications and prevalence of heart disease made their development headline news. Beta blockers and bile-acid sequestrants were both covered in national media outlets and Massachusetts newspapers where my study sample is located.[7] For example, a 1976 Boston Globe article discussed the benefits and uses of propranolol and in large font declared, "Encouraging Reports from hospitals here and abroad" (Galton, 1976). The media coverage of both drugs provides a path of information to increase public awareness of the clinical benefits of the medications without visiting a doctor or prescription. It also provides reasoning for the slower take-up of the cholesterol-lowering drug which had sparser coverage.

Both beta blockers and bile-acid sequestrants remained the last innovations to treat hypertension or hyperlipidemia until 1981. The introduction of these medications during a drought of development before and after their FDA approval offers an opportunity to identify the effect of medication availability on behavior.

[7] A search of term "propranolol" in The Boston Globe news archives using Newspapers Publishers Extra from 1963 through 1983 resulted in 71 matches, and a search for "cholestyramine" returned 6 results. A search of news archives using Nexis Uni of national media from 1963 through 1983 for the term "propranolol" resulted in 70 articles from multiple publications. The search for "cholestyramine" resulted in 14 articles from a similar grouping of media outlets.

1.2.3 Behavior, Health and Medication

The first diet to receive attention for reducing hypertension was the Kempner Rice Diet which was notable for its low-salt content (Kempner, 1948). Nine-years later in 1957, the American Heart Association (AHA) recommended that decreasing dietary fat would reduce the risk of heart disease (Krauss et al., 1996). This was promoted by Congress when the Senate Committee on Nutrition and Human Needs published *Dietary Goals for the United States* in 1977 (La Berge, 2007). By this time, the Surgeon General's report on Smoking and Health had been out for 13 years, and Americans had a clearer picture of how lifestyle impacted their risk for CVD (CDC, 2014).

There have been many studies since that consider the combined efficacy of medication and health behavior in the prevention and treatment of CVD. Khera et al. (2016) found that even among people with genetic risk of heart disease, making healthy-lifestyle changes reduced the risk of a coronary heart event by 46 percent. Multiple randomized-control trials have demonstrated that the use of a beta blocker with sodium restriction was significantly more effective at lowering blood pressure when compared to salt restriction or beta blockers alone (Erwteman et al., 1984; Luft and Weinberger, 1988; Ha, 2014). Similarly, smoking cessation complements the hypotensive effects of beta blockers while smoking blunts drug efficacy (Trap-Jensen, 1988). In a study of men at risk for heart disease, adherence to five-lifestyle factors (nonsmoking, moderate alcohol consumption, BMI under 25 kg/m^2, healthy diet and physical activity) could prevent 62% of potential coronary events; among the men who were already on medication, adopting a "low-risk" lifestyle would reduce coronary events by 57%. Only adopting two of the five lifestyle changes resulted in a 25% decrease in the risk of a coronary event (Chiuve et al., 2006). Medication and a healthy lifestyle are biological complements in reducing the risk of disease.

Despite ample evidence on the preventative effects of healthy behaviors, physician recommendations about lifestyle changes to reduce the risk of CVD are generally reserved

for patients that exhibit obvious high-risk behaviors such as obesity or sedentary lifestyle or for whom medication is not an option (Grundy et al., 2004). Even with consistent evidence of the complementary therapeutic nature of behavioral changes and medication use to treat hypertension and hyperlipidemia, medication often remains the clinical focus (Hyman and Pavlik, 2000).

1.3 Data

The Framingham Heart Study began in 1948 to collect epidemiological data on CVD (Mahmood et al., 2014). Undertaken at a time when thirty percent of men in the U.S. were developing heart disease, the study was to determine the factors that influence disease development and trajectory. The original cohort consisted of 5,209 participants who were not initially exhibiting signs of heart disease. The participants underwent exams biennially throughout their lifespans – a total of 32 exams. The tests administered and data collected vary across exams but generally focus on all aspects of cardiovascular health with additional measures of socioeconomic status and lifestyle. Eventually, the Framingham Heart study expanded to include the children of the original cohort and recruited additional participants. The Framingham Heart Study is unique in providing a long-run panel. All participants in the original cohort are from Framingham, Massachusetts (Oppenheimer, 2005). This city was selected in part because it was considered to be representative of the general U.S. population at its inception (Kelleher, 2018). However, limiting the sample to one geographic area does limit external validity. Prior research has found that the Framingham Heart Study does predict heart disease well compared to a nationally representative sample of white adults from the National Health and Nutrition Examination Survey (NHANES) I Epidemiologic Followup Study (Leaverton et al., 1987).[8] An additional concern with the sample is that

[8]Table A4 presents means for the Framingham sample population compared to a nationally representative sample from the weighted National Health Interview Survey (NHIS) for years that CVD diagnostic questions were asked during this study sample time period. The available statistics from the NHIS were limited during this time period. Among participants in both samples who were diagnosed with CVD, the Framingham

participants in the Framingham Heart Study volunteered be in the study. while individuals did not initially exhibit signs or symptoms of heart disease, volunteering is a signal that they may be more interested in heart health than the general population. This introduces the potential for bias from sample selection into the results.

I focus exclusively on the original cohort from exam number 7 through 16 which span the years 1960 through 1982. The FDA approval of propranolol (beta blocker) and cholestyramine (bile-acid sequestrant) occurred during exam 12. There are no medication introductions to treat hypertension or hyperlipidemia during any other exams in the sample time period with the exception of exam 16.[9]

The research design relies on knowing if the participant has a diagnosis of CVD. Diagnoses are validated through physical examination as part of the Framingham Heart Study and by review of medical records generated between exams as opposed to self-reported diagnosis.[10] In addition to a definitive diagnosis of CVD, the data includes validated measures of age, sex, cholesterol, blood pressure and smoking status collected at each exam. These measures are used to calculate the Framingham Risk Score (FRS), the 10-year risk probability of developing CVD, see Appendix A.1 for the formula (D'Agostino et al., 2008). To be included in the sample, the individual must attend the exam prior to a CVD diagnosis, the diagnosis exam and both exams after diagnosis. Deceased individuals are removed from the sample when they die. The sample is lastly limited to exclude anyone who was over 60 years old at exam 1. The final sample is comprised of 1,275 individuals across 10 exams, representing 34% of the non-deceased participants who attended exam 9.

participants are, on average, 7 years older than in the NHIS sample. The samples are comparable for the percentage of individuals who are married, but NHIS has an 8 percentage point higher rate of people who are divorced, widowed or separated. Lastly, 2% more men are in the Framingham sample compared to NHIS.

[9]In 1981, toward the end of the time frame for exam 14 (1979 - 1982), the FDA approved the first angiotension-converting enzyme (ACE) inhibitors to treat high blood pressure and fibrates to treat high cholesterol. See Table A1.

[10]If the study participant reports any symptoms of CVD such as chest pain, circulation problems or arrhythmia, or if they report any cardiac procedures or diagnoses, the research team reviews the medical records of the participant to confirm the diagnosis and timing of CVD and/or any other cardiac events such as stroke or AMI.

As described above, the time frame of the study aligns with the period where the impact of behavior on CVD was becoming widely known. The behavioral outcomes considered are those directly related to the prevention and treatment of heart disease and for which data are available.[11] The first outcome assessed is if the participant is a nonsmoker since smoking is a well-documented threat to heart health. Two dietary outcomes that were recognised to decrease the risk factors of CVD at the time are also considered: following a low-salt diet and/or a low-fat diet.[12] Regulating salt intake is an important behavioral treatment for hypertension and is often advised to regulate blood pressure. Similarity, a low-fat diet was advised to treat hyperlipidemia at the time (La Berge, 2007). Both of these outcomes are self reported during a participant's physical exams. Body-mass index (BMI) is used as an outcome measure of body size as opposed to weight or obesity. Weight does not account for height and obesity may not quickly respond to behavioral changes.[13] Each regression includes rich measures of age to control for any age-related BMI trends.[14] BMI cannot change in response to a diagnosis at the same exam a diagnosis is made. However, 98.4% of first diagnoses are made between exams and validated at the biennial Framingham exam. Thus, there is adequate time to detect changes in BMI that results from a CVD diagnosis.

1.3.1 Summary Statistics

Table 1.1 presents summary statistics for the sample of Framingham participants separating by men and women. Women are 1.7 years older, on average, than men, at 64.7 years. More

[11] Alcohol usage and level of physical activity are both important behaviors that can contribute to CVD. However, the Framingham Heart Study does not include consistent measures of these during the study-sample-time period.

[12] At exam 7, participants were asked if they followed a "salt restriction" or "hypocholesterol" diet with responses for yes, no or unknown. At exam 8, participants were asked if they followed a "salt restriction" or "low fat" diet singularly, together or in combination with other diet types. At exam 9, participants were asked if they avoid salt intake with responses for yes, no or unknown. Low fat or hypocholesterol dietary questions were not asked at this exam. For exams 10 through 15, participants were each asked if they followed a "low salt" or "low fat" diet with responses for yes, no or unknown. Additionally at exam 10, participants were asked if they avoided salt or salty food.

[13] The calculation for BMI is 703 times the participant's weight divided by their height squared.

[14] Age-related controls include: age, age squared, 5-year age group, and an indicator for being over 64 years old.

Table 1.1: Summary Statistics for Individuals in Sample

	(1) Male		(2) Female	
Age	63.021	(9.298)	64.711	(9.687)
Over 64 Years Old	0.523	(0.500)	0.573	(0.495)
Married	0.753	(0.431)	0.464	(0.499)
Widowed-Divorced-Separated	0.068	(0.253)	0.311	(0.463)
Less than HS Education	0.420	(0.494)	0.434	(0.496)
HS Graduate	0.275	(0.446)	0.332	(0.471)
College Education	0.142	(0.349)	0.141	(0.348)
Post College Education	0.060	(0.238)	0.018	(0.132)
AMI or Stroke	0.618	(0.241)	0.486	(0.215)
Diagnosed with Cancer	0.027	(0.161)	0.021	(0.142)
Diagnosed with Diabetes	0.071	(0.257)	0.073	(0.260)
Framingham 10-Year Risk Score	0.150	(0.055)	0.079	(0.057)
High Risk (20% or more)	0.276	(0.447)	0.060	(0.238)
Intermediate Risk (10% to 20%)	0.581	(0.493)	0.268	(0.443)
Low Risk (less than 10%)	0.143	(0.350)	0.672	(0.470)
Nonsmoker	0.645	(0.479)	0.735	(0.442)
On a Low-Salt Diet	0.058	(0.233)	0.101	(0.301)
On a Low-Fat Diet	0.055	(0.229)	0.063	(0.244)
BMI	26.836	(3.698)	26.533	(5.045)
N	6,470		6,280	
Individuals	647		628	

Notes: This table reports summary statistics for the sample of individual men and women included in the main analysis. See the Research Design section for detail on sample construction. Each characteristic and behavior is at the individual-exam level spanning exams 7 through 16. Risk score is defined as the Framingham Risk Score (FRS), see Appendix A.1 for formula details.

men are married, 75.3%, compared to women at 46.4%; conversely, more women are widowed, divorced or separated. Also, less than 45% of the sample did not graduate high school, and while women have a 6 percentage point higher high school graduation rate, men are more likely to earn college and post-college degrees.

With respect to overall health, by design 100% of the sample will experience a diagnosis

of CVD, but 61.8% of men and 48.6% of women will also experience an AMI or stroke. Cancer and diabetes have similar rates of diagnosis across the samples at 2.4% and 7.2% respectively. Men have a 7 percentage point higher probability of a CVD event within ten years based on their Framingham risk score (FRS) compared to women who have an average ten-year risk score of 7.9%. Men are more often classified as high or intermediate risk (10% or greater probability of a CVD event within 10 years) compared to women for whom 67.2% are classified as low risk (less than 10%).

Women have a 9.2 percentage point higher rate of nonsmoking compared to men at 73.5%. Men and women have comparable BMIs, but women follow diets at higher rates than men. Considering salt, 10.1% of women report being on a low-salt diet versus men at 5.8%, and 6.3% of women follow a low-fat diet compared to 5.5% of men.

1.4 Research Design

The research design is described in stages for clarity. It begins with estimating risk compensation and is then extended to incorporate the impact of a CVD diagnosis on behavior. Central to identifying the risk-compensation effect of new medication on behavior is the exogenous FDA approval of beta blockers and bile-acid sequestrants in 1973 which occurred during Framingham exam 12. Both medications are used to prevent CVD prior to a diagnosis and as a treatment after CVD has manifest. This effect can be estimated with a fixed-effects regression:

$$Y_{it} = \eta_1 FDA_t + \alpha_i + \Lambda X_{it} + \epsilon_{it} \tag{1.1}$$

Four behavioral outcomes, Y_{it}, are considered: nonsmoking at exam time t, if individual i is on a low-salt diet at exam time t, if individual i is on a low-fat diet at exam time t, and the decrease in individual $i's$ BMI. Outcomes are presented as healthy behaviors. The variable

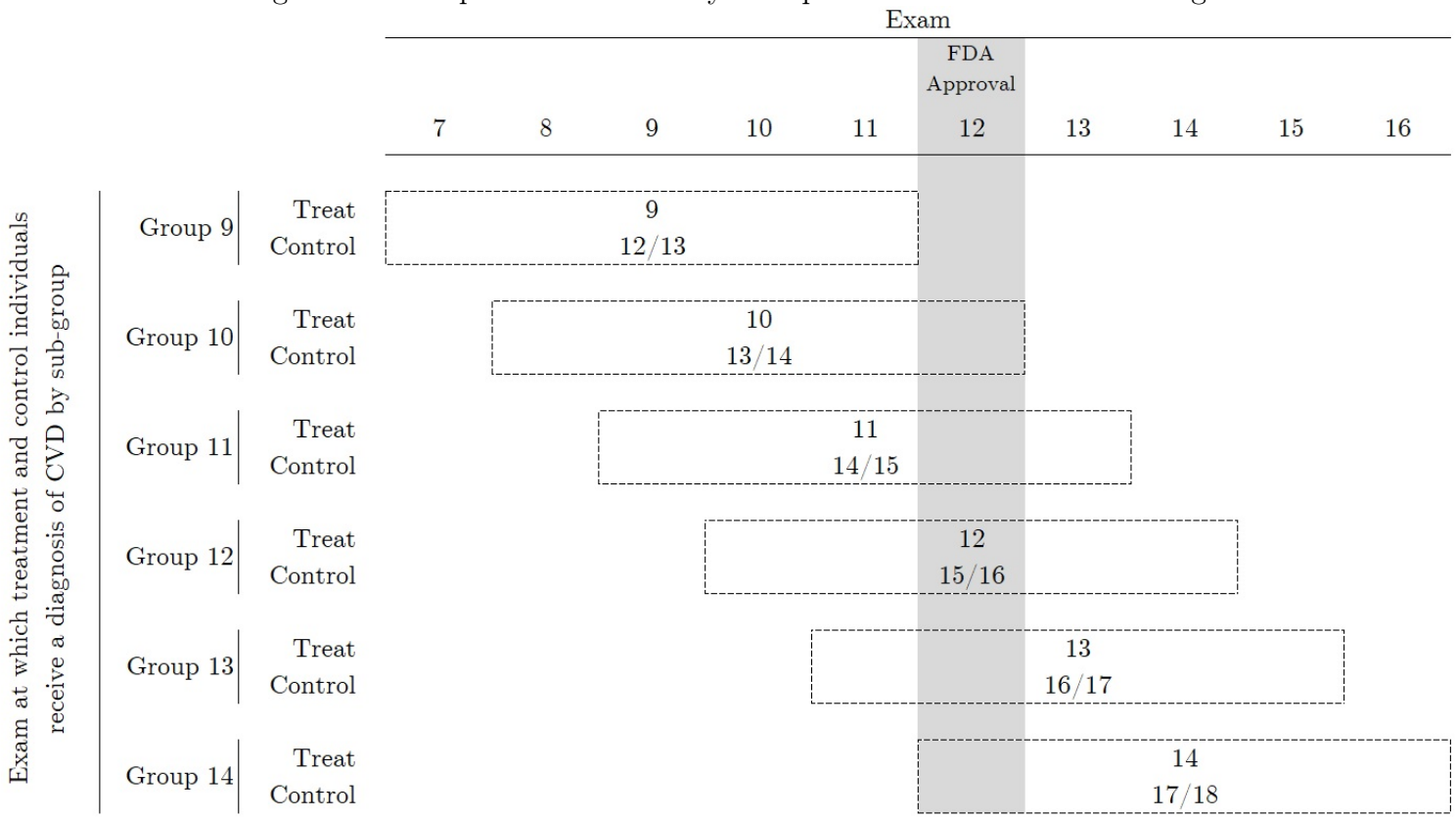
FDA_t indicates the FDA approval of new medication beginning at exam 12. Individual-level controls are indicated by X_{it} and include age, age-squared, 5-year age groups, if the participant is over 64-years old, marital status, and if they are under treatment for cancer or diabetes. Individual-fixed effects, α_i, account for unobserved personal characteristics that do not change over time. Individual-fixed effects are important in this model to control for unobserved personal characteristics that may impact behavior.

This basic regression model is expanded to consider how a diagnosis of CVD impacts the risk-compensation effect of new medication. For the moment, I set aside FDA_t, to develop a difference-in-differences model that identifies the impact of a CVD diagnosis on healthy behavior. This helps to simplify each component of the model before combining them. The difference-in-differences research design follows and extends a quasi-experimental approach proposed by Fadlon and Nielsen (2019) based on matching estimators as detailed in Imbens and Wooldridge (2009). A diagnosis of CVD is not random in the broad population, but treatment and control groups can be constructed such that within the study sample, the manifestation of CVD is assumed random within a specified time frame.[15] I begin by constructing a treatment group of individuals who receive an initial diagnosis of CVD at exam time, t, where $t = [9, ..., 14]$. I estimate the impact of the diagnosis on behavior for the exam the diagnosis occurs and for the two subsequent exams, $t + 1$ and $t + 2$, a total of four years after the diagnosis.

The corresponding control group consists of individuals who also experience a first diagnosis of CVD three or four exams after the treatment group, $t + 3$ and $t + 4$, six or eight years later. No one in the treatment or control group experiences CVD prior to exam 9. See Figure 1.1 for a visual representation of the sample. The identifying assumption is that absent a diagnosis, the treatment and control groups would experience similar trends in

[15]The majority of CVD diagnoses, 63%, were due to an AMI or stroke which is thought to have uncertain timing in prior research (Chandra and Staiger, 2007; Fadlon and Nielsen, 2019). As a robustness exercise, the sample is limited to individuals in the treatment and control groups that have an AMI or stroke as the first episode of CVD. See Appendix Table 1.5.

Figure 1.1: Sample Construction by Group Based on Treatment Timing



Notes: The treatment group is comprised of individuals who receive a diagnosis of CVD at one of the exams 9 to 14. The corresponding control group is individuals who receive the same diagnosis 3 or 4 exams after each treated group. Each group of combined treatment and control individuals are observed for two exams prior to the diagnosis of the treatment group and for the subsequent two exams after diagnosis. Hence, the sample time period is exams 7 through 16.

behavior. It would be ideal to select a control group who experience the diagnosis at exam time $t+1$, but there is a trade-off between the length of time that the effects of the shock can be identified with the comparability of the control group. The control group selected is diagnosed with CVD within a 10-year time period (the standard window used in calculations of CVD risk) from their treated comparisons, but still allows for estimating the impacts of a diagnosis on behavior over a longer time period.

I check for randomness in the timing of a CVD diagnosis between the treatment and control groups in the sample in two ways. First, Appendix Table A2 presents the mean ten-year risk of a CVD diagnosis for the treatment and control groups at the time the treated group is diagnosed. For all exams, with the exception of exam 14, there is no statistical difference between the ten-year risk of CVD between treatment and control groups. At exam 14, the treated group is 1.7 percentage points more likely to be diagnosed with CVD in the subsequent ten years. Second, Table A3 presents results from regressing ten-year risk of CVD prior to the treated groups' CVD diagnoses. I find that ten-year risk is not a reliable predictor of being in the treated group. As a robustness exercise, an alternative control group is developed using risk score matching at $t-1$. The method for this exercise is described in Appendix A.2.

For clarity, the final model will be constructed by starting with a single group of treatment-and-control individuals (based on the timing of the treated-individuals' diagnosis) and then pooled with all groups. First, consider a treated group of individuals who are diagnosed with CVD at exam 11. The corresponding control group is individuals who are diagnosed with CVD at exam 14 or 15. This sub-sample of treatment and control individuals are observed from exam 9 through 13. The impact of a diagnosis on behavior for this sample is can be estimated using a simple difference-in-differences design:

$$Y_{it} = \sigma_1 POST_t + \sigma_2(CVD_i \times POST_t) + \alpha_i + \Lambda X_{it} + \epsilon_{it} \tag{1.2}$$

The variable $POST_t$ indicates the exam of the treated group's diagnosis and following two exams. $POST_t$ serves as a counterfactual – as if the control group had also experienced the shock at exam time t (Fadlon and Nielsen, 2019). In this example, $POST_t$ is equal to 1 for exams 11, 12 and 13 and is zero otherwise for both the treatment and control groups. The treatment group is denoted as CVD_i which is an indicator for individuals who are diagnosed with CVD at exam 11 and is equal to 1 for all exam time t. Hence, $(CVD_i \times POST_t)$ indicates the effect of being diagnosed with CVD. As in equation 1.1, α_i denotes individual-fixed effects and X_{it} are controls. Note that α_i in equation 1.2 is collinear with the effect of being in the treatment group, CVD_i, in this single treatment-and-control-group model. As a robustness check, the model is estimated without individual-fixed effects, see Table 1.5.

To capture the effect of medication before and after receiving a CVD diagnosis, the FDA approval of new medications, FDA_t, is fully interacted with the difference-in-differences variables as constructed in equation 1.2. This results in the following triple-differences specification for a single grouping of treatment and control individuals:

$$\begin{aligned} Y_{it} = {} & \rho_1 FDA_t + \rho_2 POST_t + \rho_3 (POST_t \times FDA_t) \\ & + \rho_4 (CVD_i \times FDA_t) + \rho_6 (CVD_i \times POST_t) \\ & + \rho_7 (CVD_i \times (POST_t \times FDA_t)) + \alpha_i + \Lambda X_{it} + \epsilon_{it} \end{aligned} \tag{1.3}$$

As in equation 1.2, α_i is collinear with CVD_i. Equation 1.3 above is estimated by group sub-sample based on treatment timing in each of the 5-exam-time-period windows. This is done to address potential weighing issues resulting from the difference-in-differences design with variation in treatment timing (Goodman-Bacon, 2021). This exercise reveals any variation in the estimates due to the particular timing of a diagnosis and gets around issues concerning negative weighting related to treatment effects that may change over time. Results are presented in Table 1.2. Note that each sub-group regression covers 5 exam time periods: two exams prior to diagnosis, the diagnosis exam and two exams after diagnosis.

Certain cells in the sub-group results are missing due to the timing of the FDA approval of new medication at exam 12. For example, the sample time period for group 9 is exam 7 through exam 11 which all occur before FDA approval. The sample time period for group 14 is exam 12 through exam 16 which all occur after the FDA approval.

The combined analysis with all treatment and control groups is done by appending each sub-sample by exam following procedures outlined in Deshpande and Li (2019). The variable, τ, indexes the sub-sample group diagnosis timing to which a treatment or control individual belongs; hence, $i(\tau)$ refers to individual i in group τ. Groups are defined by the exam that the treated individuals experience a diagnosis of CVD. Thus, the variable $POST_t$ becomes $POST_{i(\tau)t}$ and varies based on which sub-sample each individual is in. This counterfactual variable is equal to one for the exam the treatment group receives a diagnosis and for the two subsequent exams and is zero otherwise for treatment and control individuals in the sub-sample. The treatment variable, $CVD_{i(\tau)t}$, is equal to one for all exams prior to a treated individual's diagnosis and for the two exams after diagnosis and is zero otherwise. Individuals who are treated in exams 12, 13, and 14 serve as controls for exams 9, 10, 11 and are repeated in the sample, but they are distinguished by τ and are assessed as separate individuals. The time frame considered is from exam 7 (two exams prior to the first diagnosed treatment group) through exam 16 (two years after the last treatment group is diagnosed). The corresponding control groups are made up of individuals who experience the same diagnosis, but between exams 12 and 18. See Figure 1.1 for an illustration of treatment and control groups by exam. Beginning with the difference-in-differences specification, equation 1.2 expands to encompass the total sample as follows:

$$\begin{aligned} Y_{i(\tau)t} = \gamma_1 CVD_{i(\tau)t} + \gamma_2 POST_{i(\tau)t} + \gamma_3 (CVD_{i(\tau)t} \times POST_{i(\tau)t}) \\ + \alpha_{i(\tau)} + \Lambda X_{i(\tau)t} + \epsilon_{i(\tau)t} \end{aligned} \tag{1.4}$$

The above specification of this portion of the model averages over the impacts of a health

shock after it occurs. To address the comparability of the treatment group with the constructed counterfactual including matched controls, Figure 1.2 presents a plot of the behavioral outcomes considered in the analysis. The plots demonstrate similar patterns in behavior before the treated group is diagnosed with CVD.

Equation 1.4 is expanded to the full-triple-differences model which includes the FDA approval of beta blockers and bile-acid sequestrants as additional interaction terms. The final specification is as follows:

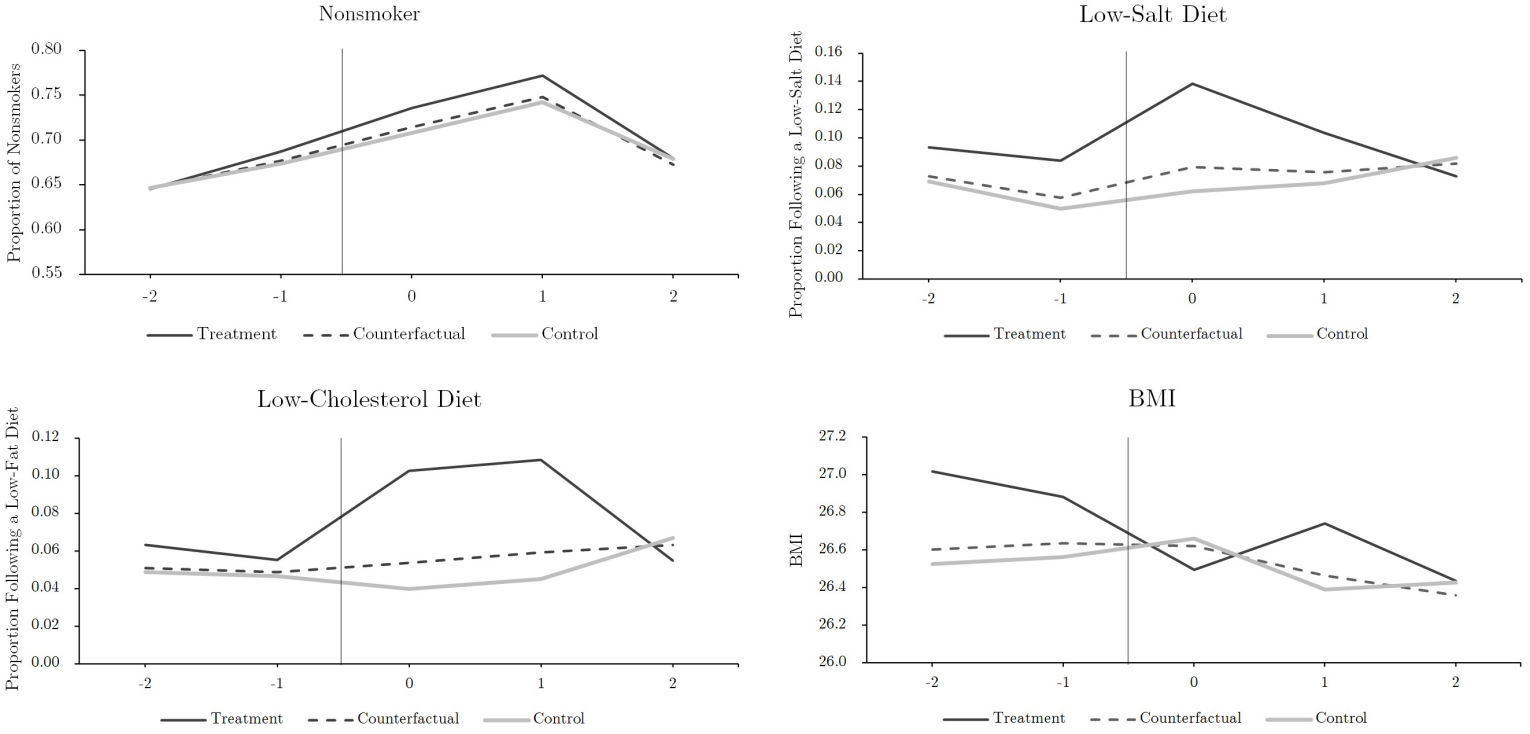
$$\begin{aligned} Y_{i(\tau)t} = {} & \beta_1 FDA_t + \beta_2 CVD_{i(\tau)t} + \beta_3 POST_{i(\tau)t} + \beta_4 (POST_{i(\tau)t} \times FDA_t) \\ & + \beta_5 (CVD_{i(\tau)t} \times FDA_t) + \beta_6 (CVD_{i(\tau)t} \times POST_{i(\tau)t}) \\ & + \beta_7 (CVD_{i(\tau)t} \times (POST_{i(\tau)t} \times FDA_t)) + \Lambda X_{i(\tau)t} + \alpha_{i(\tau)} + \epsilon_{i(\tau)t} \end{aligned} \tag{1.5}$$

The variables FDA_t, $CVD_{i(\tau)t}$ and $POST_{i(\tau)t}$ are as described above. The interaction term, $(CVD_{i(\tau)t} \times (POST_{i(\tau)t} \times FDA_t))$ indicates whether the medication was available at the time the diagnosis was experienced by treated individuals. All regressions are estimated with robust standard errors clustered at the individual level.[16]

The coefficients of interest are: β_6 is the impact of a diagnosis on behavior before the FDA approval (when FDA_t is zero and $CVD_{i(\tau)t}$ and $POST_{i(\tau)t}$ are one), and β_7 is the additional effect of a diagnosis on behavior after the FDA approval (when $CVD_{i(\tau)t}$, $POST_{i(\tau)t}$ and FDA_t are equal to one). The total impact of the FDA approval of new medication on behavior is calculated as $\beta_1 + \beta_4\pi' + \beta_5\pi'' + \beta_7\pi'''$ where π' is the mean of $POST$, π'' is the mean of CVD and π''' is the mean of $(CVD \times POST)$ for the regression

[16]One concern is that the FDA approval of new medication may be associated with the probability of being diagnosed with CVD if the medication is taken once available and prevents disease from manifesting. Individuals successful in preventing diagnosis are not included as controls in the sample. This is addressed in two ways. First, the probability of a diagnosis prior to FDA approval was estimated using a two-way, fixed-effects model. The individual predicted probability of CVD is not significantly correlated with FDA approval - the correlation was calculated to be 0.39. Secondly, for robustness, a secondary model was estimated using Framingham risk score (FRS) matching at the exam prior to each treated group's diagnosis. The results from this exercise do not demonstrate a significant change in findings. See Appendix Table 1.5.

Figure 1.2: Trends in Behavior by Diagnosis Timing



Notes: This figure shows each of the behavioral outcomes for treatment and control individuals in the sample by event time with a diagnosis of CVD occurring at $t = 0$ and also the behavior of the constructed counterfactual group including control individuals with event time constructed such that $t = 0$ is three exams before a diagnosis of CVD.

sample (Solon et al., 2015). The hypothesis is that medication availability decreases the motivation to engage in healthy behaviors, but a diagnosis of CVD, mitigates the risk-compensation effect due to the updated information about one's health. Thus, there would be a positive probability of healthy behaviors when medication is available as a treatment option after a diagnosis.

1.5 Results

1.5.1 Impact of Medication Approval and Diagnosis on Behavior

Table 1.2 presents the results from estimating equation 1.5 for the sample in total, column (1), and for each of the sub-samples as defined by the exam in which the treated group receives a diagnosis of CVD, Columns (2) thorough (7), labeled as "Group #" where "#" represents the diagnosis exam. The sub-sample group results are presented to address recent concerns about difference-in-differences research designs with variation in the timing of treatment (Goodman-Bacon, 2021). Considering the results as a whole and by sub-sample allows for nuances in the estimates by the timing of a diagnosis in relation to the FDA approval of beta blockers and bile-acid sequestrants at exam 12.

The FDA approval of new medication causes a consistent and statistically significant decrease in the probability of engaging in healthy behaviors. For each behavior, the calculated coefficient for the total impact of FDA approval is negative and all are statistically significant. This result points to clear evidence of risk compensation caused by the availability of beta blockers and bile-acid sequestrants, regardless of take-up. However, the marginal impact of a CVD diagnosis after FDA approval is less consistent. There is a decrease in smoking (reported as a increase in the healthy behavior of nonsmoking in Table 1.2) in response to being diagnosed after the FDA approval. Yet, for following a diet and BMI decrease, there is no additional impact of a CVD diagnosis after FDA approval on risk compensation.

Table 1.2: Impact of Medication Availability and Cardiovascular Disease Diagnosis on Behavior

	(1) Total Sample		(2) Group 9		(3) Group 10		(4) Group 11		(5) Group 12		(6) Group 13		(7) Group 14	
Nonsmoker														
CVD X POST	-0.01	(0.02)	0.01	(0.04)	0.00	(0.04)	-0.13 ***	(0.04)	---	---	---	---	---	---
FDA X CVD X POST	0.08 ***	(0.03)	---	---	0.04	(0.03)	0.19 ***	(0.05)	0.10 ***	(0.03)	0.06 ***	(0.02)	0.04 **	(0.02)
Total Impact of FDA Approval	-0.11 ***	(0.01)	---	---	-0.18 ***	(0.02)	-0.18 ***	(0.02)	-0.20 ***	(0.02)	-0.15 ***	(0.02)	-0.04 ***	(0.01)
N	18,399		3,275		3,524		2,908		3,407		3,832		2,812	
On Low-Salt Diet														
CVD X POST	0.07 ***	(0.02)	0.06	(0.04)	0.13 ***	(0.04)	0.05	(0.04)	---	---	---	---	---	---
FDA X CVD X POST	-0.02	(0.03)	---	---	-0.02	(0.05)	0.00	(0.05)	-0.02	(0.02)	0.04 **	(0.02)	0.01	(0.01)
Total Impact of FDA Approval	-0.04 ***	(0.01)			-0.07 ***	(0.02)	0.00	(0.02)	-0.02	(0.01)	-0.02 *	(0.01)	0.004	(0.01)
N	17,186		3,275		3,524		2,908		3,407		3,832		2,274	
On Low-Fat Diet														
CVD X POST	0.06 ***	(0.02)	0.03	(0.05)	0.11 ***	(0.04)	0.05	(0.04)	---	---	---	---	---	---
FDA X CVD X POST	0.003	(0.03)	---	---	0.04	(0.04)	0.01	(0.03)	0.07 ***	(0.02)	0.02	(0.02)	0.02	(0.02)
Total Impact of FDA Approval	-0.01 *	(0.01)			-0.08 ***	(0.02)	-0.003	(0.02)	-0.02	(0.01)	-0.03 ***	(0.01)	0.002	(0.01)
N	15,121		2,614		2,811		2,323		3,407		3,832		2,274	
BMI Decrease														
CVD X POST	0.54 ***	(0.18)	0.75 **	(0.32)	0.36	(0.24)	0.07	(0.32)	---	---	---	---	---	---
FDA X CVD X POST	-0.08	(0.30)	---	---	-0.63 **	(0.30)	-0.01	(0.31)	0.52 ***	(0.17)	-0.34	(0.28)	0.69 *	(0.37)
Total Impact of FDA Approval	-0.27 ***	(0.08)			-0.44 ***	(0.11)	-0.22 *	(0.12)	-0.67 ***	(0.13)	-0.43 ***	(0.13)	0.23 ***	(0.09)
N	18,399		3,275		3,524		2,908		3,407		3,832		2,812	

Notes: Estimation results demonstrating the impact of FDA approval and diagnosis of CVD on behavior with fixed effects. The total impact of FDA approval is calculated from equation 1.5 as: $\beta_1 + \beta_4\pi^{'} + \beta_5\pi^{''} + \beta_7\pi^{'''}$ where $\pi^{'}$ is the mean of $POST$, $\pi^{''}$ is the mean of CVD and $\pi^{'''}$ is the mean of $(CVD \times POST)$. Controls include age, age-squared, 5-year age group, marital status, over 64-years-old and under treatment for diabetes and/or cancer diagnosis. The time period is exams 7 through 16. Column (1) includes the total sample of treatment and control individuals. Columns (2) through (7) are the results for each group, τ, where the diagnosis of CVD occurs at the exam indicated. The group time period is two exams prior to diagnosis through two exams after diagnosis. If the respondent was on a low-fat diet was not asked at exam 9. Dietary questions were not asked at exam 16. Robust standard errors clustered at the individual level are in parenthesis. * Significant at the 10% level, ** significant at the 5% level, *** significant at the 1% level.

This is evidenced by the coefficients in column (1) on $(FDA \times CVD \times POST)$. Hence, the effect of a diagnosis is particularly meaningful for smoking behavior which motivates a decrease in current smoking after medication is available. The results by each behavioral outcome in Table 1.2 are assessed below:

Nonsmoker

The most striking estimates are on current smoking behavior as measured by an indicator for nonsmoking. In the absence of new medication, there is not a significant change in smoking in response to a diagnosis. However, there is a significant 11 percentage point increase in the probability of smoking due to the availability of new medication. This represents a 29.6% increase in current smoking, significant at the 1% level.[17] The negative and significant result in the total sample persists in most sub-samples. For this addictive behavior, the mere availability of medication presents a strong incentive to not give up smoking.

Also significant is the marginal impact a CVD diagnosis on smoking behavior after medication availability. There is an 8 percentage point, 13.3%, increase in nonsmoking, significant at the 1% level. This finding is consistently positive across sub-groups. The effect is not large enough to offset the total risk-compensation effect as the full impact of new medication on health behavior is negative.

Low-Salt Diet and Low-Fat Diet

When new medication is not yet available, there is an increase in the probability of following a low-salt or low-fat diet in response to receiving a CVD diagnosis of 7 and 6 percentage points respectively, significant at the 1% level. The FDA approval of new medication causes a statistically significant 4 percentage point, 44.2%, decrease in following a low-salt diet and a 1 percentage point, 18.7%, decrease in low-fat dieting; however, the impact on low-fat dieting is only significant at the 10% level. The additional impact of a CVD diagnosis

[17] Table 1.2 reports changes in nonsmoking to maintain consistency in the direction of the estimates across health behaviors.

after medication approval is not statistically different from zero. For both dietary outcomes, the sub-group sample sizes are small, and the findings are mostly null with some exceptions.

Particularly with dieting, there is a stark change in approach from treating CVD before and after medication approval. Both low-salt and low-fat diets are used at higher rates prior to new medication in response to a CVD diagnosis, but after the medication is available, risk compensation adjusts behavior such that there are no detectable changes in healthy behavior.

BMI Decrease

BMI is reported in Table 1.2 as a BMI decrease - a negative value represents an increase in BMI (a decrease in healthy behavior). Before the FDA approval of new medication, a diagnosis of CVD prompts a larger and significant decrease in BMI of 0.54, 2.0%. However, after the medications are approved, there is a statistically-significant increase in BMI of 0.27, 1.0%. A diagnosis of CVD, after when medication is available, does not impact BMI. People are inclined to increase BMI in response to the FDA approval of medication to treat and prevent CVD, regardless of use.

Considering results by sub-sample, estimates are consistent in direction for a diagnosis prior to FDA approval and for total impact of FDA approval. However, the estimated impact of a CVD diagnosis after new medication is available varies by sub-sample.

Participants selected into the Framingham Heart Study by volunteering. This raises concern that the study participants may be more interested in preventing heart disease than the general population. If there is selection bias in the estimates, it would be in the direction of engaging in healthier behaviors to prevent and treat CVD assuming that participants wanted to maintain heart health. The direction of this bias would be toward healthier behaviors, in the opposite direction of risk compensation (a increase in the probability of engaging in healthy behavior). Hence, the findings on the total impact of FDA approval,

which are less than zero for all behaviors, would be an upper bound. In contrast, the positive estimates for diet prior to FDA approval and for smoking after FDA approval in response to CVD diagnosis may be lower than is estimated for a general population.

1.5.2 Heterogeneity: Personal Characteristics

Table 1.3 displays estimates from equation 1.5 by a variety of different personal characteristics. Women are more likely than men to have a negative behavioral response to the availability of new medication with the exception of smoking where men's response is of larger magnitude. Men are more likely to engage in healthy behavior in response to a diagnosis prior to the FDA approval which is mainly due to the behavior of married men. Non-married people have a significant increase in the probability of nonsmoking after a CVD diagnosis when medication is available as compared to smoking. The responses to the FDA approval of new medication are relatively similar between married and non-married people for low-salt dieting, but non-married people have a significant increase in BMI of 1.0 due to new medication for which is driven by non-married females.

The estimates by level of education, find that individuals with less than a high school education are less likely than others to engage in healthy behaviors of nonsmoking, low-fat diet and BMI decrease and when new medication is available, and have no change in behavior in response to a diagnosis with the exception of BMI which decreases BMI by 1.2 prior to FDA approval and increases BMI by an 0.88 after FDA approval. On the other hand, college graduates are more likely to follow a low-fat diet or be nonsmokers in absence of new medication after a diagnosis, and they are significantly more likely to decrease BMI by 1.2 after a CVD diagnosis and FDA approval.

Table 1.3: Heterogeneity by Individual Characteristics

	(1) Male		(2) Female		(3) Married		(4) Non-Married		(5) Married Male		(6) Married Female		(7) Non-Married Male		(8) Non-Married Female		(9) Less than HS Education		(10) HS Graduate		(11) College or More	
Nonsmoker																						
CVD X POST	0.05	(0.03)	-0.09 ***	(0.02)	0.01	(0.03)	-0.10 ***	(0.03)	0.07 **	(0.04)	-0.09 ***	(0.03)	-0.14 *	(0.08)	-0.09 ***	(0.03)	0.00	(0.03)	-0.08 **	(0.04)	0.13 **	(0.06)
FDA X CVD X POST	0.02	(0.05)	0.15 ***	(0.03)	0.05	(0.04)	0.15 ***	(0.05)	-0.01	(0.05)	0.15 ***	(0.05)	0.31 ***	(0.12)	0.12 **	(0.05)	0.05	(0.05)	0.15 ***	(0.05)	-0.01	(0.08)
Total Impact of FDA Approval	-0.12 ***	(0.01)	-0.10 ***	(0.01)	-0.11 ***	(0.01)	-0.11 ***	(0.02)	-0.11 ***	(0.01)	-0.11 ***	(0.02)	-0.20 ***	(0.05)	-0.09 ***	(0.02)	-0.12 ***	(0.01)	-0.12 ***	(0.02)	-0.08 ***	(0.02)
N	9,310		9,089		13,320		5,079		8,256		5,064		1,054		4,025		7,952		5,585		3,283	
On Low-Salt Diet																						
CVD X POST	0.09 ***	(0.03)	0.06 *	(0.04)	0.07 **	(0.03)	0.10 *	(0.05)	0.08 **	(0.03)	0.05	(0.05)	0.22	(0.15)	0.07	(0.05)	0.02	(0.03)	0.13 ***	(0.05)	0.08	(0.06)
FDA X CVD X POST	-0.01	(0.04)	-0.01	(0.04)	-0.02	(0.03)	-0.06	(0.06)	-0.02	(0.04)	0.00	(0.06)	-0.10	(0.15)	-0.05	(0.07)	0.04	(0.04)	-0.06	(0.05)	-0.05	(0.07)
Total Impact of FDA Approval	-0.02 **	(0.01)	-0.06 ***	(0.01)	-0.03 ***	(0.01)	-0.05 ***	(0.02)	-0.01	(0.01)	-0.06 ***	(0.01)	-0.06 **	(0.03)	-0.05 ***	(0.02)	-0.03 **	(0.01)	-0.04 ***	(0.01)	-0.05 ***	(0.02)
N	8,718		8,468		12,574		4,612		7,765		4,809		953		3,659		7,445		5,203		3,063	
On Low-Fat Diet																						
CVD X POST	0.07 **	(0.03)	0.05	(0.03)	0.05 **	(0.03)	0.06 *	(0.04)	0.07 **	(0.03)	0.02	(0.05)	-0.01	(0.06)	0.08 *	(0.04)	0.02	(0.03)	0.07 **	(0.04)	0.13 **	(0.06)
FDA X CVD X POST	0.01	(0.03)	-0.01	(0.04)	0.02	(0.03)	-0.01	(0.05)	0.02	(0.04)	0.01	(0.06)	0.12	(0.11)	-0.04	(0.06)	0.00	(0.04)	0.02	(0.05)	-0.03	(0.08)
Total Impact of FDA Approval	-0.01	(0.01)	-0.02	(0.01)	-0.01	(0.01)	-0.03 **	(0.01)	0.00	(0.01)	-0.02	(0.01)	-0.07 **	(0.03)	-0.02	(0.02)	-0.01 *	(0.01)	-0.01	(0.01)	0.01	(0.02)
N	7,657		7,464		10,961		4,160		6,787		4,174		870		3,290		6,542		4,581		2,699	
BMI Decrease																						
CVD X POST	0.52 **	(0.25)	0.55 **	(0.25)	0.39 *	(0.20)	1.09 ***	(0.38)	0.48 *	(0.26)	0.23	(0.32)	1.18	(1.15)	1.08 ***	(0.40)	1.20 ***	(0.26)	0.02	(0.31)	-0.27	(0.46)
FDA X CVD X POST	-0.01	(0.31)	-0.07	(0.52)	0.30	(0.30)	-1.09	(0.87)	-0.03	(0.32)	0.92	(0.59)	0.67	(1.32)	-1.50	(1.04)	-0.88 *	(0.48)	0.61	(0.56)	1.19 **	(0.57)
Total Impact of FDA Approval	0.22 **	(0.10)	-0.76 ***	(0.12)	-0.04	(0.08)	-1.00 ***	(0.18)	0.27 ***	(0.10)	-0.56 ***	(0.14)	-0.41	(0.33)	-1.14 ***	(0.21)	-0.51 ***	(0.12)	-0.17	(0.12)	-0.18	(0.20)
N	9,310		9,089		13,320		5,079		8,256		5,064		1,054		4,025		7,952		5,585		3,283	

Notes: Estimation results demonstrating the impact of FDA approval and diagnosis of CVD on behavior with fixed effects. The total impact of FDA approval is calculated from equation 1.5 as: $\beta_1 + \beta_4\pi^{'} + \beta_5\pi^{''} + \beta_7\pi^{'''}$ where $\pi^{'}$ is the mean of $POST$, $\pi^{''}$ is the mean of CVD and $\pi^{'''}$ is the mean of $(CVD \times POST)$. Controls include age, age-squared, 5-year age group, marital status, over 64-years-old and under treatment for diabetes and/or cancer diagnosis. The time period is exams 7 through 16. The sample is limited to the characteristic indicated in each column. If the respondent was on a low-fat diet was not asked at exam 9. Dietary questions were not asked at exam 16. Robust standard errors clustered at the individual level are in parenthesis. * Significant at the 10% level, ** significant at the 5% level, *** significant at the 1% level.

1.5.3 Heterogeneity: Behavior Prior to FDA Approval

To determine if the risk-compensation response to new medication varies based on behavior prior to FDA approval, I segment the sample into people that have healthy and unhealthy behavior prior to exam 10. Equation 1.5 is re-estimated for exams 10 through 16 for the aggregated sample. The behavior during exams 7 through 9 from which the sample is selected is excluded from the data included in the analysis period.[18] Segmenting the sample in this way may bias the estimates for $(CVD_{i(\tau)} \times POST_{i(\tau)t})$ and $(CVD_{i(\tau)} \times (POST_{i(\tau)t} \times FDA_t))$ because the sample is selected on behavior which can impact the timing of a CVD diagnosis. Results in Table 1.4 report the total impact of FDA approval only.[19] Odd-numbered columns present the results of people with healthy behavior and even numbered columns present results from people with unhealthy behavior prior to exam 10. The outcomes remain the same as in the baseline analysis.

I find that risk compensation for nonsmoking is driven by people who smoked prior to the FDA approval. Smokers are 21 percentage points less likely to become nonsmokers after medication is available, significant at the 1% level. This points to a lack of persistent action by people who have already engaged in an addictive behavior. However, for diet, I find that people who follow a low-salt or low-fat diet prior to FDA approval, have a significantly higher probability of switching behavior as compared to those who did not diet. The FDA approval of new medication as a preventative decreases the probability of being on a low-salt diet by 14 percentage points and a low-fat diet by 12 percentage points for people that dieted before exam 10. In this case, the "cost" of dieting paid prior to new medication is forgone once the medication is available. Interestingly, is does not matter if an individual's BMI is above or below the average BMI for their 5-year age group, the response to the FDA approval of new medication is to increase BMI. There is a slightly greater increase in BMI from those below the 5-year age group mean compared to those below the mean of 0.40 and 0.38 respectively.

[18] Diet questions were not asked prior to exam 7 which limits the time frame for which behavior prior to FDA approval can be selected upon.

[19] This analysis relies on the assumption that the variable FDA is exogenous to all other regressors.

Table 1.4: Risk Compensation Segmented by Behavior Prior to FDA Approval

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
	Nonsmoker		On a Low-Salt Diet		On a Low-Fat Diet		BMI Decrease	
	Prior to Exam 10		Prior to Exam 10		Prior to Exam 10		Prior to Exam 10	
	Nonsmoker	Smoker	On Low-Salt Diet	Not On Low-Salt Diet	On Low-Fat Diet	Not On Low-Fat Diet	Below 5-Year Age Group Mean BMI	Above 5-Year Age Group Mean BMI
Total Impact of FDA Approval	0.002 (0.00)	-0.21 *** (0.02)	-0.14 *** (0.02)	-0.01 (0.01)	-0.12 *** (0.04)	-0.02 ** (0.01)	-0.40 *** (0.09)	-0.38 *** (0.10)
N	4,834	7,370	2,511	8,480	1,042	9,949	8,298	8,955

Notes: Notes: Estimation results demonstrating the impact of FDA approval and diagnosis of CVD on behavior with fixed effects. The total impact of FDA approval is calculated from equation 1.5 as: $\beta_1 + \beta_4\pi^{'} + \beta_5\pi^{''} + \beta_7\pi^{'''}$ where $\pi^{'}$ is the mean of $POST$, $\pi^{''}$ is the mean of CVD and $\pi^{'''}$ is the mean of $(CVD \times POST)$. Controls include age, age-squared, 5-year age group, marital status, over 64-years-old and under treatment for diabetes and/or cancer diagnosis. The sample is segmented to the behavior listed prior to exam 10. The sample time period is limited to exams 10 through 16. If the respondent was on a low-fat diet was not asked at exam 9. Dietary questions were not asked at exam 16. Robust standard errors clustered at the individual level are in parenthesis. * Significant at the 10% level, ** significant at the 5% level, *** significant at the 1% level.

1.5.4 Robustness

Table 1.5 presents estimates from three robustness checks. Column (1) shows the baseline results from Table 1.2. Column (2) re-estimates equation 1.5 but excludes individual-fixed effects. Excluding fixed effects changes the significance of certain estimates. However, the direction of the estimates is consistent for most behavioral outcomes. The exceptions are smoking and low-fat diet for which the total impact of FDA approval are not statistically different from zero, and BMI for which the estimate estimated impact of a CVD diagnosis prior to medication availability is no longer significant but does remain positive. This exercise demonstrates that some proportion of individuals who do not change their behavior over the sample-time period in response to FDA approval. Hence, including fixed effects controls for individual-specific persistent non-response in behavior.

As a second check of robustness, an alternative matching method was used to generate the control group for estimating equation 1.5. The details for this procedure are outlined in Appendix A.2. Table 1.5, column (3), presents the results from this exercise. The estimated impact of FDA approval maintains similar magnitude and significance for all behaviors. Also, the impact of a diagnosis (prior to FDA approval) is positive and significant for both dietary outcomes and BMI decrease. The additional impact of a diagnosis on nonsmoking behavior after FDA approval is positive and significant.

The remaining test of robustness limits the diagnosis of CVD to AMI or stroke as the first instance of diagnosis. The results are presented in Appendix Table 1.5, column (4). Limiting the sample in this way does not affect the direction of the results. There is still significant evidence of risk compensation in relation to the availability of medication for all healthy behaviors. The evidence that prior to medication, individuals followed a low-salt diet or low-fat diet and /or decrease BMI remains and is significant at the 1% level for each outcome. The direction of the coefficient on a CVD diagnosis after FDA approval maintains

Table 1.5: Impact of Medication Availability and Cardiovascular Disease Diagnosis on Behavior: Robustness

	(1) Baseline		(2) without Individual FE		(3) Risk Matching		(4) AMI/Stroke Only	
Nonsmoker								
CVD X POST	-0.01	(0.02)	0.04	(0.03)	-0.02	(0.02)	0.03	(0.03)
FDA X CVD X POST	0.08 ***	(0.03)	0.09 *	(0.05)	0.06 **	(0.03)	0.01	(0.04)
Total Impact of FDA Approval	-0.11 ***	(0.01)	-0.01	(0.02)	-0.15 ***	(0.01)	-0.11 ***	(0.01)
N	18,399		18,399		111,903		14,204	
On Low-Salt Diet								
CVD X POST	0.07 ***	(0.02)	0.07 ***	(0.03)	0.08 ***	(0.02)	0.11 ***	(0.04)
FDA X CVD X POST	-0.02	(0.03)	0.01	(0.03)	-0.01	(0.03)	-0.06	(0.04)
Total Impact of FDA Approval	-0.04 ***	(0.01)	-0.03 ***	(0.01)	-0.03 ***	(0.00)	-0.03 ***	(0.01)
N	17,186		17,186		102,301		13,441	
On Low-Fat Diet								
CVD X POST	0.06 ***	(0.02)	0.05 *	(0.02)	0.05 **	(0.02)	0.13 ***	(0.03)
FDA X CVD X POST	0.00	(0.03)	0.05	(0.03)	0.002	(0.03)	-0.01	(0.04)
Total Impact of FDA Approval	-0.01 *	(0.01)	-0.002	(0.01)	-0.02 ***	(0.00)	-0.02 **	(0.01)
N	15,121		15,121		90,678		11,773	
BMI Decrease								
CVD X POST	0.54 ***	(0.18)	0.36	(0.34)	0.57 ***	(0.17)	0.90 ***	(0.24)
FDA X CVD X POST	-0.08	(0.30)	-0.20	(0.57)	-0.13	(0.30)	-0.45	(0.35)
Total Impact of FDA Approval	-0.27 ***	(0.08)	-0.53 ***	(0.17)	-0.24 ***	(0.06)	-0.26 ***	(0.09)
N	18,399		18,399		111,903		14,204	

Notes: Estimation results demonstrating the impact of FDA approval and diagnosis of cardiovascular disease on behavior with fixed effects. Total impact of FDA approval is calculated from equation 1.5 as: $\beta_1 + \beta_4\pi^{'} + \beta_5\pi^{''} + \beta_7\pi^{'''}$ where $\pi^{'}$ is the mean of $POST$, $\pi^{''}$ is the mean of CVD and $\pi^{'''}$ is the mean of $(CVD \times POST)$. Controls include age, age-squared, 5-year age group, marital status, over 64-years-old and under treatment for diabetes and/or cancer diagnosis. Column (1) is the baseline result from Table 1.2. Column (2) excludes individual-fixed effects. Column (3) presents results from using risk-score matching. The treatment group is individuals who will have a diagnosis of CVD between exam 9 and exam 14. Controls are matched based on Framingham risk score at the exam prior to diagnosis and weighted based on the representation in each match cell. In column (4), treatment is limited to individuals who will have a CVD shock (AMI or stroke). The time period is exams 7 through 16. If the respondent was on a low-fat diet was not asked at exam 9. Dietary questions were not asked at exam 16. Robust standard errors clustered at the individual level are in parenthesis.
* Significant at the 10% level, ** significant at the 5% level, *** significant at the 1% level.

the direction of the estimate but is not significant for smoking status. This is possibly due to the lower sample size as a result of limiting the definition of who is diagnosed.

1.6 Cardiovascular Disease and Selection of Treatment

1.6.1 Approach

Assessing the impact of medication availability resulting from the FDA approval of new medication does not answer questions about treatment choices patients make after a diagnosis. Cardiovascular disease is treated non-invasively with medication and behavior, and these treatment choices are often made simultaneously. Medication and behavior can be complements in treatment or substitutes. To extend the initial analysis, I consider treatment choices after FDA approval of beta blockers and bile-acid sequestrants. The first outcome to consider is the choice to take medication regardless of behavior.[20] Next, I examine medication as a complement or substitute to healthy behavior. For brevity, I have simplified the outcomes presented in the main text. Medication as a complement is defined as taking medication and engaging in at least two healthy behaviors of nonsmoking, on low-salt diet, on low-fat diet or BMI decrease (calculated as BMI in the current exam, t, minus BMI from the prior exam, $t-1$). Medication as a substitute is defined as taking medication and having zero healthy behaviors.

Each behavior is considered independently in Appendix A.4. This results in eight possible outcomes. The complementary outcomes for individual behaviors are taking medication and engaging in one healthy behavior (nonsmoking, on a low-salt, on a low-fat diet or decreased BMI). The substitute outcomes for individual behavior are taking medication and engaging in an unhealthy behavior (smoking, not on a low-salt diet, not on a low-fat diet or an increase in BMI).

[20]Taking medication as an outcome is defined as self-reported medication use to treat hypertension or hyperlipidemia collected during each Framingham examination.

The same quasi-experimental difference-and-differences design as in equation 1.4 is used to estimate the impact of a shock on treatment choice. Hence, the sample cohorts and identifying assumption for CVD diagnosis are as previously described. The model specification for the impact of a diagnosis on treatment choice is as follows:

$$\begin{aligned} C_{i(\tau)t} = \delta_1 CVD_{i(\tau)t} + \delta_2 POST_{i(\tau)t} + \delta_3 (CVD_{i(\tau)t} \times POST_{i(\tau)t}) \\ + \delta_4 LOW_{i(\tau)t} + \delta_5 HIGH_{i(\tau)t} + \alpha_{i(\tau)} + \Lambda X_{i(\tau)t} + \varepsilon_{i(\tau)t} \end{aligned} \tag{1.6}$$

The dependent variable, C_{it} is an indicator corresponding to each of the treatment choices explained above. The variables $POST_{i(\tau)t}$ and $CVD_{i(\tau)t}$ are as defined in equation 1.4 and identify the treatment and control groups as they relate to each exam. Variables are included to indicate if an individual has low risk, $FRS < 10\%$, for developing CVD, notated $LOW_{i(\tau)t}$, or high risk, $FRS \geq 20\%$, for developing CVD, notated $HIGH_{i(\tau)t}$. Low-risk and high-risk variables are relative to intermediate risk ($\geq 10\%$ and $< 20\%$) which is excluded as a reference category. The specification includes the same control variables as used in estimating equation 1.5 and individual-fixed effects, α_i. Equation 1.6 is estimated with robust standard errors clustered at the individual level. The sample is limited to exams 12 through 16 after beta blockers and bile-acid sequestrates are FDA approved.

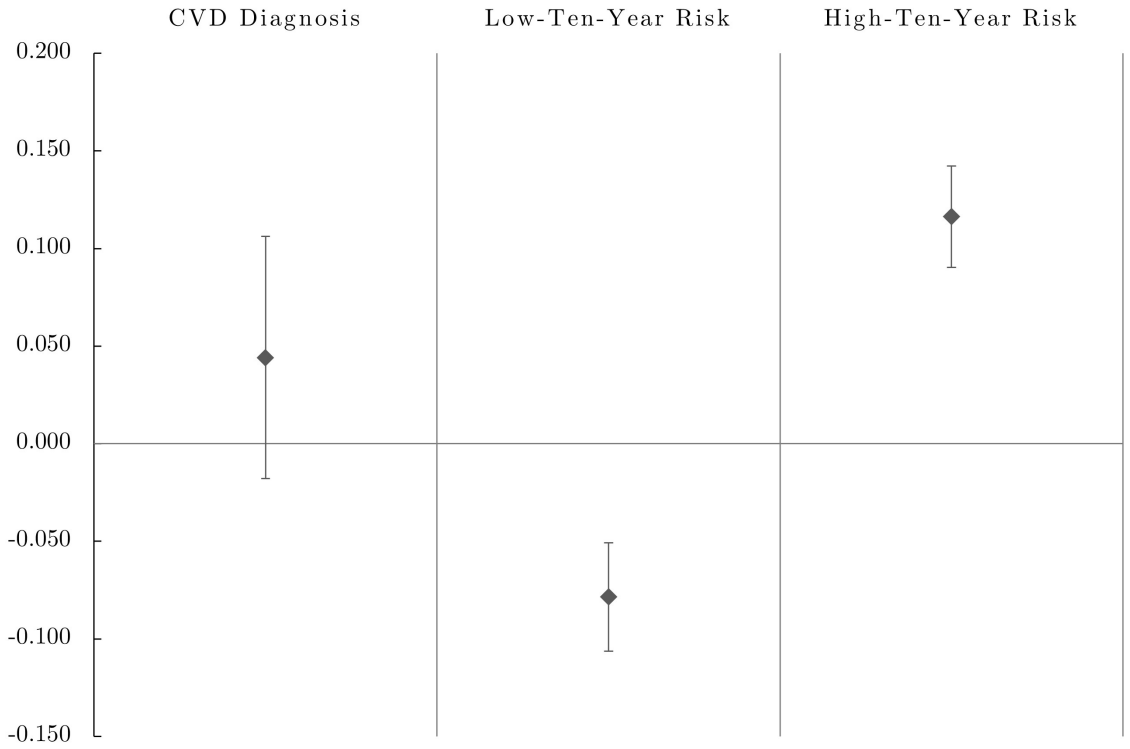
The coefficient of interest is δ_3 which indicates the average treatment effect of receiving a CVD diagnosis on the combined choice of medication and behavior. The hypothesis is that a diagnosis will increase the probability that the patient will take medication and make positive lifestyle changes. Also of interest are δ_4 and δ_5 on $LOW_{i(\tau)t}$ and $HIGH_{i(\tau)t}$ respectively. With the inclusion of individual-fixed effects, the categorical-risk variables are identified off of the individuals whose risk changes from one exam to the next. Between 14% and 35% of participants change risk classification at each exam in the sample period. The estimates provide useful signposts to how people approach preventative care absent a diagnosis but who have some level of risk.

1.6.2 Medication and Behavior as Substitutes or Complements

Figure 1.3 plots the impacts of CVD diagnosis, low-risk (FRS under 10%) and high-risk (FRS of 20% or more) on medication use. Having a greater than 20% chance of CVD in the next ten years is associated with a 11.6 percentage point, 27.3%, increase in the probability of taking hypertension or hyperlipidemia medication compared to individuals with intermediate risk, significant at the 1% level. This implies that risk screening is being implemented for medication use. On the other hand, being low risk for CVD is associated with a 7.9 percentage point, 64.9%, decrease in the probability of taking medication compared to intermediate risk. The coefficient on receiving a CVD diagnosis is positive but not a significant. Hence, results suggest there is no difference in the probability of taking medication for individuals diagnosed now as compared to individuals who will experience a CVD diagnosis in the future when controlling for level of risk.

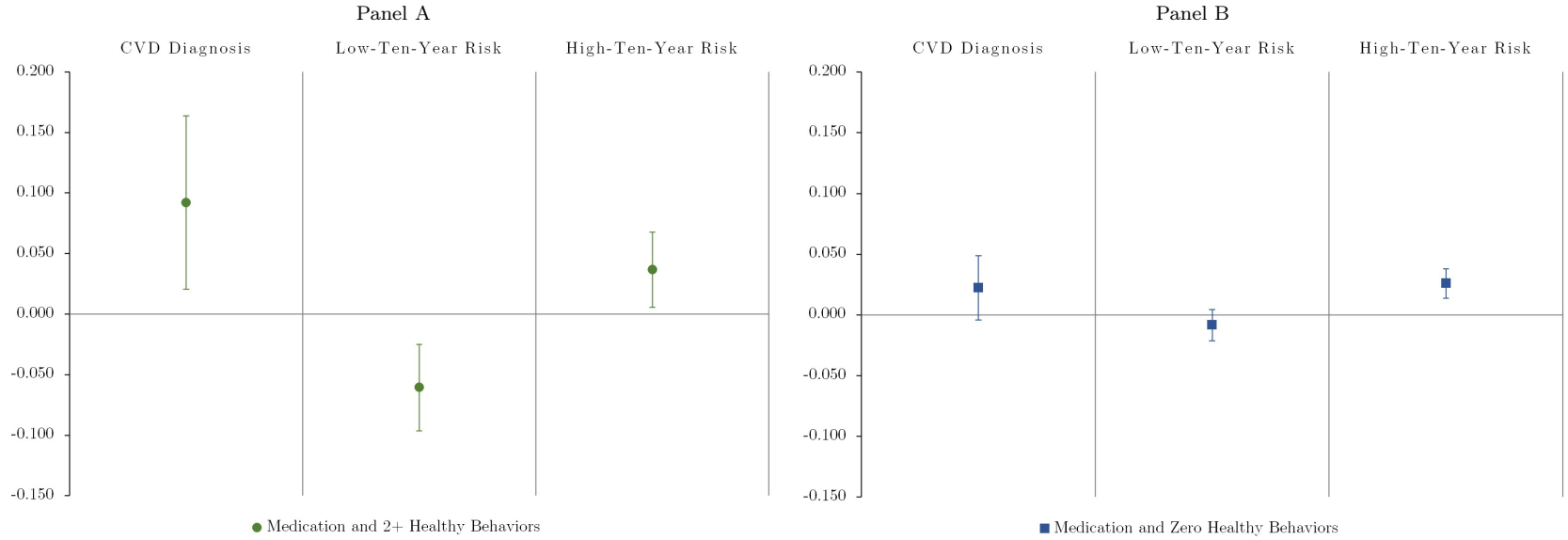
Figure 1.4 plots the coefficients from estimating equation 1.6 for taking medication and engaging in two-or-more-healthy behaviors (Panel A) or taking medication and engaging in zero-healthy behaviors (Panel B). Once medication is available, having high risk of CVD is associated with treatment - both complementary treatment where medication and healthy behaviors are used together and where medication is used to substitute not engaging in healthy behaviors. Having a diagnosis of CVD increases the use of medication as a complement to multiple healthy behaviors by a statistically significant 9.2 percentage points which is greater than using medication without any healthy behaviors. High-risk individuals also use medication to complement at least two healthy behaviors at a greater rate than they use medication in lieu of any healthy behavior. However, when behaviors are considered individually (see Appendix A.4), there is a higher likelihood that any one behavior is used as a substitute to medication than a complement for high-risk individuals. This implies that individuals mix-and-match behaviors which choosing which healthy behaviors to adopt when they are at high risk of CVD because medication is more likely to be used as a substitute to

Figure 1.3: Impact of Cardiovascular Disease Diagnosis and Risk Score on Choice to Take Medication



Notes: This figure plots the coefficients from estimating equation 1.6 where the outcome is an indicator for taking hypertension and/or hyperlipidemia medication. There are three variable coefficients reported: the impact of a CVD diagnosis for treated individuals (those who had a diagnosis of CVD at exam 12, 13 or 14) as compared to matched controls who will have a diagnosis of CVD three or four exams after the treated group, low risk for CVD in the next 10 years (<10%), and high risk of CVD in the next 10 years (20% or more). The time frame is exam 12 through exam 16 after the FDA approval of beta blockers and bile-acid sequestrants. Controls include age, age-squared, 5-year age group, marital status, over 64-years-old and under treatment for diabetes and/or cancer diagnosis plus individual-fixed effects. Error bars show 95% confidence intervals estimated with robust standard errors clustered at the individual level.

Figure 1.4: Impact of Cardiovascular Disease Diagnosis and Risk Score on Choice to Use Medication as a Complement or Substitute in Treatment



Notes: This figure plots the coefficients from estimating equation 1.6 where the outcome is an indicator for taking hypertension or hyperlipidemia medication and engaging in 2 or more healthy behaviors (green bar) or zero healthy behaviors (blue bar). There are three variable coefficients reported: the impact of a CVD diagnosis for treated individuals (those who had a diagnosis of CVD at exam 12, 13 or 14) as compared to matched controls who will have a diagnosis of CVD two or three exams after the treated group, low risk for CVD in the next 10 years (<10%), and high risk of CVD in the next 10 years (20% or more). The time frame is exam 12 through exam 16 after the FDA approval of beta blockers and bile-acid sequestrants. Controls include age, age-squared, 5-year age group, marital status, over 64-years-old and under treatment for diabetes and/or cancer diagnosis plus individual-fixed effects. Error bars show 95% confidence intervals estimated with robust standard errors clustered at the individual level.

any one behavior but a complement to multiple healthy behaviors.

The group of concern is those with low-risk of developing CVD in the next 10 years. Individuals in this group will eventually be diagnosed with CVD (based on the sample design which only includes individuals diagnosed with CVD) even though their 10-year risk of disease is less than 10%. This group is less likely to use medication as a complement by 6.1 percentage points, significant at the 1% level. Low-risk individuals also select into medication use at a lower rate compared to individuals with intermediate risk which is partially driving these estimates. Considering behaviors individually, being low risk is associated with a significant decrease in probability of using medication as a substitute. This implies that if a low-risk individual does take medication they are generally more likely to engage in other healthy behaviors.

1.7 Discussion and Conclusion

Medication and behavior are the two non-invasive means of preventing and treating CVD. While clinical research has demonstrated that they serve as complements in efficacy for treating hypertension and hyperlipidemia, the implementation of these treatments is subject to risk compensation. The mere availability of a new medication through FDA approval causes a significant decrease in healthy behaviors. There is an 11 percentage point (29.6%) increase in the probability of smoking, a 4 percentage point (44.2%) decrease in the probability of following a low-salt diet, 1 percentage point (18.7%) decrease in the probability of following a low-fat diet and a 0.27 (1.0%) increase in BMI. A CVD diagnosis does partially offset the negative response to new medication for smoking - one of the largest risk factors for CVD. However, for dieting and BMI, a diagnosis after the FDA approval has no impact on the risk-compensation effects of new medication. Conversely, when medication is not available, a CVD diagnosis causes a modest increase in diet usage for both low-salt and low-fat diets.

Behavior change in response to a diagnosis after medication is available is not consistent

across behaviors. Prior research on diabetes found that there is not a big dietary response to a diagnosis, and individuals generally view medication as more important to treatment than healthy behaviors (Oster, 2018; Kim et al., 2019). The findings for diet and BMI support this. Yet, individuals are more likely to become nonsmokers (partially offsetting risk compensation) after a diagnosis when medication is available. It may be that care providers emphasize the detrimental effects of smoking more stringently than other behaviors or that quitting smoking is easier to understand than diet modification. Even still, the positive probability of nonsmoking after a CVD diagnosis and FDA approval is not large enough to fully offset the total risk-compensation effect of new medication.

Medication effectively decreases the "expense" of avoiding CVD through positive behavior change. As was seen with car-safety regulations, PREP, statins and diabetes medication, risk compensation can cause increased take-up of risky behavior behavior. Furthermore, even the *possibility* of using a drug can prompt risk compensation. For smokers, there is a decreased incentive to change behavior. For people dieting, new medication prompts a behavior switch.

It is an open question if medication availability decreases the current cost of prevention or the expected future cost of disease. Individuals may offset unhealthy behavior with medication as a disease preventative. In contrast, they may engage in unhealthful behavior before disease manifestation knowing that a treatment is available if necessary. There is a rational paradox in health care. Individuals often wait until a disease is diagnosed to take-up the treatments that could have prevented it (Zweifel, 2017). This is rational in the sense that preventative care requires upfront costs of time and money but does not guarantee the absence of disease and its associated costs. Furthermore, health behaviors are often hard to change resulting in sparse adoption patterns (Ogden et al., 2014; Kaestner et al., 2014). I assume individuals derive utility from unhealthy behaviors but also from health. This may partially explain the risk-compensation trade-off between medication and healthy behavior

as a utility maximization strategy. Unfortunately, for many patients this presently rational calculation may result in long-run-health spending and decreased life expectancy, especially if present risk of CVD is incorrectly assessed.

I do find that once medication is FDA approved, having a 20% or greater chance for CVD is associated with medication use, but a CVD diagnosis does not change medication take-up. The implication is that risk screening for prescription medication is implemented and that people use medication. High-risk individuals are also associated with a higher probability of using medication to complement two-or-more healthy behaviors, but they still have a positive probability of using medication as a substitute. However, diagnosed individuals have the highest probability of using medication as a complement for multiple healthy behaviors. Of concern is the negative association between having a low risk of CVD ($< 10\%$) and medication use. Low risk is still risk. Each respondent in the analysis will be diagnosed with CVD (by study design), but they are less likely to be treated. This group's risk may be incorrectly assessed in risk formulas or formulas may not take into account a broad-enough spectrum of factors to predict disease (Wilson, 2021b). For those that do take medication, they are less likely to use it as a substitute when considering individual behaviors. These individuals may be prevention minded and cluster positive health behaviors.

This study does have some limitations. The outcomes available in the data did not include consistent measures of physical activity and alcohol consumption which are both risk factors for heart disease. The criteria restrictions placed on the data to create a balanced panel resulted in a relatively small sample size from 1960 through 1981. Additionally, the sample was limited to Framingham, Massachusetts which reduces the external validity of these estimates especially for non-white populations (Leaverton et al., 1987). Despite these shortcomings, this study has implications for preventative health care.

There is clear clinical evidence that healthy behaviors increase the efficacy of medications (Erwteman et al., 1984; Luft and Weinberger, 1988; Trap-Jensen, 1988; Chiuve et al.,

2006). Yet, recommendations to adopt healthy behaviors are often reserved for patients with obvious CVD risk factors or a diagnosis (Grundy et al., 2004; Hyman and Pavlik, 2000). Broader promotion of healthy living through diet modification, physical activity and smoking cessation targeted toward individuals at low-clinical risk of CVD, or those without obvious risk factors such as obesity, may benefit from a better understanding how behavior contributes to CVD. The findings also highlight the importance of disease salience for motivating patients to adopt medication use and positive-lifestyle changes ahead of a diagnosis. The introduction of new medication to treat high blood pressure and high cholesterol leads to risk compensation. However, when prevention does not work, receiving a diagnosis attenuates the risk-compensation effect and increase the likelihood of adopting healthy behaviors. Finding ways to motivate patients ahead of a diagnosis is of paramount importance to decrease the risk and prevalence of cardiovascular disease.

Chapter 2

Technology Adoption and Market Allocation: The Case of Robotic Surgery[1]

2.1 Introduction

The healthcare sector accounts for almost one-fifth of the U.S. economy, a share that has grown dramatically in the last quarter-century (CMS, 2020b). Technology adoption in health care is a key determinant of productivity in this sector, and technology is widely considered the central driver of long-term productivity gains in the broader economy (Jorgenson, 2011). However, unique features of the healthcare sector, like information frictions and insurance, can distort the quality and quantity of technology adoption. If patients or their agents (such as referring physicians) have a preference for technology or use it as a proxy for quality, the introduction of a new technology will increase demand and prompt adoption by care providers. New technology has the potential to promote a wave of adoption as hospitals compete over the same set of patients, resulting in service duplication and increased cost. In

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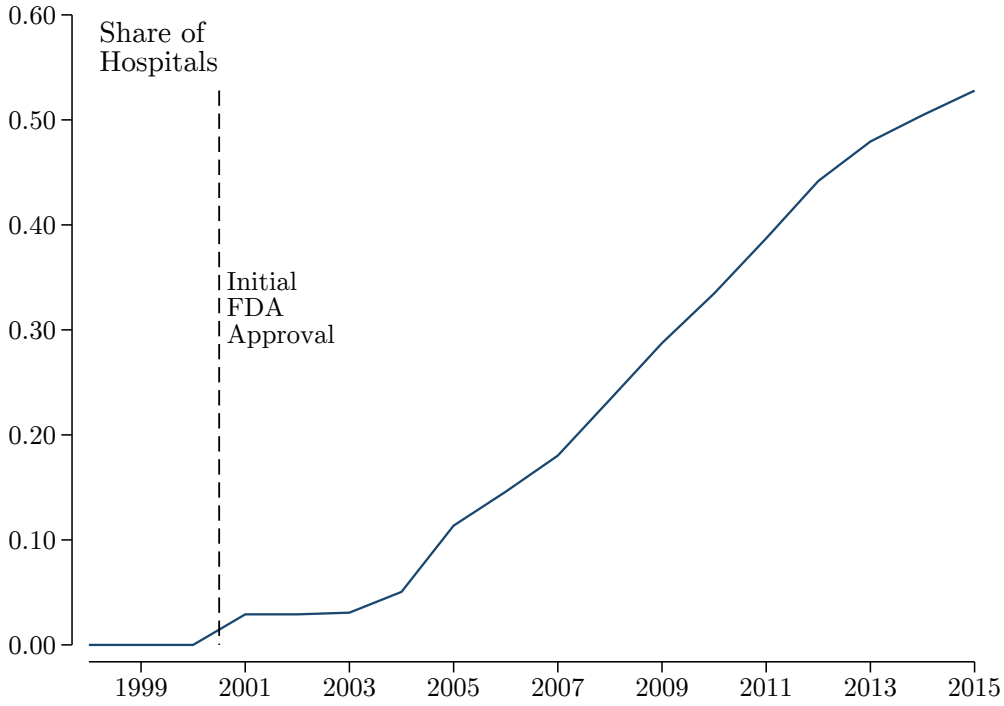
this way, adoption could theoretically go beyond the socially optimal level, a phenomenon known in health care as the "medical arms race."

In this study, we ask how technology adoption impacts utilization of hospital care to better understand its role in the performance of the healthcare sector. We use the diffusion of robotic surgery for the treatment of prostate cancer to investigate how patients or their agents respond. Adoption of surgical robotics proceeded exceptionally rapidly: from its introduction in 2001 through 2015, more than half of hospitals in the U.S. that treat cancer patients adopted a robot (Figure 2.1). Focusing on surgical removal of the prostate, termed prostatectomy, allows us to assess how patient volume changes in response to a new technology from inception along its trajectory to becoming the predominant method of intensive intervention for these patients. Additionally, surgical robots are a frequent focus of hospital advertising, pointing toward their potential use by patients as a signal of quality (Schwartz and Woloshin, 2019; Sheetz et al., 2020).

Our differences-in-differences research design exploits variation in the timing of adoption across hospitals in the U.S. to estimate the effect of robotic surgery on patient volume and characteristics. We show that adoption leads to a statistically significant and economically meaningful rise in hospital volume: prostate cancer admissions (the risk set for robotic surgical intervention) increase by 59 log points and prostatectomies (in which the robot can be used) increase by 69 log points. In event study plots, we show that these estimates average over effects that increase over time. These results suggest that patients – or their agents – have a preference for robotic surgery or view it as as signal of quality.

Increases in patient admissions would arise if robotic device adoption expands the market for robotic surgery. On the other hand, our estimates are also consistent with business stealing in which hospitals adopt surgical robots to compete over the same patients. To distinguish between market expansion and business stealing, we also implement our research design at the healthcare market level. We show that as hospitals in a market adopt surgical

Figure 2.1: Robotic Adoption Over Time



Notes: This figure shows the share of U.S. hospitals adopting a surgical robot according to data from the Intuitive Surgical Website (2001-2005) and the AHA survey (2005-2015). Adoption assumed to be 0% in 2000, the year in which surgical robots were first approved for use in the U.S.

robots, the volume of prostate cancer patients and prostatectomies in the entire market rises in response. Surgical robot adoption thus leads to meaningful expansions in the market for intensive intervention. These effects are statistically and economically significant, but are just under half the magnitude of the hospital-level results. Using event study plots to illustrate dynamics of the effects, we find that they grow over time but on a shallower trajectory than their hospital-level counterparts. Taking these findings together, we conclude that some of the hospital-level effects also reflect business stealing in which adoption leads to a re-shuffling of patients.

Our results raise the question of who receives treatment at the margin when a hospital adopts a surgical robot and patient volume expands. We apply our main estimation strategy to study two key characteristics of patients, age and pre-existing burden of illness. We

find that adoption of surgical robots brings relatively younger and healthier patients to the hospital for treatment. A key concern is that prostatectomy induced by robot adoption could provide little value to patients and society because the recipients may have short remaining life expectancy (they would likely die of another competing health risk) or have severe existing health conditions (they are at a high risk of adverse surgical outcomes) (Lepor, 2000). Our findings reject the idea that surgical robotics is expanding treatment among this group. Thus we find no sign that adoption broadens eligibility criteria for surgical intervention in a way that would attract patients who, at least on observable characteristics, are likely to benefit little from treatment.[2]

Robotic surgery is well-suited to the study of healthcare technology and its diffusion for several reasons. First, barriers to entry are relatively low for surgical robots. The initial capital investment of $1 to $2.5 million is significantly less than other intensive technologies like cardiac catheterization laboratories which have been the focus of much prior research (Barbash and Glied, 2010; Cutler et al., 2010). Additionally, a majority of states do not have certificate of need (CON) laws or have laws that would not be triggered by the purchase of a surgical robot (NCSL, 2019).[3] Second, whether physicians use a robot for prostate surgery has no bearing on the Medicare physician or hospital payment for the procedure, and evidence for clinical benefit of the robot for prostate cancer treatment relative to non-robotic surgery is essentially nonexistent (Sandoval Salinas et al., 2013; Yaxley et al., 2016; Ilic et al., 2017). The lack of direct financial incentive and clinical benefit points to the potential adoption of surgical robots as a pure signal to patients, rather than an attempt to improve outcomes or bill more for the same cases. Third, Medicare patients are largely protected from the costs of intervention, and so out-of-pocket costs should play little role

[2]While these results show that adoption of surgical robots did not lead to the clearest socially wasteful overuse for prostate cancer treatment, we cannot ascertain that the expansion of the intervention to the younger, healthy group is necessarily cost-effective. Such analysis is beyond the scope of this study but an important topic for future work.

[3]Thirty states either do not have certificate of need (CON) laws or the law does not apply to medical equipment purchases, and an additional 10 states have low-stringency laws as defined by Jacobs et al. (2013) as having an equipment expenditure threshold over $1.3 million (NCSL, 2019).

in the decision to initiate surgery with or without the robot. Finally, robots are sufficiently new that we observe hospital adoption and the universe of Original Medicare prostate cancer patients starting from initial FDA approval.

This study contributes to the literature in three key ways. First, we add to the evidence on the efficiency of technology diffusion in the health care sector. The most relevant prior studies have focused on the potential for a socially wasteful medical arms race in which hospitals compete for patients by providing care of questionable value and acquiring costly high-tech equipment (Dranove et al., 1992; Kessler and McClellan, 2000). This research is related to the concept that free entry can lead to social inefficiencies through business stealing (Mankiw and Whinston, 1986). As we show, adoption of surgical robots leads to business stealing as well as market expansion, which the literature would interpret as a signpost of an arms race – though the presence of market expansion rules out that adoption was wholly the result of such a phenomenon. Still, the welfare impacts of technology adoption depend on the costs and benefits of the technology for patients who use it at the margin. Our finding that the patients who are induced to get treatment due to the robot are younger and healthier suggests that the worst fears for social inefficiencies were not realized. However, combining our results with clinical literature finding minimal benefits of the robot for patient outcomes calls into question whether this adoption was socially beneficial.

These results also relate to research on productivity variations in the health care sector. Much of this work has focused on the adoption of evidence-based, low-cost technology like beta blockers in the treatment of heart attacks (Skinner and Staiger, 2007; Chandra and Staiger, 2007). Disparities in the use of these technologies are hypothesized to be a key determinant of productivity variations across regions (Baicker and Chandra, 2004; Skinner and Staiger, 2015). The benefits of adopting costly, high-tech equipment for the efficiency of the sector are more equivocal as, for example, Cutler et al. (2010) shows in the case of coronary bypass surgery for heart attacks. We add new evidence on the adoption of costly

technology with few *de jure* restrictions on adoption and even less evidence backing its use. As we show, the surgical robot drove large volumes of patients to the hospital even as its clinical value remained unsubstantiated.

Finally, our work connects research on demand responses to quality information with the literature on hospital market responses to technology adoption. One piece of conventional wisdom suggests that unique characteristics of the health care market, such as the lack of accurate quality information and the prevalence of insurance coverage, dampens demand-side competition and gives providers little incentive to innovate (Cutler et al., 2010; Skinner, 2011). More recent studies challenge this view and show evidence that the allocation of patient volume across hospitals does respond to quality information (Chandra et al., 2016). Recent developments in health care markets like increased public reporting of patient outcomes may make the demand response to quality, or perceived quality, even stronger. The strong volume increases we see in response to innovation demonstrates that there can be strong demand-side competition in health care. Our results suggest that patients and their agents view hospitals that have adopted the robot as higher quality and thus more preferable. This robust response to innovation has been found in technologies relating to treatments for cardiovascular disease, but the magnitude is not as stark as what we have found here (Hodgkin, 1996; Grossman and Banks, 1998).

The chapter continues as follows: Section 2.2 provides background on robotic surgery devices and prostate cancer. Section 2.3 presents the data used in the analysis. Section 2.4 describes the estimation methodologies. Section 2.5 details the results. Section 2.6 discusses the findings and concludes.

2.2 Background

Robotic assisted surgical devices were first introduced to the general U.S. hospital setting in 2000 when Intuitive Surgical, Inc. received FDA approval to bring its da Vinci device to

market. Due to patent protection, the da Vinci surgical robot remained the only surgical robot available in the U.S. through our analysis period.[4] This device augments laparoscopic surgery, assisting physicians in procedures conducted through small incisions (Mack, 2001). Robotics aim to expand a surgeon's capabilities by increasing their dexterity, flexibility and visual field. During a robot-assisted procedure the surgeon sits at a console and controls robotic arms with specially-designed instruments. In contrast, in traditional laparoscopic surgery the physician would manipulate instruments directly.

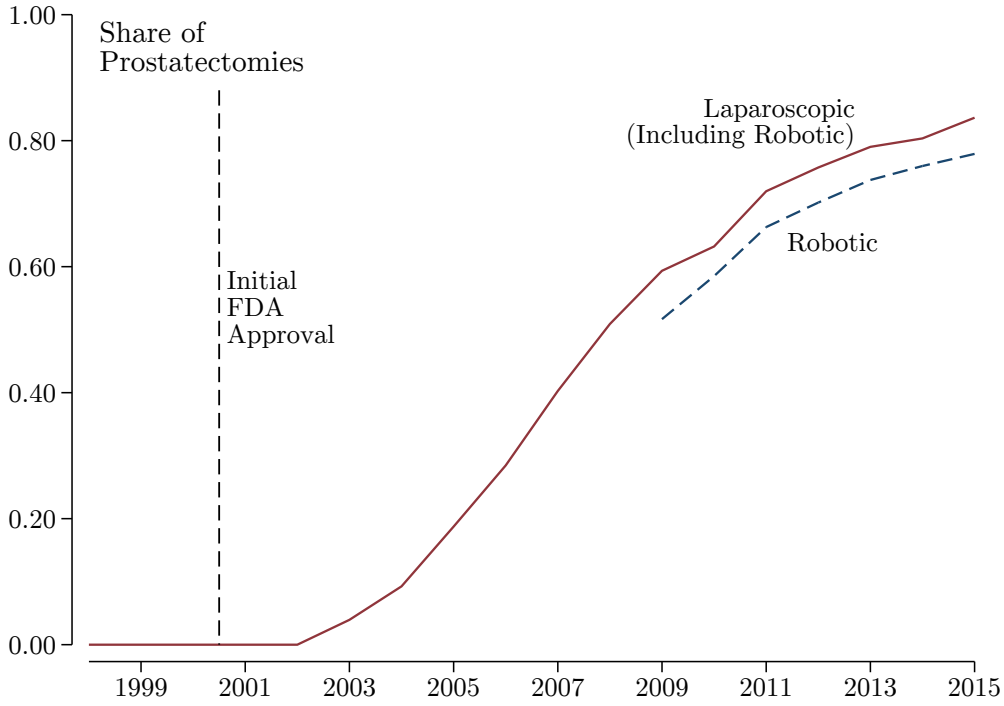
Purchasing a robotic surgical system requires an initial capital investment of approximately $1 to $2.5 million, and robotic procedures cost hospitals an average of 13 percent more than traditional laparoscopic or open-site surgical procedures (Barbash and Glied, 2010). However, Medicare hospital and physician reimbursement do not differentiate between robotic surgery and laparoscopic surgery (the reimbursement systems are agnostic to the surgical instrument, though pay differs more for invasive open procedures). Given Medicare's tendency to reimburse at average rather than marginal cost, robot adoption and use can still be profitable for hospitals, particularly if the device receives heavy use. Hospitals may thus seek to increase the volume of procedures after adoption (Sheetz et al., 2020). Perhaps unsurprisingly given the appeal of a volume-oriented strategy, hospitals heavily advertise their surgical robots (Schwartz and Woloshin, 2019).

We focus on robotics in the context of prostate cancer because the robot has played a notably large role in transforming how prostatectomy is performed in comparison to other conditions intensively treated with the robot (Chandra et al., 2011). Prior to robotics, prostatectomy was usually an open-site procedure because the prostate is hard to access with a laparoscope (Finkelstein et al., 2010). Figure 2.2 shows that by 2008, just 8 years after the FDA approval of the robot, open-site procedures were no longer the dominant method of prostatectomy. The market implications of this phenomenon have received surprisingly

[4]Intuitive Surgical faced one major competitor, Computer Motion, Inc., whose ZEUS surgical-robotic system received FDA approval in 2001. After patent battles, the firms merged in 2003 and ZEUS was removed from the market (SEC, 2003).

little study; perhaps the most relevant work in this area is Ko and Glied (2021), which found that hospital robot adoption increased robot use and decreased costs for New York state Medicaid patients.

Figure 2.2: Use of Robotic Surgery for Prostatectomies Over Time



Notes: This figure depicts the share of prostatectomies conducted using surgical robots from 1998 to 2015. The blue dashed line plots the robotic share, defined as the share of prostatectomies with a robot-assisted procedure code (it begins in 2009 because the robot-assist hospital procedure code was only created in late 2008). The red solid line plots the laparoscopic share for the full period, which we can observe well throughout by linking to physician procedural billing. In this series, the denominator is the subset of prostatectomy hospitalizations for which there was concurrent physician billing for any prostatectomy procedure during the stay (patient admission through discharge) while the numerator is further restricted to those with physician billing for a laparoscopic prostatectomy procedure. All procedure codes are listed in Appendix Table B1. Essentially all robotic prostatectomies are laparoscopic and the vast majority of laparoscopic prostatectomies use a robot.

The transition to laparoscopic intervention was driven by adoption of the robots, and we exploit this rapid roll-out in our differences-in-differences research design. Yet this dramatic change in intervention modality was backed by essentially no randomized trial data. To date,

only one randomized trial has compared the robotic and open approaches head-to-head; it was published after our sample period and detected no benefit of the robotic approach (Yaxley et al., 2016). Systematic reviews of randomized trials find that the outcomes of open, laparoscopic, and robotic prostatectomy are similar (Sandoval Salinas et al., 2013; Ilic et al., 2017).

Prostate cancer is the second most common cancer behind skin cancer in men and results in approximately 33,000 deaths each year (ACS, 2020; CDC, 2020). Prostatectomy, or the removal of the prostate gland, is the key surgical treatment for prostate cancer. However, the treatment can come with significant side effects like incontinence and sexual dysfunction that may dramatically impact a patient's life. The high personal and accounting costs of aggressively treating this slow-growing cancer has led to a shift toward a watch-and-wait strategy to avoid over-treating a disease that may not become fatal (Lepor, 2000). Prostatectomy hospitalizations decreased by 32 percent in Medicare over our sample period as watch-and-wait became more widespread in managing prostate cancer (Appendix Figure B1). The introduction of robots overlays this reduction in aggressively treating prostate cancer, and so increases in prostatectomy volume induced by surgical robots may only partially offset the general decline in intensive intervention.

2.3 Data

The key allocation analyses in this study measure the volume of prostate cancer and prostatectomy inpatients at each hospital in each year. Both volume measures are key to this study because adoption of a surgical robot could attract patients to the hospital whether or not they ultimately receive surgical intervention; they provide, respectively, a broader and narrower view of the impact of adoption on allocation. We source these measures from 1998-2015 inpatient hospitalization records (called MEDPAR) for 100% of Medicare beneficiaries.[5]

[5]We focus on inpatient stays because Medicare only covers open and robotic/laparoscopic prostatectomy in this setting during our analysis period (CMS, 2015). A related procedure, transurethral resection of the

We count patients with a principal diagnosis of prostate cancer and, separately, those with prostate cancer who also received a prostatectomy. Appendix Table B1 lists the diagnosis and procedure codes we use to identify patients. When we analyze patient characteristics, we do so through a linkage to patient summary data (the Master Beneficiary Summary File). We omit patients under age 65, who can enter Medicare due to disability or end-stage renal disease, to focus on the older adult population for whom coverage is near-universal. We also exclude managed care patients, for whom reporting is incomplete, from all analyses.

To observe if and when hospitals acquire surgical robots, we rely on snapshots of the Intuitive Surgical website posted on the Wayback Machine (archive.org) from 2002-2005 and American Hospital Association (AHA) survey data from 2005-2015. Intuitive Surgical is the manufacturer of the da Vindi robot which was the only surgical robot available in the U.S. through our analysis period. The Intuitive Surgical website listed da Vinci providers by state and year starting in 2002. Hence, our first view of adoption thus occurs 12 to 18 months after the robot was approved by the FDA.[6]. To account for the lag between very early adoption and initial reporting, we assign hospitals listed in the 2002 archive of the website an adoption year of 2001.

The Medicare setting has a number of advantages for this research. The size of the program allows us to observe patient allocation in essentially all U.S. markets and the vast majority of hospitals. The Original Medicare program imposes no network restrictions on patients. The cost-sharing structure of Medicare and patients' frequent enrollment in secondary coverage of these costs mean that patients have little financial incentive to choose one hospital over another. Together, these features of Medicare insulate our findings from potentially endogenous changes in networks and cost-sharing that might occur in private insurance.

prostate (TURP), is covered in the outpatient setting but is most often used to treat an enlarged prostate as opposed to prostate cancer (Hopkins, 2021). In more recent years post-dating our analysis period, Medicare began expanding its coverage of prostatectomy procedures in the outpatient setting (CMS, 2020a).

[6]The FDA approved the da Vinci surgical robot on July 17, 2000 (FDA, 2000)

Our analysis period spans 1998 through 2015. All analyses presented in this study use a balanced panel of hospitals that treated at least 1 patient with any condition in every year.[7] To ensure we observe at least 3 years of pre- and post-adoption patient volumes at all facilities, hospital-level analyses omit facilities that acquire a robot after 2012. We also restrict to the plausible hospital choice set for patients seeking cancer care. First, we limit to short-term and critical access hospitals. Second, hospitals in the analysis sample must admit a minimum of 50 patients annually with at least 5 of those patients being admitted for cancer treatment (we do not count skin cancer). In robustness analyses we show that our findings are preserved when we add back late adopters and facilities that fail to meet the patient thresholds.[8]

Table 2.1 provides summary statistics for the 2,261 hospitals in our sample, split nearly evenly into those that do and do not adopt. Compared to non-adopters, hospitals that adopt a robot tend to be larger, in urban areas and are more often teaching institutions. Adopters also treat more cancer patients overall and treat more prostate cancer patients. In turn, adopting hospitals also have three to four times the prostate cancer and prostatectomy market shares of non-adopting hospitals. These differences may partly reflect the effect of robot adoption itself in driving these patients to the hospitals.

2.4 Analytic Approach

Our research design exploits the staggered adoption of surgical robots across hospitals to identify the effect of acquiring a robot on patient volume and characteristics. We conduct analyses at the hospital and market levels. Analyses at the latter level are key to evaluating

[7]To ensure that hospitals that change Medicare provider numbers are consistently tracked, we draw on a provider number transition matrix graciously provided to us by Jon Skinner and the Dartmouth Institute for Health Policy and Clinical Practice. We map together all provider numbers that ever refer to the same facility into one synthetic hospital. A synthetic hospital is considered to have adopted a robot if any of its component provider numbers has adopted one.

[8]The hospitals in our main analysis sample capture 87 percent of all Original Medicare prostate cancer patients and 88 percent of all prostatectomy patients. The expanded set of hospitals analyzed in the robustness section captures 94 percent of prostate cancer patients and 95 percent of prostatectomy patients.

Table 2.1: Summary Statistics for Hospitals in Sample

	(1) Non-Adopters	(2) Adopters
Beds	186.4	413.7
	(139.1)	(272.6)
Urban	0.61	0.94
	(0.49)	(0.24)
Teaching Hospital	0.13	0.32
	(0.34)	(0.47)
Patients (Annual)		
Cancer (ex. skin)	87.2	324.9
	(77.9)	(308.9)
Prostate Cancer	4.5	18.9
	(6.4)	(23.3)
Prostatectomy	3.3	15.7
	(5.2)	(21.0)
Market Share		
Prostate Cancer	0.06	0.20
	(0.12)	(0.23)
Prostatectomy	0.05	0.20
	(0.12)	(0.24)
Hospitals	1,168	1,093
Observations	21,024	19,674

Notes: This table shows summary statistics for the sample of hospitals included in the main hospital-level analyses. See text for more information on sample construction. All characteristics are at the hospital-year level spanning 1998-2015. Market share defined as the hospital's patient count divided by the patient count in its market. Standard deviations presented in parentheses.

the market-expanding effect of surgical robots because there is less scope for patients to reallocate across markets than across hospitals. When analyses at the hospital-level show stronger allocation effects than those at the market-level, it suggests the presence of business stealing since patients have more scope to change the hospital where they receive treatment within a market.

We implement this research design at the hospital level by estimating differences-in-differences Poisson regressions of the following form:

$$N_{ht} = \exp\left(\alpha_t + \alpha_h + \beta \cdot interim_{ht} + \gamma \cdot post_{ht} + X_{ht}\Omega\right) + \varepsilon_{ht}, \tag{2.1}$$

where h and t index hospitals and years, respectively. The outcome N_{ht} is a measure of patient volume; α_t and α_h are year and hospital fixed effects, respectively; $interim_{ht}$ indicates whether the hospital adopted the robot in year t; $post_{ht}$ indicates whether the hospital adopted the robot in year $t-1$ or earlier; and X_{ht} is a vector of time-varying hospital controls. Our primary analyses include no controls in X_{ht}, but in robustness analyses we show our results are similar as we add controls of varying richness. The key coefficient of interest is γ, the log-point effect of adopting a robot on volume omitting the initial adoption year. This log-point interpretation is similar to that of a log-linear model.

The identifying assumption of this model is that absent acquiring a surgical robot, adopters and non-adopters would have followed common proportional trends in patient volume. Equivalently, it assumes that patient volume at adopters and non-adopters would have grown at common rates. To this end, we run event-study specifications:

$$N_{ht} = \exp\left(\alpha_t + \alpha_h + \delta_{-3} adopt^{pre}_{h,t-3} + \gamma_{-2} adopt_{h,t-2} + \ldots + \gamma_2 adopt_{h,t+2} + \delta_3 adopt^{post}_{h,t+3}\right) + \varepsilon_{ht}, \tag{2.2}$$

where $adopt^{pre}_{h,t-k}$ indicates that the hospital adopted robotics in year $t-k$ or earlier, $adopt_{h,t}$

indicates adoption in year t, and $adopt^{post}_{h,t+k}$ indicates adoption in year $t+k$ or later. We omit $adopt_{h,t-1}$ as the reference year. This specification emits pre-trend coefficients $(\delta_{-3}, \delta_{-2})$ to test if volume grew at common rates *before* adoption, a key falsification exercise for the counterfactual parallel trends assumption. It also yields post-adoption coefficients $(\delta_0, \ldots, \delta_3)$ illustrating the dynamics of the impacts.

The Poisson model has several advantages for our setting. First, compared to a log-linear regression, it accommodates zeroes without adding an arbitrary constant or switching to an alternative functional form like inverse hyperbolic sine (though we show that our findings are preserved under such alternatives). Second, unlike the bulk of nonlinear models it is robust to fixed effects, which we use in our core models and (in higher dimensional form) in our robustness exercises (Hausman et al., 1984). Finally, the model makes few assumptions about the data-generating process beyond that the conditional mean takes the form in equations 2.1 and 2.2; it does not require that N_{ht} is Poissonian much as linear regression does not require the outcome to be normally distributed (Gourieroux et al., 1984; Wooldridge, 1999).

We also run the models given by equations 2.1 and 2.2 at the market level, replacing all hospital subscripts h with market subscripts r. As a market concept, we use Dartmouth Hospital Referral Regions (HRRs), which partition the U.S. into 306 regions within which patients tend stay when they receive specialty care. The outcome N_{rt} counts patient volume at all hospitals in the market rather than at one hospital. To measure market-wide adoption of the robot, we define $interim_{rt}$ as the beds-weighted share of hospitals in market r that adopted the robot in year t and $post_{rt}$ as the beds-weighted share of hospitals that adopted the robot in year $t-1$ or earlier. For the event study we define the $adopt_{rt}$ variables analogously as the beds-weighted averages of $adopt_{ht}$ across the hospitals in the market. We construct the adoption measures this way to maximize their comparability with the hospital-level estimates; the market-level coefficients we report give the log-point effect of *all* hospitals

in the market adopting a robot.

2.5 Results

2.5.1 Patient Allocation

Table 2.2 presents our main estimates of the effect of robot adoption on patient volume based on equation 2.1. We focus on γ, the coefficient on *post*, which provides a single estimate of the long-term effect of adoption averaging over its dynamics. At the hospital level, adoption raises prostate cancer patient volume unconditional on surgical intervention by 59 log points, an expected absolute increase of 7.8 patients per year at the average hospital. Prostatectomy patient volume rises 69 log points or 7.6 patients. Effects at the market level are just under half the log-point magnitude. Going from 0% to 100% adoption in a market is expected to raise market-wide prostate cancer patient volume by 28 log points (27.8 patients) and prostatectomy patient volume by 34 log points (27.7 patients). All of these effects are highly statistically significant.

Figure 2.3 plots the event study estimates from equation 2.2 for prostate cancer volume (Panel A) and prostatectomy volume (Panel B) outcomes. The panels illustrate three key facts. First, they show limited differences in pre-adoption trends in patient volume between adopting and non-adopting hospitals and between relatively slow-adopting and fast-adopting markets, a key falsification exercise for the parallel counterfactual trends assumption of differences-in-differences. Pre-trends are quantitatively small at the hospital level; at the market level they reverse trajectories after adoption, suggesting our findings will be, if anything, conservative.

Second, the effect of adopting a robot on patient volume grows over time. For example, hospital-level prostate cancer patient volume increases by a statistically significant 17 log points in the adoption year, an effect that rises to 73 log points in the third year and

Table 2.2: Estimates of Effect of Adoption on Patient Volume

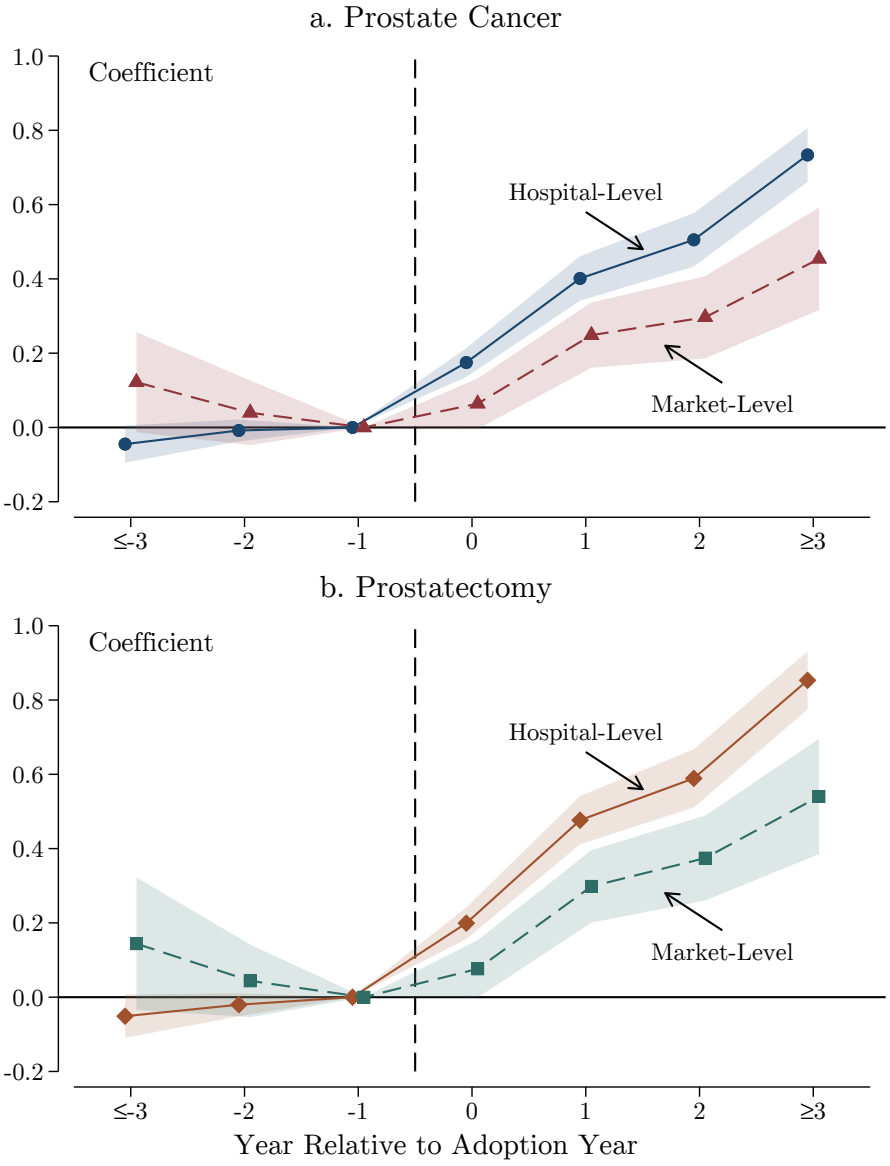
	(1)	(2)	(3)	(4)
	Hospital-Level		Market-Level	
Patients:	Prostate Cancer	Prostatectomy	Prostate Cancer	Prostatectomy
Interim	0.17	0.19	-0.04	-0.05
	(0.03)	(0.03)	(0.06)	(0.07)
Post	0.59	0.69	0.28	0.34
	(0.04)	(0.04)	(0.07)	(0.08)
Marginal Effect	7.8	7.6	27.8	27.8
	(0.5)	(0.5)	(7.8)	(6.8)
DV Average	11.5	9.5	90.2	73.1
Hospitals/Markets	2,255	2,212	306	306
Observations	40,590	39,816	5,508	5,508

Notes: This table depicts the results of estimating equation 2.1 (columns 1 and 2) and its market-level analog (columns 3 and 4). The dependent variable is prostate cancer patient volume (columns 1 and 3) and prostatectomy patient volume (columns 2 and 4). Interim indicates the first year the hospital reports having a robot while Post indicates the subsequent years. Coefficients have a log-point interpretation, e.g. a coefficient of 0.2 implies a 20 log point change. Marginal effect is the expected absolute change in patient volume derived from the Post coefficient. DV average is the average dependent variable (patient volume) in the regression. Robust standard errors clustered at the market level in parentheses. Regressions control for year and level (hospital or market) fixed effects.

beyond. Essentially the same pattern holds for prostatectomy patients, though magnitudes are slightly larger. These results highlight the importance of effect dynamics for patient allocation following robot adoption. They suggest that the long-term effect is greater than the single average effect estimated in Table 2.2.

Third, effects at the market level are also highly significant and growing over time, but they expand on a shallower trajectory than hospital-level effects. The market-level estimates are very roughly half the magnitude of those at the hospital level, much as we found in Table 2.2. The divergence in magnitudes between the regressions at the two levels informs whether adoption leads to market expansion or business stealing. The economically meaningful and statistically significant market-level impacts suggest that robots expand the market, since there is less scope for patients to be "stolen" across markets. Yet the greater magnitudes at the hospital level imply that adoption further leads to business stealing as patients re-allocate

Figure 2.3: Event Studies of Patient Allocation



Notes: This figure plots event study coefficients from estimating equation 2.2 and its market-level analog. The outcome is prostate cancer patients in Panel A and prostatectomy patients in Panel B. The year prior to adoption is the reference year. The outcome is the volume of prostate cancer patients. Coefficients have a log-point interpretation, e.g. a coefficient of 0.2 implies a 20 log point change. Shaded areas depict 95% confidence intervals based on robust standard errors clustered at the market level. Regressions control for year and level (hospital or market) fixed effects.

across facilities in the same market.[9]

[9]The market-level estimates report the effect of 100% of hospitals in a market adopting to make them comparable to the hospital-level estimates. Since the typical market has lower levels of adoption, the effect of surgical robots on total volume would be attenuated accordingly.

2.5.2 Robustness

Appendix Tables B2 and B3 provide a number of robustness checks on the hospital-level prostate cancer and prostatectomy results, respectively. The tables first test adding varying controls to the baseline estimating equation 2.1. Our key findings are preserved when adding hospital-specific trends, hospital size decile-by-year interactions, and market by year interactions (effects attenuate somewhat with the inclusion of trends and expand somewhat when controlling for markets). We also consider controls for rest-of-market robot adoption to directly model the potential for one hospital's adoption to attract patients away from other facilities. Point estimates on the rest-of-market coefficients are negative, as expected, but own-adoption effects are unchanged.

The tables next test robustness to alternative hospital samples. In a more restrictive approach, we limit the sample to adopters so that identification comes solely from comparing hospitals that acquired a robot early vs. late in the period. Estimates shrink somewhat but remain highly economically and statistically significant.[10] Results are qualitatively unchanged from baseline when we use the broadest sample possible by including hospitals that acquired a robot after 2012 as well as those that failed to meet the minimum total patient and cancer patient thresholds. We additionally test robustness to alternative functional forms by running linear regressions with $\ln(N_{ht}+1)$ and $\text{asinh}(N_{ht})$ as the outcomes, respectively. Our results are little changed under these alternatives.

Appendix Tables B4 and B5 report robustness checks for the market-level analyses. Effects remain significant with the inclusion of market-specific trends, and while they attenuate somewhat, the ratios of these effects to their hospital-level analogs reported in the prior

[10] One reason for this attenuation may be that restricting the sample puts more weight on the short-term effects of adoption, which are smaller according to the event studies. To explore this concern, we model the adoption effect dynamics as having a constant (given by γ, as before) and a linear slope (we add the interaction $post_{ht} \times [t - adoptyear_h - 1]$, where the bracketed term is the hospital's adoption year relative to the post period). Columns 10 and 11 of Appendix Tables B2 and B3 augment the baseline and adopters-only models, respectively, with this interaction. The results are consistent with this concern: the constant terms converge and the slope terms are similar between the models.

robustness tables remain similar. We also show estimates nearly identical to those reported in the main text when we calculate market-level patient volume and adoption rates from the broadest possible set of hospitals (adding those that had failed to meet minimum patient and cancer patient thresholds). Finally, we provide estimates from linear models which yield significant (albeit expanded) coefficients.

2.5.3 Characteristics of Marginal Patients

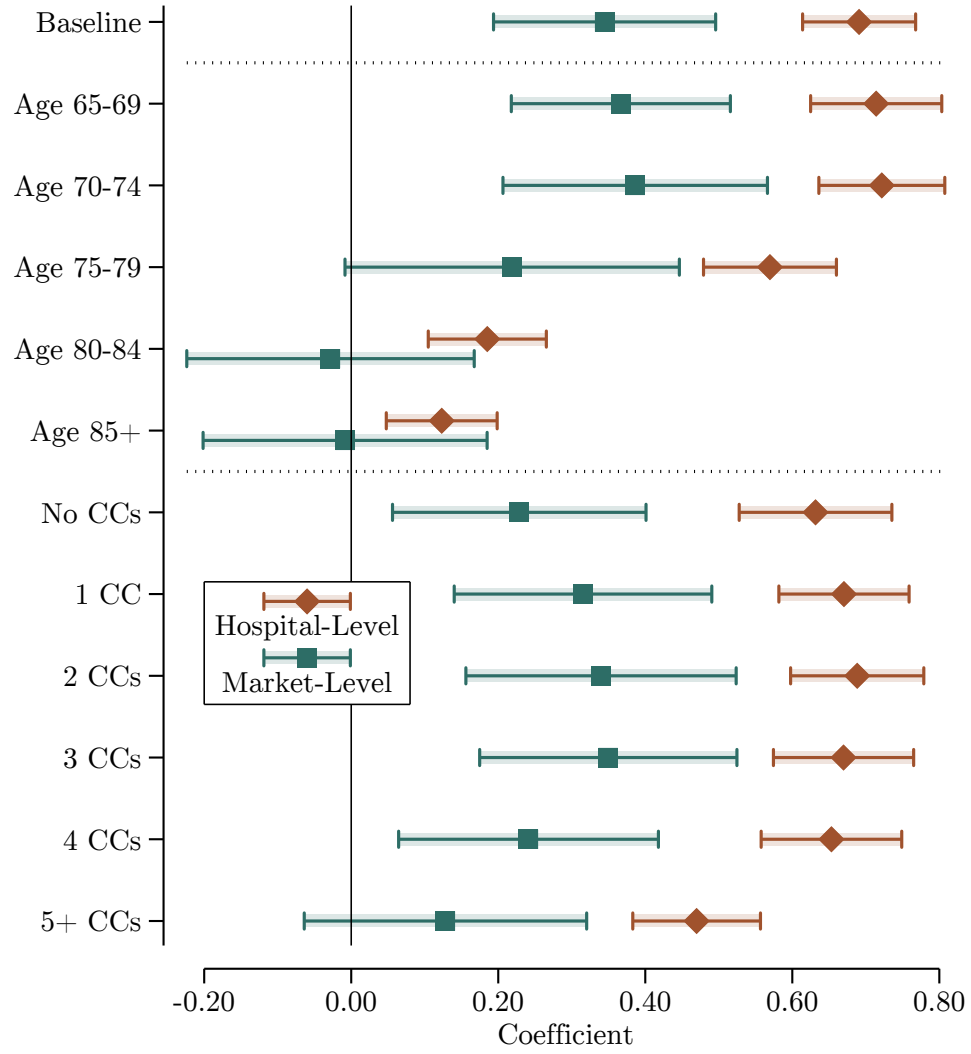
Having demonstrated substantial increases in patient volume in response to robot adoption, we now analyze the characteristics of the marginal patients drawn in to treatment. We focus on prostatectomy patients for brevity and since their hospital stay makes direct use of the robot; results for prostate cancer yield essentially identical patterns and are presented in Appendix Table B6. We characterize patients on two dimensions, each key for assessing their suitability for surgical intervention: age and burden of illness. We measure illness by counting the number of chronic conditions (CCs) according to the patients diagnoses prior to the hospitalization.[11]

Figure 2.4 plots the coefficient γ on *post* from estimating equation 2.1 with the outcome redefined as the number of prostatectomy patients in the specified age or CC bin (Appendix Figure B2 presents the results for prostate cancer). The volume increases at both the hospital and market levels are driven by younger patients. At both levels, effects attenuate greatly as the age bin rises; at the market-level we fail to detect effects at age 75 and up and point estimates are close to zero for ages 80 and up.

Effects by history of illness follow an upside-down U-shaped path. At both the hospital and market levels we detect significant increases in the volume of patients with up to 4 CCs, those with low and intermediate levels of prior illness. Point estimates for the volume of

[11] We track 22 CCs measured in the Medicare Chronic Conditions data at 6-month intervals using the observation most immediately predating the patient's admission. This data was not available before 1999 so these estimates are limited to the years 2000 to 2015.

Figure 2.4: Effect on Prostatectomy Volume by Patient Age and Chronic Conditions



Notes: This figure plots estimates from equation 2.1 of the effect of adopting a robot on the volume of prostatectomy patients in the specified age and chronic condition (CC) bins. Hospital-level effects depicted with diamonds and market-level effects depicted with squares. Estimates of effects on the total volume of patients reported at the top of the figure ("Baseline", repeated from Table 2.2). Coefficients have a log-point interpretation, e.g. a coefficient of 0.2 implies a 20 log point change. Error bars depict 95% confidence intervals based on robust standard errors clustered at the market level. Regressions control for year and level (hospital or market) fixed effects.

patients with no CCs, those who are observably the healthiest, are slightly smaller. Effects on the volume of patients with 5 or more CCs are the smallest; they are still significant at the hospital level but not the market level.

To provide a sense of how the patients induced to receive treatment due to robot adoption compare to incumbent patients, we directly estimate the effect of adoption on the average characteristics of the patients. Our approach draws on Gruber et al. (1999) and adapts their two stage least squares method to our context, which uses a Poisson model. Specifically, for each patient characteristic of interest we estimate two Poisson regressions: a first stage on patient volume, which repeats equation 2.1, and a reduced form with the same specification but the outcome redefined as the average characteristic of patients at the hospital or in the market. We then report the first stage estimates, which repeat our prior volume findings; the reduced form estimates, which indicate the log point effect of adoption on the average characteristic of the patients; and the ratio of the reduced form to the first stage, similar to an indirect least squares estimate. As the ratio of two log-point effects, this object is an elasticity. Under the assumption that adopting a surgical robot brings new patients into treatment without pushing old patients out of treatment (i.e. there are no "defiers" to adoption), the elasticity can be interpreted as the log point difference in the average characteristic between marginal patients and the incumbents. Appendix B.1 provides more details on this model.

Table 2.3 reports the estimates from these regressions. Panel A reports the first stage with similar estimates to those presented earlier (when they differ, it is because we omit observations where the average characteristic could not be calculated, e.g. when a hospital or market has no patients or the characteristic is not observed). Panel B reports the reduced forms. Columns 1-4 show the effect of adoption on average age and CCs. As expected, adoption tends to lower the age of the average patient at both the hospital and market level. For example, when a hospital adopts, average patient age is expected to fall by 2.9 log points or 2.1 years off the average; when 100% of a market adopts, average age falls by 2.3 log points or 1.6 years off the average. Panel C scales the reduced form by the first stage. These elasticities indicate that the marginal prostatectomy patient is statistically significantly 5.4 log points younger at the hospital level (3.9 years off the average) and 6.7 log points younger

at the market level (4.7 years off the average) than the incumbents. Results on CCs indicate that marginal patients are healthier, with elasticities that are 4-5 times larger than age elasticities at both levels but only statistically significant at the hospital level.

These results suggest that markets and hospitals grow in response to robot adoption by attracting younger, healthier prostate cancer patients. The attraction to robotics does not seem to be as strong for relatively sick patients. These findings imply that the influx of patients after adoption is not caused by widening eligibility criteria to patients in observably poorer health, particularly on the basis of age.

In columns 5-7 of Table 2.3 we consider how adoption changed the features of the average hospital in a market performing prostatectomy. Specifically, we test if markets that adopt tend to shift their prostatectomy patients to larger, higher-volume, and teaching hospitals.[12] The directions of these effects are *a priori* unclear: adoption by large well-resourced hospitals could further entrench their market dominance while adoption by smaller hospitals could give them a new opportunity to compete with their larger counterparts. While we do not find any significant effects on these metrics, the point estimates are all positive indicating that if there is adjustment in response to adoption it tends to concentrate patients at bigger hospitals with teaching infrastructure.

[12]To ease interpretation, we measure hospital size and volume at baseline (1998) levels, which avoids exploiting growth in size and volume due to adoption of the robot itself.

Table 2.3: Effect of Adoption on Characteristics of Prostatectomy Patients

	Hospital-Level		Market-Level				
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Characteristic:	Age	Chronic Conditions	Age	Chronic Conditions	Beds (Baseline)	Volume (Baseline)	Teaching Hospital
A. First Stage: Outcome is Patient Volume							
Post	0.542	0.490	0.342	0.260	0.342	0.342	0.342
	(0.035)	(0.040)	(0.077)	(0.082)	(0.077)	(0.077)	(0.077)
B. Reduced Form: Outcome is Average Characteristic							
Post	-0.029	-0.136	-0.023	-0.064	0.021	0.037	0.084
	(0.002)	(0.015)	(0.005)	(0.034)	(0.025)	(0.029)	(0.065)
C. Ratio of Reduced Form to First Stage: Elasticity of Average Characteristic with Respect to Volume							
Elasticity	-0.054	-0.277	-0.067	-0.248	0.061	0.107	0.245
	(0.004)	(0.033)	(0.020)	(0.149)	(0.075)	(0.088)	(0.191)
Average Characteristic	73.32	2.68	72.24	2.50	413.08	22.02	0.46
Hospitals/Markets	2,191	2,164	306	306	306	306	306
Observations	62,046	53,808	10,956	9,732	10,956	10,942	8,925

Notes: This table reports results from estimating the impact of robotic adoption on the characteristics of prostatectomy patients. Panel A reports the "first stage" results from estimating equation 2.1 and differs only from Table 2.2 because it omits observations (hospital- or market-years) with no prostatectomy patients. Panel B reports the "reduced form" estimates of the same specification with the outcome redefined as the average characteristic of prostatectomy patients. Coefficients in Panels A and B have a log-point interpretation, e.g. a coefficient of 0.2 implies a 20 log point change in volume or the average characteristic. Panel C reports the ratio of the reduced form estimate to the first stage estimate. These coefficients have an elasticity interpretation, i.e. the elasticity of the average characteristic with respect to volume. In columns 5-7, the outcome is the average characteristic of the patients' hospitals. Columns 5 and 6 measure the hospital's beds and prostatectomy patient volume at baseline (1998) levels. See text for more details. Robust standard errors clustered at the market level in parentheses. Regressions control for year and level (hospital or market) fixed effects.

2.6 Discussion and Conclusion

Robotic surgery diffused quickly through the health care system, and during our analysis period it became the primary surgical modality to treat prostate cancer. Our results clearly indicate that when hospitals adopt this technology they attract more prostate cancer patients. We find signs that this increase in patient volume occurs through both business stealing and market expansion following adoption. As hospitals in a market adopt surgical robots, prostate cancer volume increases in the whole market; since it is relatively difficult to "steal" patients across regions, this result shows the market-expanding power of surgical robots. Still, this phenomenon does not explain the totality of the increase in volume that occurs after a hospital adopts, since we find a hospital-level effect that is roughly twice the market-level effect. The gap between the results at each level points to a significant role for business stealing.

The welfare implications of this result are nuanced. One interpretation of these findings is that they indicate a wasteful medical arms race, since hospitals had few regulatory constraints on adoption, frequently took up a new technology with nontrivial fixed costs, and engaged in business stealing from one-another. If hospitals do not otherwise differ in their quality of care, this service duplication could be welfare-damaging. However, when hospitals differ in quality, business stealing has the potential to improve — or further reduce — welfare by redirecting patients to better or worse hospitals. For example, outcomes from robotic surgery are widely believed to depend on provider experience with the device (Savage and Vickers, 2009). If low-volume facilities attract patients by adopting robots, patient outcomes could deteriorate throughout the market because provider experience could become more diluted. On the other hand, if facilities that adopt robots tend to be higher-performing, the marginal patients attracted to them could benefit. Such a channel may operate here: adopting hospitals tend to be bigger and are more likely to be teaching facilities, two features that are associated with better patient outcomes (see e.g. Birkmeyer et al., 2002; Burke

et al., 2017); we also note signs in Section 2.5.3 that as markets adopt, patients are more likely to receive treatment at these facilities.

Market expansion is generally considered a sign of welfare improvement in traditional sectors, since a rise in quantity would tend to signal more consumers with access to the good. The market imperfections typical of the health care sector add some complication to this interpretation, however. Market expansion may be welfare-decreasing if it occurs due to moral hazard, when patients or their agents are shielded from the true costs of the technology due to insurance and overuse it as a result, or from behavioral hazard, when patients or their agents are attracted to hospitals with robotics because they have biased beliefs about the benefits of the technology (Baicker et al., 2015).

A full accounting of these welfare effects would require detailed clinical data on patient characteristics like cancer staging. Still, the relatively coarse data that we observe in claims is informative for ruling out a key welfare-damaging moral and behavioral hazard story in which poor candidates for intensive treatment are attracted to the hospital after adoption. During our analysis period, prostate cancer treatment guidelines increasingly sought to discourage older patients with competing risks from intensive testing for and management of this condition (USPSTF, 2008; Lepor, 2000). We find that the increase in prostatectomy patient volume in response to robot adoption is comprised of relatively younger patients that have fewer chronic conditions; we fail to detect increases in volume for patients age 80 and up or those with 5 or more chronic conditions. Our findings therefore suggest that robot adoption had small-to-nonexistent market-expanding effects on poor matches for surgery, an encouraging though not definitive sign that welfare was not harmed through at least one channel.[13]

In this study, we sought to evaluate the effects of hospital technology adoption on

[13]While we can rule out that marginal patients are poor candidates because they are relatively old or have competing risks, we cannot determine if they have early-stage prostate cancer and are seeking aggressive (and potentially low-value) treatment. Such analyses would require electronic medical record or cancer registry data and are an important topic for future study.

hospital utilization through the lens of surgical robotics in prostate cancer. We found striking impacts of adoption on patient volume at both the hospital- and market-level. These results raise key questions for future work on robotics and technology in the health care sector. While robotics has diffused particularly rapidly in prostate cancer treatment, its welfare effects in other areas of health care remain an open question that merits further study. In the space of prostate cancer treatment, future work could exploit electronic medical record or cancer registry data to observe an even richer view of patient outcomes. Taken together, our work highlights the power of technology diffusion to rapidly change the health care delivery system with concomitant implications for patient welfare.

Chapter 3

Direct-to-Consumer Pharmaceutical Advertising Influence on Generic Market Entry

3.1 Introduction

Prescription-drug spending increased by 58.3% in the ten years from 2005 to 2015 (CMS, 2018). By 2016, 12.1 per-capita prescriptions were filled at retail pharmacies amounting to $379.2 billion (KFF, 2018). Over this same period, direct-to-consumer advertising (DTCA) of pharmaceutical drugs increased 17.4% to $5.4 billion in 2015 (Mack, 2016). The advertising and market-entry decisions of pharmaceutical firms shape the increases observed in recent years.

Figure 3.1: Per Capita Direct to Consumer Advertising and Prescription Drug Spending

Notes: This figure shows the increase in prescription-drug spending and direct-to-consumer advertising (DTCA) from 1990 through 2017. The blue curve is per capita prescription drug spending, and the yellow curve is per capita DTCA in millions of dollars. All dollar amounts are real dollars adjusted using the 2010 consumer price index. Sources: CMS (2018); Census (2020); Palumbo and Mullins (2002); Kornfield et al. (2013); Mack (2016); Mahoney (2018); BLS (2010).

Prescription-drug companies receive a 20-year patent for new-drug formulations. Part of profit maximization during the patent-protection period is advertising. Firms advertise to physicians, termed detailing, to make them aware of the existence and quality of new pharmaceutical products (Gellad and Lyles, 2007). On top of physician advertising, the U.S., along with New Zealand, are the only countries that allow DTCA of prescription-pharmaceutical drugs. In 1997, DTCA regulations were relaxed by the Food and Drug Administration (FDA) which facilitated radio and television advertising. This coincided with a significant rise in both per-capita-advertising expenditures and prescription-drug spending. See Figure 3.1. One study found that for a sample of 2,601 older adults exposed to DTCA, 31% requested

the advertised drug. Of those that requested the drug, 69% received a prescription; though the research was unable to distinguish if the prescription the patient received was for the DTCA drug (Datti and Carter, 2006).

There is an active debate surrounding DTCA. Proponents believe DTCA provides valuable information to consumers about the existence of new pharmaceutical products to treat conditions that may not otherwise receive medical attention. On the other hand, critics of DTCA believe that these advertisements prompt clinically inappropriate prescribing of DTCA drugs or that they have prompted non-medical conditions to be medicalized (Weinmeyer, 2013). Both sides of the argument have direct implications for consumer welfare.

To understand how DTCA impacts welfare, it is vital to assess how DTCA influences generic entry into pharmaceutical markets. After a patent expires, the brand-name-pharmaceutical manufacturer faces the potential for increased competition from generic manufacturers entering the market. Generic drugs have bioequivalence to brand-name counterparts but are often less expensive. Research by Fischer and Avorn (2003) found that Medicaid could have saved $229 million from increased use of generic drugs in 2000. Even though there is clinical equality, there can be perceived quality differences by physicians and patients (Shrank et al., 2009, 2011).

In this paper I use a vertical-differentiation model to study the impact of DTCA on detailing, price, demand and the resulting entry decision of generic pharmaceutical manufacturers after patent expiration. The approach taken can be illustrated with a simple example. In 2004 the FDA approved eszopiclone for the treatment of insomnia. It is marketed under the brand name Lunesta. During the patent-protection period for eszopiclone, its manufacturer, Sepracor, made decisions about how to advertise Lunesta to physicians and the public.

Information on the benefits and clinical indications for prescribing Lunesta were directed to physicians. The public became aware of Lunesta as a sleep aid through various

forms of media advertising. Many people have now been made aware of Lunesta from commercials that feature a luna moth. Some consumers would have visited their physician for symptoms of insomnia regardless of seeing an advertisement. Yet, there is a portion of consumers who were unaware of the existence of a treatment for insomnia and are prompted to visit their physician after viewing an advertisement. In this way, the market for eszopiclone is expanded by the patients who would not have gone to the doctor without seeing an advertisement for Lunesta.

The patent for Lunesta expired in 2014.[1] As the patent neared expiration, a generic manufacturer observed the market conditions around insomnia medication including market size and the price of Lunesta and decided to enter the market. To enter, the manufacturer proved bioequivalence of a generic form of eszopiclone to Lunesta (as manufactured by Sepracor) and received FDA approval. After 2014, Serpacore competed with the generic manufacturer for market share.

For simplicity, my model considers the market for a pharmaceutical drug that treats a condition not addressed by other medications on the market. During patent protection there is only the brand-name drug available and the firm acts as a monopolist. After patent expiration, a single generic manufacturer observes market conditions and makes an entry decision. If the generic enters the market, oligopolistic competition ensues. If the generic does not enter, the brand-name firm maintains its monopoly.

I find that DTCA increases market size and profit for both brand-name and generic firms. Additionally, DTCA is a complement to detailing. DTCA prompts more consumers to visit the doctor which increases the marginal revenue of detailing and creates incentives for the brand-name firm to invest more in detailing as a response to DTCA allowance. Due to this relationship between detailing and DTCA, DTCA indirectly increases the monopoly

[1]Patents for pharmaceutical products are approved for 20 years; however, FDA approval is post-patent approval after clinical trials. This decreases the patent-protected marketing and sales period of new pharmaceutical products.

price during patent protection. After patent expiration, DTCA indirectly decreases price. Additionally, where prior research has found that there is a threshold past which detailing serves as an entry deterrent, DTCA extends this threshold and promotes generic entry. Hence, brand-name firms that invest in DTCA during the patent-protection period face increased competition after patent expiration.

This chapter is organized as follows. Section 3.2 is a review of the relevant literature. Section 3.3 lays out the model. Section 3.4 considers model equilibrium. Section 3.5 assesses the market entry decision of the generic firm. Section 3.6 analyzes the advertising decision of the incumbent firm. Section 3.7 is a simulation of the vertical differentiation model. Lastly, section 3.8 concludes.

3.2 Literature Review

Hurwitz and Caves (1988) completed one of the first studies to look at the market power of brand-name versus generic pharmaceutical drugs. The authors found that during the patent-protection period, goodwill accumulates with health-care providers for the brand-name drug which is enhanced by advertising. This was confirmed by Shrank et al. (2011) who surveyed 506 physicians. The authors found that fifty-percent of respondents believed that generics were of poorer quality than the equivalent brand-name counterpart, and over twenty-five percent would not use generics as a first prescription for themselves or family members.

Considering that goodwill accumulates during the patent-protection period, the best predictors of generic-manufacturing firms gaining market share were the passage of time and an increase in the number of suppliers (Hurwitz and Caves, 1988). Grabowski and Vernon (1992) extended this research to show that providers are price insensitive to what they prescribe, which gives brand-name firms an extreme first-mover advantage. After entry, generics compete in price; in contrast, brands decrease advertising and instead introduce a variant to the original drug with a new feature, for example slow release (Grabowski and

Vernon, 1992; Morton, 2002).

In 2007, Königbauer used a vertical-differentiation model to study the impact of persuasive detailing on the market entry decision of generic manufacturers. Königbauer's model predicts that, up to a certain threshold, advertising during the patent-protection period promotes generic entry, reduces average market price and raises consumer welfare after patent expiration. Beyond this threshold, advertising deters entry because the generic perceives that it will be unable to compete considering existing brand loyalty. This results in a higher-average price and reduction in consumer welfare.

Most pharmaceutical-market modeling has focused on advertising to physicians. Yet, in 2000, DTCA made up 15.9% of pharmaceutical-advertising budgets. A study by Brekke and Kuhn (2006) considered both forms of advertising. The authors used a horizontal differentiation model to assess competition between two brand-name manufacturers during the patent-protection period. Brekke and Kuhn find that detailing and DTCA are complementary strategies that result in higher price and decreased welfare if small co-payments are assumed. Dave and Saffer (2012) demonstrated empirically that DTCA does increase prescription drug prices and consumer demand by 9.5% and 21.0% respectively.

There are two additional studies which have brought together detailing and DTCA. Rosenthal et al. (2002) and Wosinska (2002) distinguished the impacts of pharmaceutical advertising as either informative or persuasive. Detailing generates brand goodwill. In contrast, DTCA increases demand for the overall drug class. Rosenthal et al. (2002) estimated elasticities for DTCA and detailing for pharmaceutical drug classes and individual products. DTCA elasticities are greater for the drug class than for individual brands while the opposite is true for detailing.

In contrast to Brekke and Kuhn (2006), I assume that during patent protection the incumbent firm is a monopolist. This approach lends itself to utilizing a vertical-differentiation model which will allow for assessing market entry after patent expiration. I contribute to the

existing literature by expanding the vertical-differentiation model from Königbauer (2007) to include DTCA. The model is an assessment of the 1997 regulation change that allowed for the expansion of DTCA and its influence on generic entry into pharmaceutical markets. To my knowledge, this study is the first pharmaceutical research paper to distinguish the impacts detailing and DTCA have on market entry in a single vertical-differentiation model.

3.3 Theoretical Model

This is a two-period model. During the first period the brand-name firm, B, has patent protection. During the second period, the patent has expired and a generic-drug manufacturer, G, can enter the market. The notation, assumptions and structure of the model remain consistent with Königbauer (2007) except where it has been extended to include DTCA. This maintains comparability to discern how the addition of DTCA impacts market outcomes. Hence, the foundation of Königbauer's model is replicated below for completeness to facilitate understanding the full impacts of DTCA.

My model begins with a proportion of consumers, $h \in [0, 1]$ in the market who visit the doctor based on their current experience of symptoms. In line with Brekke and Kuhn (2006), I assume that patients cannot observe the specific condition they have nor the effectiveness of available treatments. A higher h indicates a more widespread condition and symptom severity.

For the portion of patients, h, that go to the doctor, the physician perfectly observes each patient's symptoms and determines the value the patient would receive from a prescription drug, the "treatment" denoted by t. Assume each physician faces a uniform distribution of patients who each have a corresponding treatment value of t on the interval $[0, T]$. In Period 1, there is only a brand-name drug available as treatment which is priced at p_B. As the patient's agent, the physician maximizes her perception of the patient's utility function.

$$U = t - p_B \tag{3.1}$$

In this model, consumers pay the market price of the drug, p_B. Currently, adults in the United States pay 14% of prescription-drug costs out of pocket (Centers for Medicare and Medicaid, 2018). Assuming that co-payments do not exist does not impact the qualitative implications of the analysis presented here.

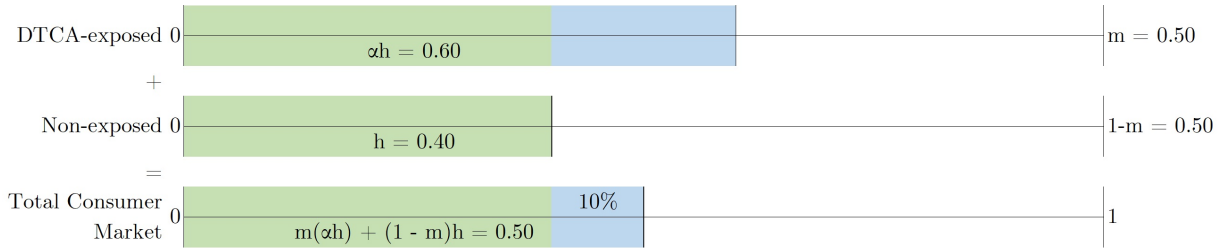
3.3.1 Period 1: Patent Protection - Monopoly

During Period 1, the brand-name firm has patent protection and can choose to advertise a new drug in two ways: as detailing to physicians and as DTCA through mass media. The firm chooses the proportion, k, of physicians to detail to and the proportion of consumers, m, to expose to DTCA. Detailing and DTCA have differing impacts in pharmaceutical markets (Wosinska, 2002). DTCA expands the market for the entire class of drugs by increasing the proportion of patients who visit the doctor based on exposure to drug advertising. On the other hand, detailing enhances brand loyalty by making physicians aware of the benefits of the brand-name drug.

Direct-to-Consumer Advertising

DTCA enters the model by making consumers' symptoms more salient which expands the fraction of DTCA-exposed consumers, m, who visit the doctor by α, $1 < \alpha < 2$, with the condition that $max(\alpha h) = 1$. The α term can be interpreted as the brand-name firm's ability to impact symptom salience through advertising. DTCA will be more effective if the condition targeted is more widespread or if belief in treatment and/or symptom salience is malleable. With DTCA, the proportion of consumers who visit the doctor is now the sum of the DTCA-exposed and non-exposed consumers and increases from h to $m(\alpha h) + (1 - m)h$. See below for an illustrative example using values $m = .5$, $h = 0.4$ and $\alpha = 1.5$:

Figure 3.2: Consumer Market with DTCA



Notes: This figure illustrates that the proportion of consumers that visit a physician is the sum of DTCA-exposed and non-exposed consumers. The green-shaded area indicates the proportion of the population that would visit a physician in absence of DTCA based on his or her health. The green-shaded area represents the additional share of the population that visits a physician as a result of DTCA exposure.

Figure 3.2 demonstrates that the consumer market is the sum of DTCA-exposed and non-exposed consumers. Exposing 50% of the market to advertising results in an additional 10% of patients choosing to visit the doctor. As the brand-name firm increases m by one-percentage point, the market expands by $h(\alpha - 1)$ which is the percentage change in h resulting from advertising effectiveness.

As will be shown, DTCA expands demand in the market by rotating the demand curve out, but maintains the same price intercept. The demand derived in the vertical-differentiation model as presented in Königbauer (2007) is scaled up by the inclusion of DTCA. Therefore price derivations are unchanged, but profit is impacted.

Detailing

In Brekke and Kuhn (2006), physicians are assumed to be perfectly uninformed about newly FDA-approved pharmaceutical drugs and only learn of them through detailing; however, this would imply that there is no market of un-detailed physicians. Here, I follow Königbauer (2007) and assume that physicians have some information about the new drug (for example by reading medical journals) and its corresponding benefits which is represented as normalized quality of $\theta = 1$. If a physician has been detailed to, she has an enhanced

understanding of the drug's properties and is aware of additional drug benefits. Detailed physicians assess the drug's quality at, $\theta > 1$. Recall that k physicians are detailed to and $(1-k)$ physicians are not exposed to advertising. Adding in that a patient may see either a detailed or non-detailed physician, the utility function is expanded as follows:

$$U = \begin{cases} \theta t - p_B \text{ utility perceived by a detailed physician} \\ t - p_B \text{ utility perceived by a non-detailed physician} \end{cases} \tag{3.2}$$

The DTCA term αh does not enter the utility function, even if there is DTCA exposure. This is due to the physician correctly assessing the patient's health and corresponding value of treatment as t even if DTCA exposure increased the salience of the patient's symptoms.

Demand and Profit in Period 1

For consumers who visit the doctor in Period 1, the brand-name drug is prescribed if $U \geq 0$. The points of indifference are based on the advertising exposure present in each physician-patient pairing.

$$\begin{aligned} t &\geq \frac{1}{\theta} p_B \text{ if the patient visits a detailed physician} \\ t &\geq p_B \text{ if the patient visits a non-detailed physician} \end{aligned} \tag{3.3}$$

Given k and m with the above indifference points, the brand-name firm's demand function in Period 1 is constructed. The inclusion of DTCA in the equation below expresses how DTCA impacts the size of the market, which is the sum of the DTCA-exposed, m, and non-exposed, $(1-m)$, market segments times the sum of the detailed and non-detailed markets, k and $(1-k)$. The resulting formulation reflects the four physician-patient pairs in the market:

1. Detailed physician and DTCA-exposed patient
2. Detailed physician and non-DTCA-exposed patient
3. Non-detailed physician and DTCA-exposed patient
4. Non-detailed physician and non-DTCA exposed patient

The superscript 1 in the demand function represents the first period.

$$\begin{aligned} D_B^1 &= k\left[\Big[m\alpha h + (1-m)h\Big]\Big[T - \frac{1}{\theta}p_B^1\Big]\right] + (1-k)\left[\Big[m\alpha h + (1-m)h\Big]\Big[T - p_B^1\Big]\right] \\ &= \left[m\alpha h + (1-m)h\right]\left[k\Big[T - \frac{1}{\theta}p_B^1\Big] + (1-k)\Big[T - p_B^1\Big]\right] \end{aligned} \tag{3.4}$$

Period 1 variable profit is equal to gross revenue minus the cost of production, the cost of advertising to physicians, $C(k)$, and the cost of DTCA, $C(m)$. Marginal cost is assumed to be constant and is normalized to zero. The fixed cost of product development and FDA approval is sunk and does not enter the profit function. The brand-name firm's revenue in Period 1 is scaled by the length of the patent, δ. The timing of patent protection is an important policy variable that can be regulated.

$$\pi_B^1(\theta, h, k, m) = \delta D_B^1 p_B^1 - C(k) - C(m) \tag{3.5}$$

The advertising cost functions follow Cabrales (2003) and Königbauer (2007) with $\gamma > 0$ and $\rho > 0$. The functions are strictly convex and increasing in the proportion of physicians, k, and consumers, m, advertised to. The parameters in the cost functions, γ for detailing and ρ for DTCA, reflect cost differences in the deployment of these advertising strategies. Plugging in demand and cost, Period 1 brand-name profit is:

$$\pi_B^1(\theta, h, k, m, p_B^1) = \delta\Bigg[p_B^1\Big[m\alpha h + (1-m)h\Big]\Big[k\Big[T - \frac{1}{\theta}p_B^1\Big] + (1-k)\Big[T - p_B^1\Big]\Big]\Bigg] - \Big[\frac{1}{1+\gamma}\Big]k^{1+\gamma} - \Big[\frac{1}{1+\rho}\Big]m^{1+\rho} \tag{3.6}$$

3.3.2 Period 2: Patent Expiration

In this period, the generic manufacturing firm observes the market conditions and makes its entry decision. To enter, the generic firm faces fixed-entry costs of F. If the firm enters the market, then the brand-name and generic firms compete in price. If the firm does not enter, the brand-name firm continues to act as a monopolist. There is no advertising in Period 2 (Grabowski and Vernon, 1992). Hence, k and m are exogenous in this period.

Scenario 1: The generic does not enter:

In this case, the brand-name firm maximizes the sum of its Period 1 and Period 2 profit functions. The patent-protection period has length δ; thus, Period 2 is length $(1-\delta)$ such that the sum of both periods has normalized length 1. Without entry, the brand-name firm will reaffirm its monopoly price, p_B^1, such that $p_B^1 = p_B^2 = p_B^M$. The brand-name firm's profit over both periods is:

$$\pi_B = \delta\pi_B^1 + (1-\delta)\pi_B^2 = \delta\pi_B^M + (1-\delta)\pi_B^M = \pi_B^M \tag{3.7}$$

Plugging in the demand derived during Period 1 the complete formulation is:

$$\pi_B(\theta, h, k, m) = p_B^1 \Big[m\alpha h + (1-m)h \Big] \Big[k\Big[T - \frac{1}{\theta} p_B^1\Big] + (1-k)\Big[T - p_B^1\Big] \Big] - \Big[\frac{1}{1+\gamma}\Big] k^{1+\gamma} - \Big[\frac{1}{1+\rho}\Big] m^{1+\rho} \tag{3.8}$$

Scenario 2: The generic enters:

With entry, the utility function now includes that the brand, B, or generic, G, may be prescribed. In this case, detailed physicians believe there is a difference in effectiveness between the brand and generic. Non-detailed physicians know that the brand and generic drugs are bioequivalent and therefore conclude quality to be equivalent, $\theta = 1$. Hence, non-detailed physicians exclusively prescribe the drug with the lowest price, and detailed physicians choose between the brand or generic based on whichever yields the higher perceived patient utility.

To determine if the brand or generic has the lowest price, observe that if the generic enters and $p_G^2 > p_B^2$ then the generic captures zero demand, $D_G^2 = 0$, which results in a profit loss of the generics firm's fixed entry costs, $\pi_G^2 = -F$. This is true regardless of DTCA, $m = 0$ or $m > 0$, because detailed physicians would still prefer the brand and non-detailed physicians would prescribe whatever is cheapest to maximize patient utility. In all physician-patient pairs, if $p_G > p_B \Rightarrow U_G < U_B$. In this scenario, the generic would have an incentive to reduce its price below the brand. For the generic to observe positive profit and enter the market, $p_G^2 < p_B^2$. It follows from this that non-detailed physicians exclusively prescribe the generic drug, $p_G^2 < p_B^2 \Rightarrow U(t, p_G) = t - p_G^2 > U(t, p_B) = t - p_B^2$. The utility function with generic entry is:

$$U = \begin{cases} \theta t - p_B \text{ utility perceived by a detailed physician prescribing the brand-name drug} \\ t - p_G \text{ utility perceived by a physician prescribing the generic drug} \end{cases} \tag{3.9}$$

To construct the demand functions for the brand-name and generic firms, the points of indifference are found. Non-detailed physicians will prescribe the generic drug if $U(t, p_G) \geq 0$. Detailed physicians will prescribe the generic drug if $U(t, \theta, p_B) < 0$ and $U(t, p_G) \geq 0$ and will prescribe the brand-name drug if $U(t, \theta, p_B) \geq U(t, p_G) \geq 0$. Hence, to prescribe the drug, the utility will need to be at least as great as the utility at the lowest-prescribing threshold which is $t - p_G = 0 \Rightarrow t = p_G$ since $p_G^2 < p_B^2$. The indifference points relative to advertising exposure are as derived in Königbauer (2007) and follow:

Detailed Physician

Prescribes the brand-name drug if:

$$\begin{aligned} \theta t - p_B &\geq t - p_G \\ \theta t - t &\geq p_B - p_G \\ t(\theta - 1) &\geq p_B - p_G \\ t &\geq \frac{1}{(\theta - 1)}(p_B - p_G) \end{aligned} \tag{3.10}$$

Prescribes the generic drug if:

$$\begin{aligned} t - p_G &\geq 0 \\ t &\geq p_G \end{aligned} \tag{3.11}$$

In the non-detailed market, physicians do not believe that there is a quality difference between brand and generic; thus, they will exclusively prescribe the drug that is less

expensive, which, given the above, is the generic, $p_B > p_G$.

Non-detailed Physician

Prescribes the generic drug if:

$$\begin{aligned} t - p_G &\geq 0 \\ t &\geq p_G \end{aligned} \tag{3.12}$$

With the above indifference points, brand-name and generic demand is constructed. DTCA again enters as an increase in the number of patients who visit the doctor based on advertising exposure and health status. In Period 2, detailing, k, and DTCA, m, are exogenous.

$$D_B^2 = [m\alpha h + (1-m)h]\left[k\left(T - \left(\frac{1}{(\theta-1)}(p_B - p_G)\right)\right)\right] \tag{3.13}$$

$$D_G^2 = [m\alpha h + (1-m)h]\left[k\Big(\Big(\frac{1}{(\theta-1)}(p_B - p_G)\Big) - p_G^2\Big) + (1-k)\Big(T - p_G^2\Big)\right] \tag{3.14}$$

Period 2 profits for the brand-name and generic firms with detailing and DTCA are as follows. The generic firm's fixed cost of entry is included as F.

$$\pi_B^2(\theta, h, k, m) = (1-\delta)p_B^2\Big[m\alpha h + (1-m)h\Big] \quad \Big[k\Big(T - \Big(\frac{1}{(\theta-1)}(p_B^2 - p_G^2)\Big)\Big)\Big] \tag{3.15}$$

$$\begin{aligned} \pi_G^2(\theta, h, k, m, F) = (1-\delta)p_G^2\Big[m\alpha h + (1-m)h\Big]\Big[k\Big(\Big(\frac{1}{(\theta-1)}(p_B^2 - p_G^2)\Big) - p_G^2\Big) \\ + (1-k)\Big(T - p_G^2\Big)\Big] - F \end{aligned} \tag{3.16}$$

3.4 Equilibrium Prices

The price and advertising levels are solved for recursively. First by maximizing Period 2 profit and then using p_B^{2*} to solve for advertising levels of k^* and m^* in Period 1. The brand-name firm considers two possible scenarios in Period 2: Either the generic firm does not enter, or the generic firm enters.

If the generic does not enter. The brand-name firm will reaffirm its monopoly price. This is found by maximizing the brand-name firm's total profit function without entry:

$$\max_{p_B^2} \pi_B(\theta, h, k, m) = p_B^1 \Big[m\alpha h + (1-m)h \Big] \Big[k\Big[T - \frac{1}{\theta} p_B^1\Big] + (1-k)\Big[T - p_B^1\Big] \Big] - \Big[\frac{1}{1+\gamma}\Big] k^{1+\gamma} - \Big[\frac{1}{1+\rho}\Big] m^{1+\rho} \tag{3.17}$$

The first-order condition and Period 2 monopoly price derivation is below:

$$\frac{\partial \pi_B}{\partial p_B^2} = \Big[m\alpha h + (1-m)h \Big] \Big[T - 2k(\frac{1}{\theta} p_B^{2*}) - 2(1-k)(p_B^{2*}) \Big] = 0 \tag{3.18}$$

Solving equation 3.19 for p_B^{2*} results in the brand-name firm's monopoly price.

$$p_B^{M*} = p_B^{2*} = \frac{1}{2} \Big[\frac{\theta T}{[k + \theta - k\theta]} \Big] \tag{3.19}$$

The monopoly price, p_B^{M*}, does not depend on the proportion of consumers exposed to DTCA, m. As stated earlier, this is because DTCA expands the demand in the market by rotating the demand curve out, but maintains the same price intercept. Hence, p_B^{M*} is the same as was derived in Königbauer (2007). The derived monopoly price is used in Period 1

to determine advertising levels of k and m without entry. The Period 1 monopoly price is increasing in the proportion of physicians detailed to, k, and belief in brand quality, θ.

$$\frac{\partial p_B^{M*}}{\partial k} = \frac{(\theta-1)\theta T}{2(\theta-\theta k+k)^2} > 0 \tag{3.20}$$

$$\frac{\partial p_B^{M*}}{\partial \theta} = \frac{kT}{2(\theta-\theta k+k)^2} > 0 \tag{3.21}$$

The equilibrium monopoly prices are also higher with DTCA. Even though DTCA scales the market up by rotating the demand curve out but maintaining the same price intercept, DTCA indirectly impacts price by increasing the incentive to invest in detailing, k which directly increases price. This will be demonstrated in Section 3.6.

To determine the Period 2 price, assuming generic entry, the firms simultaneously maximize Period 2 profit and compete on price. As with the monopoly price, the presence of DTCA does not impact price under generic entry for the brand-name or generic firms. This can be seen in comparison with Königbauer (2007) which derives the same Period 2 price for both generic and brand-name firms.

$$\max_{p_B^2} \pi_B^2(\theta,h,k,m) = (1-\delta)p_B^2\Big[m\alpha h+(1-m)h\Big]\Big[k\Big(T-\Big(\frac{1}{(\theta-1)}(p_B^2-p_G^2)\Big)\Big)\Big] \tag{3.22}$$

$$\max_{p_G^2} \pi_G^2(\theta,h,k,m) = (1-\delta)p_G^2\Big[m\alpha h+(1-m)h\Big] \Big[k\Big(\Big(\frac{1}{(\theta-1)}(p_B^2-p_G^2)\Big)-p_G^2\Big)+(1-k)\Big(T-p_G^2\Big)\Big]-F \tag{3.23}$$

The resulting Bertrand-Nash equilibrium prices are as follows:

$$p_B^{2*}(k,m) = \frac{T(\theta-1)(k+2\theta-1)}{3k+4\theta-4} \tag{3.24}$$

$$p_G^{2*}(k,m) = \frac{T(\theta-1)(2-k)}{3k+4\theta-4} \tag{3.25}$$

The brand-name price, with entry, in Period 2 is decreasing with detailing. This is because the larger detailing, k, is the greater the incentive for the brand-name firm to rationally reduce price to compete more aggressively in the detailed market for demand since now detailed physicians can prescribe the brand or generic drug. However, the brand-name price is increasing in advertising effectiveness. This implies that the larger the proportion of physicians exposed to advertising the lower the Period 2 Bertrand-Nash equilibrium brand price, but that downward pressure is offset by how effective the detailing is, which would increase brand loyalty. This is due to the Period 2 competition with generic entry only happening in the detailed segment of the market as the generic manufacturer captures the entirety of the non-detailed market.

$$\frac{\partial p_B^{2*}}{\partial k} = -\frac{T(\theta-1)(2\theta+1)}{(4\theta+3k-4)^2} < 0 \tag{3.26}$$

$$\frac{\partial p_B^{2*}}{\partial \theta} = \frac{1}{2}T\left(1 - \frac{3(k-2)k}{(4\theta+3k-4)^2}\right) > 0 \tag{3.27}$$

In Period 2, DTCA decreases price for the brand-name and generic firms through increased competition. Since DTCA incentivizes detailing, detailing with entry puts downward pressure on price. Hence, $m > 0$ indirectly decreases price in Period 2.

For the generic firm in Period 2, price decreases as detailing increases and decreases as advertising effectiveness, θ increases.

$$\frac{\partial p_G^{2*}}{\partial k} = -\frac{2T(\theta-1)(2\theta+1)}{(4\theta+3k-4)^2} < 0 \tag{3.28}$$

$$\frac{\partial p_G^{2*}}{\partial \theta} = -\frac{3(k-2)kT}{(4\theta+3k-4)^2} < 0 \tag{3.29}$$

3.4.1 Equilibrium Conditions

There are only certain conditions under which p_B^{2*} and p_G^{2*} are a Bertrand-Nash equilibrium. It has been established that for the generic firm to have positive profit and enter the market after patent expiration, $p_G^2 < p_B^2$. The sufficient condition for equilibrium is only dependent on k and θ which determine the size of the detailed market relative to the non-detailed market. Hence, the presence of DTCA does not impact equilibrium prices or the subsequent decisions of the brand-name or generic firms to remain at p_B^{2*} and p_G^{2*}.

The sufficient condition for p_B^{2*} and p_G^{2*} to be a Bertrand-Nash equilibrium is:

$$\theta \geq \frac{1}{2k}\Big[-k^2+2+\sqrt{k^4-5k^3+9k^2-8k+4}\Big] \tag{3.30}$$

All derivations of the brand-name firm's choices of k, given θ, must to be evaluated against the above condition because k is endogenous. The proof in Appendix A of Königbauer (2007) presents a detailed derivation and analysis of the equilibrium condition.

3.5 Generic Entry Decision

For the generic firm to enter, the variable profit of the generic must be greater than the firm's fixed cost of entry, given the advertising levels of k and m and the related parameters θ, h, α and F. That is,

$$\begin{aligned}\pi_G^{2*}(\theta,h,k,m,F) &= (1-\delta)\Big[\pi_G^*\Big] - F \geq 0 \\ &= (1-\delta)\Big[\frac{(\theta-1)(k-2)^2T^2(\theta+k-1)((\alpha-1)hm+h)}{(4\theta+3k-4)^2}\Big] \geq F\end{aligned} \tag{3.31}$$

If $k = 0$, then there is no perceived difference in effectiveness between the brand and generic drugs, even if $m > 0$. Without detailing, there is intense price competition which leads to the Bertrand paradox, and price is equal to marginal costs and $\pi_G^2 = -F$. Assuming the generic firm faces positive startup costs, $F > 0$, detailing is a necessary condition for market entry.

Assuming, $k > 0$, the values of k and m directly impact the generic firm's variable profit.

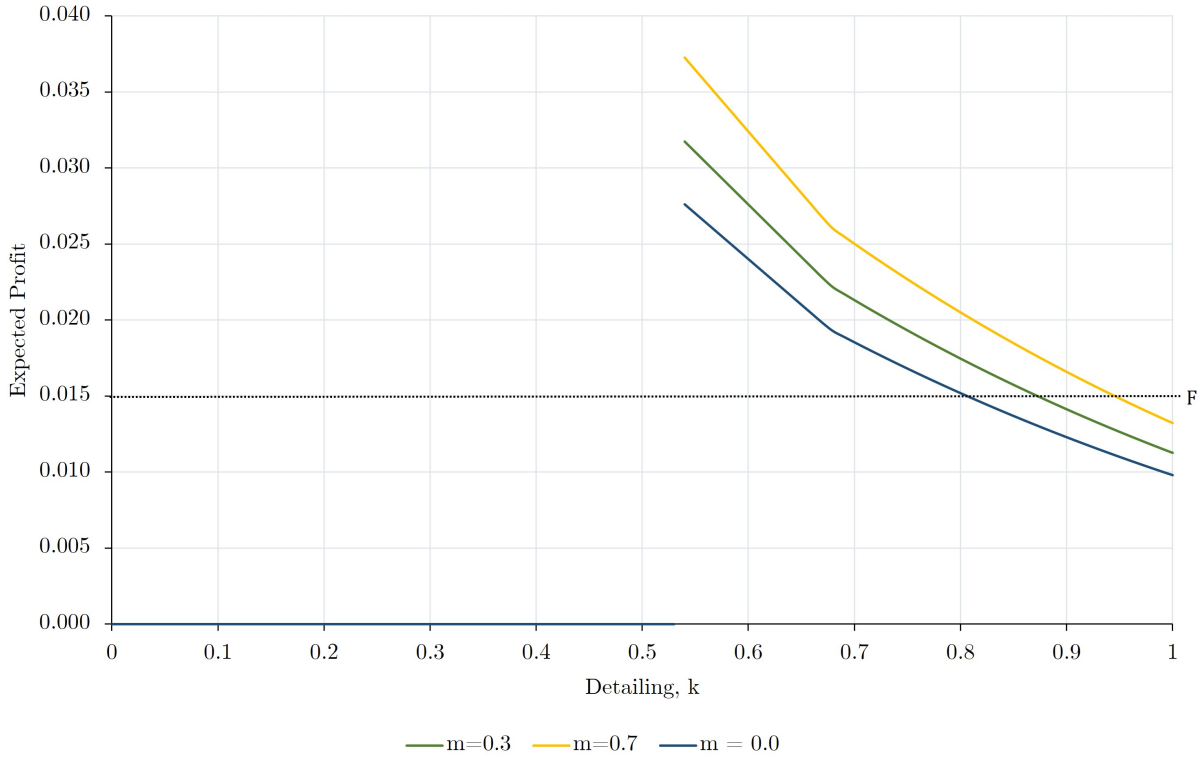
$$\frac{\partial \pi_G^{2*}}{\partial k} = (1-\delta)\frac{h(\theta-1)(k-2)T^2\left(8\theta^2+3k^2+12\theta(k-1)-6k+4\right)\left((\alpha-1)m+1\right)}{(4\theta+3k-4)^3} < 0 \tag{3.32}$$

$$\frac{\partial \pi_G^{2*}}{\partial m} = (1-\delta)\frac{(\alpha-1)h(\theta-1)(k-2)^2T^2(\theta+k-1)}{(4\theta+3k-4)^2} > 0 \tag{3.33}$$

There are two opposing forces in the generic firm's entry decision. Profit decreases as detailing, k, increases, but as DTCA spending, m, increases profit increases since the amount, m, and effectiveness, α, of DTCA increase the size of the market for the whole class of drugs (brand and generic).

The generic firm's entry decision is illustrated in Figure 3.3. The graph is a plot of the generic firm's variable profit against brand-name detailing for different levels of DTCA. The generic profit function is calculated by holding constant all parameters at the following values: $T = 1$; $\theta = 2.0$; $\delta = 0.4$; $h = 0.4$ and $\alpha = 1.5$. For $\theta = 2$, the sufficient condition for equilibrium is met at $k = 0.54$, and the generic would enter the market from $k = 0.54$

Figure 3.3: Generic Entry Decision, $\theta = 2.0$



Notes: This figure demonstrates the expected profit of the generic manufacturing firm for different values of detailing, k. Each curve represents a different level of DTCA, m, used to calculate the generic firm's profit. For values below $k = 0.54$ the sufficient condition for equilibrium price is not met and the generic firm would not enter the market. The profit is calculated by holding constant all parameters at the following values: $T = 1$; $\theta = 2.0$; $\delta = 0.4$; $h = 0.4$ and $\alpha = 1.5$.

to $k = 0.8$ with $m = 0$; however, if $m = 0.3$ or $m = 0.7$ the generic would enter up to $k = 0.86$ or $k = 0.94$ respectively. The entry points assume fixed entry costs of $F = 0.015$ as indicated by the dashed-black line. The addition of DTCA tempers the profit declines experienced from detailing and extents the detailing threshold for which the generic would choose to enter. Hence, DTCA promotes competition in Period 2 by increasing the range of k values for which the generic firm would choose to enter the market.

3.6 Advertising Decision of the Brand-Name Firm

The brand-name firm recursively chooses values of k and m to block, deter or accommodate entry. The firm has two potential profit functions to consider. The first is without entry where the brand-name maintains its position as a monopolist. The second assumes that the generic firm enters the market after patent expiration.

In both profit maximization scenarios, the optimal levels of k^* and m^* are at the point where marginal revenue from each type of advertising will equal marginal cost assuming the condition for the Bertrand-Nash equilibrium are met. The values of k and m which satisfy the following first-order conditions (FOCs) are solved for simultaneously. The levels of advertising, k^* and m^*, cannot be solved for explicitly and will be calculated in the model simulation.

Assuming the generic firm does not enter:

$$\max_{k,m} \pi_B^*(\theta, h, k, m) = \left[\frac{h\theta T^2(-\alpha m + m - 1)}{4(\theta - 1)k - 4\theta}\right] - \frac{k^{\gamma+1}}{\gamma + 1} - \frac{m^{\rho+1}}{\rho + 1}$$

First order conditions:

$$\frac{h(\theta - 1)\theta T^2((\alpha - 1)m + 1)}{4(\theta - \theta k + k)^2} = k^{\gamma} \tag{3.34}$$

$$\frac{(1 - \alpha)h\theta T^2}{4(\theta - 1)k - 4\theta} = m^{\rho} \tag{3.35}$$

Assuming the generic firm enters:

$$\max_{k,m} \pi_B^*(\theta, h, k, m) = \delta \left[\frac{h\theta T^2(-\alpha m + m - 1)}{4(\theta - 1)k - 4\theta} - \frac{k^{\gamma+1}}{\gamma + 1} - \frac{m^{\rho+1}}{\rho + 1} \right] + (1 - \delta) \left[\frac{(\theta - 1)kT^2(2\theta + k - 1)^2((\alpha - 1)hm + h)}{(4\theta + 3k - 4)^2} \right] \tag{3.36}$$

First order conditions:

$$\delta \Big[\frac{h(\theta - 1)\theta T^2((\alpha - 1)m + 1)}{4(\theta - \theta k + k)^2} \Big] + (1 - \delta) \Big[\frac{(\theta - 1)T^2(2\theta + k - 1)\left(8\theta^2 + 3k^2 + 6\theta(k - 2) - 9k + 4\right)((\alpha - 1)hm^* + h)}{(4\theta + 3k - 4)^3} \Big] = k^\gamma \tag{3.37}$$

$$\delta \frac{(1 - \alpha)h\theta T^2}{4(\theta - 1)k - 4\theta} + (1 - \delta) \Big[\frac{(\alpha - 1)h(\theta - 1)kT^2(2\theta + k - 1)^2}{(4\theta + 3k - 4)^2} \Big] = m^\rho \tag{3.38}$$

The above FOCs can be used to additionally assess how DTCA, m, impacts the optimal values of k. By comparing the marginal revenue from detailing, k, with an without DTCA, m, I am able to show the relationship between the two forms of advertising. The difference between $\frac{\partial \pi}{\partial k}|_{m>0}$ and $\frac{\partial \pi}{\partial k}|_{m=0}$ is:

$$(\alpha - 1)hm \left[\frac{\partial \pi}{\partial k}|_{m=0} \right] > 0 \tag{3.39}$$

The marginal revenue from detailing with a positive amount of DTCA is higher than without. This confirms in a vertical-differentiation model that detailing and DTCA act as complements. Additionally, the brand-name price in Period 1 increases as detailing increases, $\frac{\partial p_B^M}{\partial k} > 0$, and since DTCA is complementary to k, DTCA indirectly increases monopoly price by increasing k^*. Similarly, price in Period 2 decreases because $\frac{\partial p_B^2}{\partial k} < 0$.

3.6.1 Brand-Name Firm's Decision to Block, Deter or Accommodate Entry

Once the brand-name firm knows the optimal values of k and m for profit maximization with and without entry, it can assess the generic firm's expected profit to see if the generic firm would enter at $\{k^*, m^*\}$. Starting with the generic firm's profit function at the equilibrium prices of p_B^{2*} and p_G^{2*}, the brand-name firm can determine all of the values of k and m for which the generic firm has zero profit. Thus, by setting the above function equal to zero, DTCA, m can be expressed as a function of detailing, k, $m = f(k)$:

$$\pi_G^{2*}(\theta, h, k, m, F) = \frac{(\theta-1)(k-2)^2T^2(\theta+k-1)((\alpha-1)hm+h)}{(4\theta+3k-4)^2} - F = 0 \qquad (3.40)$$

Solving the above function for m:

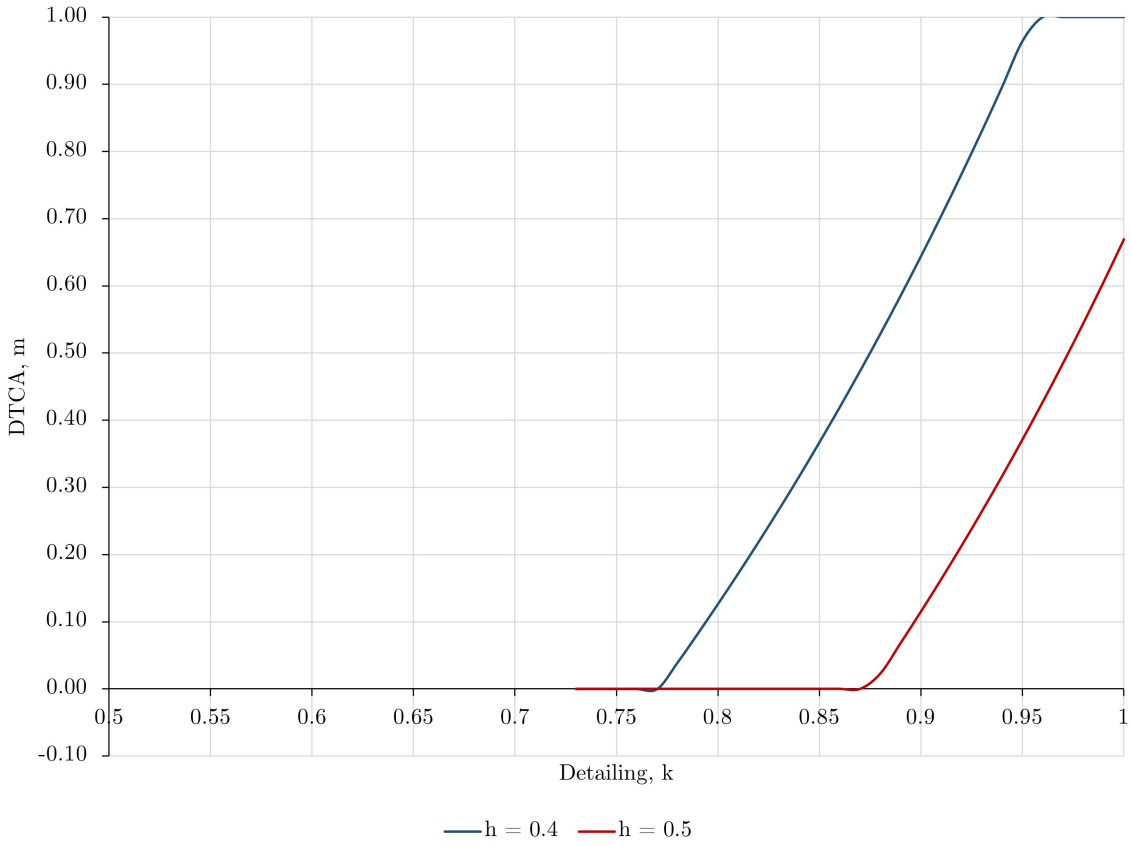
$$m = \frac{1}{1-\alpha}\Big[\frac{F(4\theta+3k-4)^2}{(\delta-1)h(\theta-1)(k-2)^2T^2(\theta+k-1)} + 1\Big],\ 0 \le m \le 1,\ 0 \le k \le 1 \qquad (3.41)$$

Figure 3.4 plots for different values of h how DTCA, m, expands the range of generic profitability across k. For example, considering the blue curve, $h = 0.4$, the generic firm has positive profit above and to the left of the curve for $0.73 \le k \le 0.96$.[2] Hence, for each combination of k and m along and to the right of the the blue curve, the brand name firm can deter entry.

If the brand-name firm maximizes its profit function for the unconstrained solution for p_B^*, and k^* and m^* lie to the right of the zero-generic profit curve then entry is blocked and the brand-name firm is unaffected. Entry is deterred automatically. However, if k^* and m^* are to the left of the curve, then the generic would enter. In practice, the brand-name firm

[2]Values of k below 0.73 do not satisfy the condition for a Bertrand-Nash Equilibrium.

Figure 3.4: Advertising Trade-off



Notes: This figure shows the values of DTCA, m, and detailing, k, for which the generic manufacturer earns zero profit. The curves correspond to generic manufacturing profit calculations for different values of h where h represents the proportion of the population that would visit a doctor in absence of DTCA.

would find the monopoly values of k^* and m^* that would deter entry and compare it to the values of k^* and m^* with entry to determine if the firm maximizes constrained profit by deterring entry. Since k^* and m^* cannot be solved for algebraically, the above exercise will be completed in simulation, see Section 7.

Additionally, Figure 3.4 shows how h shifts the trade-off curve. When $h = 0.4$ only 40% of consumers would visit the doctor (without DTCA). For the generic firm, the non-detailed market will need to be quite large to make it profitable to enter. However, if an additional 10% of consumers would visit the doctor based on symptoms, $h = 0.5$, both the detailed

and non-detailed markets are enlarged and there is a greater opportunity for generic entry. The red curve lies to the right of the blue. Similarly, as α increases the range of generic profitability widens because DTCA stimulates a larger proportion of the population to visit the doctor, not pictured.

Lastly, since k>0, is a necessary condition for entry, the brand-name firm could choose the corner solution, $k = 0$ and block entry. This solution is not viable as given the conditions for equilibrium. For low values of k, the brand-name firm would decrease its price and assume the non-detailed market and increase profit. Hence, they would always choose $k > 0$.[3]

The path that the brand-name firm takes will depend on the exogenous parameters in the profit function, θ, α, h and δ. That is, the effectiveness of advertising, the health status of the population that the drug treats and the length of the patent protection period. The specific values will be explored in the simulation.

3.7 Simulation

The logarithmic formulation of the cost functions makes solving for k^* and m^* algebraically impossible. Table 3.1 presents simulations for numerous parameter assumptions. The results demonstrate the hypotheses developed in the vertical differentiation model about the ways that DTCA impacts pharmaceutical markets. Table 3.1 is organized such that the left most columns indicate the parameter values. The top two rows (1) and (2) are the base parameter values, with and without DTCA respectively. Each simulation below row (2) uses the same base values but varies one parameter as indicated.

Columns (1) through (8) are simulations based on the brand-name firm maximizing its profit function to select k^* and m^* assuming that the generic does not enter. Columns (9) and (10) demonstrate the values for which the brand-name firm could block entry by choosing k and m different from k^* and m^*. Columns (12) through (19) show values based on

[3]See brand-name firm's decision to deter in Königbauer (2007) Appendix A.

the brand-name firm maximizing its profit while accommodating generic entry. The conditions for a Bertrand-Nash equilibrium are only satisfied if the detailed portion of the market is sufficiently large. If the conditions for equilibrium are not met, the variable price and profit values are not applicable (n/a). Give the exogenous parameters, the brand-name firm chooses a strategy: to deter, block or accommodate entry. Assuming $F = 0.015$, the values highlighted in yellow indicate the brand-name firm's best strategy.

Optimal Advertising:

The optimal value of k^* with and without entry in higher if $m^* > 0$. This implies that DTCA complements detailing by expanding the market and increasing the marginal revenue of physician advertising. This is seen by comparing the values of k^* in rows with entry to rows without entry.

Price:

DTCA indirectly increases the Period 1 monopoly price. For example, the Period 1 monopoly price in row (2) column (3) without DTCA is 3.5% lower than row (1) which increases to 0.797. This results from the increase in k^* without entry where an additional 4.4% of physicians are exposed to DTCA. This same pattern is seen for all parameter simulations when comparing the monopoly prices in columns (3) and (15) for $m = 0$ and $m > 0$. Additionally, as h increases, the monopoly price gains are exacerbated by the larger market based on baseline health, h. This would make it more profitable to target conditions where there is a naturally large market and all forms of advertising reach more potential patients. As h increases from 0.4 to 0.8 the indirect monopoly price gains from DTCA are 3.5% and 5.4% assuming no entry (column (3)), and 1.9% and 3.0% (column (15)) respectively.

In Period 2, the price response to DTCA is the opposite. DTCA reduces Period 2 price if the generic firm enters the market. While m promotes increases in k, if the generic

enters in Period 2, the downward pressure on price results from increased competition in the detailed market. This is seen by comparing the Period 2 prices in row (1) to row (2) and row (6) to row (4).

Generic Entry:

For certain parameters, DTCA promotes generic entry. Variable profit for the generic firm is presented in columns (8) and (19). Comparing simulations where $m = 0$ to $m > 0$, variable profit is consistently higher. This demonstrates that for more values of F, fixed cost, the generic firm would choose to enter the market. For example, if $F = 2.0$ the generic firm would not enter the market in row (2), column (8), without DTCA, but the firm would enter with a positive amount of DTCA, row (1), column (8). The same is true comparing rows (1) and (2) in column (19) if $F = 0.035$. This also shows that if the brand name firm accommodates entry, then they reduce the size of the detailed market by decreasing k^* and m^* which increases the generic firm's profit and likelihood of entry.

Generic entry is also more likely for high values of h. See row (11). In column (19), rows (1) and (8), the generic firms profit increases by 0.019 when h increases from 0.4 to 0.8. If h is too low, there is not enough inherent demand in the market to sustain a Bertrand-Nash equilibrium and the brand-name firm would decrease it's price to capture demand in the detailed and non-detailed market. The non-detailed market must be of an adequate size to make it profitable for the generic to enter. Hence, for conditions that more widely impact the population, generic entry is more likely if consumers can be informed about available products on the market.

Brand Profit and Strategy:

Brand profit with and without entry is higher with DTCA due to the expanded market size. In some cases, for large enough markets based on consumers health or the effectiveness

of DTCA, the brand-name firm gains more profit with DTCA and entry. This is seen by comparing row (2), column (6) with row (1) column (18). The monopoly profit without DTCA is 0.142; however, DTCA with entry increases brand-name profit to 0.148.

DTCA consistently increases the probability that the generic firm will enter the market. If generic entry is inevitable based on the value of F and the other market conditions, the brand-name firm could choose to block entry by choosing values of k and m for which the generic firm has zero profit. This is a preferred strategy if the brand-name firm is unable to engage in DTCA (for example for black-box pharmaceutical drugs).[4] However, if DTCA is allowed in the market, the brand-name firm's best strategy is to maximize profit by accommodating entry.

The values highlighted in yellow show the highest-profit choice for the brand-name firm assuming the fixed cost of the generic firm is $F = 0.015$.[5] For certain markets with high inherent demand, $h = 0.8$, the brand-name firm cannot block entry as the generic remains profitable even if 100% of the physicians are detailed to. Considering row (2), for $F = 0.015$ the generic firm would enter even if the brand-name firm tries to deter entry by maximizing it's monopoly profit function to choose k^* and m^*. In this case, their best choice is to block entry by choosing $k = 0.823$. In this case they earn 0.133 in profit which is higher than if the generic entered at k^* and m^* where profit is 0.112 in column (7). However, if DTCA is allowed, the brand-name firm's best strategy is to accommodate entry by choosing k^* and m^* assuming the generic will enter. In this scenario, DTCA is a benefit to the brand by increasing profit, even though it also prompts the brand to accommodate entry.

[4]Black-box pharmaceutical drugs are medications have have serious side effects. They cannot be marketed with advertising that only states the drug's name and excludes its use, termed reminder advertising.

[5]The values highlighted in column (18) are higher than those in column (7) to the ten thousandth place.

Table 3.1: Brand and Generic Decision Simulation

		Brand Profit Maximization Assuming No Entry								Block Entry			Brand Profit Maximization Assuming Entry						
				Price	P2 Price		Profit	Variable Profit with Entry		F = 0.015		Profit	Entry		Price	P2 Price		Variable Profit with Entry	
		k*	m*	Monopoly	Brand	Generic	Monopoly	Brand	Generic	k	m	Brand	k*	m*	Monopoly	Brand	Generic	Brand	Generic
		(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(15)	(16)	(17)	(18)	(19)
Base Values: T=1; θ=2; h=0.4; α=1.5; γ=6.0; ρ=7.0; δ=0.4																			
(1) m>0		0.745	0.697	0.797	0.601	0.201	0.190	0.148	0.023	0.963	0.716	0.144	0.724	0.674	0.784	0.603	0.207	0.148	0.039
(2) m=0		0.701	0.000	0.770	0.606	0.213	0.142	0.112	0.018	0.823	0.000	0.133	0.705	0.000	0.772	0.606	0.212	0.112	0.033
Parameter: θ																			
(3) m>0	1.8	0.709	0.688	0.730	n/a	n/a	0.177	n/a	n/a	n/a	n/a	n/a	0.707	0.665	0.729	n/a	n/a	n/a	n/a
(4) m>0	2.2	0.779	0.705	0.869	0.703	0.205	0.203	0.166	0.023	0.990	0.719	0.153	0.739	0.683	0.838	0.708	0.216	0.166	0.039
(5) m=0	1.8	0.670	0.000	0.712	n/a	n/a	0.134	n/a	n/a	n/a	n/a	n/a	0.690	0.000	0.721	n/a	n/a	n/a	n/a
(6) m=0	2.2	0.729	0.000	0.830	0.709	0.218	0.150	0.124	0.018	0.849	0.000	0.141	0.718	0.000	0.822	0.711	0.221	0.124	0.034
Parameter: h																			
(7) m>0	0.2	0.644	0.623	0.737	n/a	n/a	0.087	n/a	n/a	n/a	n/a	n/a	0.682	0.644	0.759	n/a	n/a	n/a	n/a
(8) m>0	0.8	0.871	0.781	0.886	0.585	0.171	0.421	0.325	0.036	---	---	---	0.781	0.719	0.820	0.596	0.192	0.325	0.058
(9) m=0	0.2	0.611	0.000	0.720	n/a	n/a	0.067	n/a	n/a	n/a	n/a	n/a	0.669	0.000	0.751	n/a	n/a	n/a	n/a
(10) m=0	0.8	0.810	0.000	0.840	0.593	0.185	0.303	0.238	0.030	---	---	---	0.754	0.000	0.803	0.599	0.199	0.239	0.048
Parameter: α																			
(11) m>0	1.2	0.718	0.611	0.780	0.604	0.208	0.159	0.124	0.020	0.885	0.709	0.136	0.712	0.641	0.776	0.605	0.210	0.124	0.035
(12) m>0	1.8	0.772	0.747	0.814	0.597	0.194	0.225	0.174	0.026	---	---	---	0.735	0.700	0.791	0.602	0.204	0.175	0.042
Parameter: ρ																			
(13) m>0	5.0	0.740	0.602	0.794	0.601	0.203	0.181	0.141	0.022	0.963	0.716	0.130	0.721	0.575	0.782	0.604	0.208	0.141	0.038

Notes: This table reports the results of profit maximization simulations to determine the values of detailing, k, and DTCA, m, for which the brand name firm has the highest profit given the parameters indicated. Each simulation is presented in a row, (1) to (13). The columns present three different assumptions/strategies for the brand name firm: assume no entry, block entry and assume entry. The price and profit according to each strategy are presented in the columns as indicated. The highlighted cells represent the brand-name firm's best strategy assuming the fixed cost of entry, F, for the generic firm is 0.015.

DTCA Effectiveness and Cost:

As the effectiveness of DTCA, as measured by α, increases, m^* also increases which prompts subsequent increases in k^*. See rows (11) and (12). If DTCA for a particular drug is effective at increasing symptom salience, it becomes more profitable to expose more consumers to DTCA and physicians to detailing. This may be the case for conditions for which symptoms are fairly common (insomnia) but for which consumers may not visit the doctor. It behoves brand-name firms to more broadly expose the population to information that can more effectively motivate physician visits. If a condition already prompts doctor visits or has sufficiently salient symptoms and α is low, the investment in DTCA is not as profitable.

The base cost of DTCA is assumed to be less per exposure than detailing due to media advertising being less labor intensive than some forms of detailing which involve sales calls to physicians. If the opposite is assumed and DTCA per percentage of the population exposed is more expensive than detailing per percentage of the physicians advertised to, then m^* and $k*$ are both lower than when DTCA is less expensive than detailing which decreases brand profit. This is seen by comparing the k^* and m^* values in row (13) to row (1).

Welfare:

DTCA impacts consumer and producer welfare directly and indirectly by expanding the market for the entire class of drugs. For producers, DTCA increases brand profit in Period 1 and generic profit in Period 2 through increased demand by prompting more patients to visit the doctor. The brand-name firm in Period 2 may experience increased or decreased profit depending on generic entry. If entry was inevitable based on exogenous market conditions, then brand-profit will be higher than it would have been in absence of DTCA. On the other hand, DTCA increases the threshold of detailing for which the generic firm would enter the market. This promotes increased generic entry for certain conditions.

On the consumer side, while DTCA does not directly impact price, it is a complement

to detailing and increases the brand-name firm's incentive to advertise to doctors. This increases the monopoly price in Period 1 and decreases consumer welfare. In Period 2, advertising directly to consumers indirectly decreases Period 2 price by promoting generic entry and increased competition in Period 2 through an increase in the size of the detailed market.

3.8 Conclusion

The pharmaceutical market has seen increases in prescription expenditures and advertising to both physicians and patients. The relaxation of DTCA regulations in 1997 motivated a desire to understand how DTCA impacts the market-entry decision of generic-pharmaceutical manufacturers after patent expiration. I expanded a vertical differentiation model of the pharmaceutical market from Königbauer (2007) to include DTCA. The model demonstrates that DTCA prompts the incumbent brand-name firm to increase detailing and raise monopoly price. DTCA increases the threshold of detailing under which generic entry remains profitable. Generic entry is also more likely for conditions that are more widespread. Also, as the effectiveness of DTCA increases, it is more profitable for the brand-name firm to invest in higher amounts of DTCA and detailing. DTCA decreases price after patent expiration by promoting generic entry and increased competition.

The theoretical model of generic market entry under two forms of advertising has broad policy implications for pharmaceutical markets. Additional empirical analysis can shed further light on the hypothesis generated by the model in market settings for a variety of drug classes. This will further the discussion around DTCA and the welfare impacts for producers and consumers in pharmaceutical markets.

References

ACS (2020). Facts & Figures 2020: Key Statistics for Prostate Cancer. Atlanta, GA.

AHA (2021). Heart Disease and Stroke Statistics Update Fact Sheet At-a-Glance. Technical report, American Heart Association.

Baicker, K. and A. Chandra (2004). Medicare Spending, The Physician Workforce, And Beneficiaries' Quality Of Care. *Health Affairs 23*(Suppl1), W4–184. Publisher: Project HOPE-The People-to-People Health Foundation, Inc.

Baicker, K., S. Mullainathan, and J. Schwartzstein (2015). Behavioral Hazard in Health Insurance. *The Quarterly Journal of Economics 130*(4), 1623–1667.

Barbash, G. I. and S. A. Glied (2010). New Technology and Health Care Costs — The Case of Robot-Assisted Surgery. *New England Journal of Medicine 363*(8), 701–704.

Birkmeyer, J. D., A. E. Siewers, E. V. Finlayson, T. A. Stukel, F. L. Lucas, I. Batista, H. G. Welch, and D. E. Wennberg (2002, April). Hospital Volume and Surgical Mortality in the United States. *New England Journal of Medicine 346*(15), 1128–1137.

BLS (2010). Consumer Price Index. Technical report, Bureau of Labor Statistics, U.S. Department of Labor.

Brekke, K. R. and M. Kuhn (2006). Direct to consumer advertising in pharmaceutical markets. *Journal of Health Economics 25*(1), 102–130.

Broadbent, E., L. Donkin, and J. C. Stroh (2011). Illness and Treatment Perceptions Are As-

sociated With Adherence to Medications, Diet, and Exercise in Diabetic Patients. *Diabetes Care 34*(2), 338–340.

Burke, L. G., A. B. Frakt, D. Khullar, E. J. Orav, and A. K. Jha (2017, May). Association Between Teaching Status and Mortality in US Hospitals. *JAMA 317*(20), 2105.

Cabrales, A. (2003). Pharmaceutical Generics, Vertical Product Differentiation, and Public Policy. *SSRN Electronic Journal*.

CDC (2014). *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General.* (2, Fifty Years of Change 1964–2014 ed.). National Center for Chronic Disease Prevention and Health Promotion, Atlanta (GA): Centers for Disease Control and Prevention (US): Office on Smoking and Health.

CDC (2018). Underlying Cause of Death, 1999–2018. Technical report, Centers for Disease Control and Prevention: WONDER Online Database.

CDC (2020). Prostate Cancer Statistics. Technical report, CDC: Division of Cancer Prevention and Control.

Census (2020). Population of the United States by Year, 1990 - 2017. Technical report, US Census Bureau.

Chandra, A., D. Cutler, and Z. Song (2011). Who Ordered That? The Economics of Treatment Choices in Medical Care. In *Handbook of Health Economics*, Volume 2, pp. 397–432. Elsevier.

Chandra, A., A. Finkelstein, A. Sacarny, and C. Syverson (2016). Health Care Exceptionalism? Performance and Allocation in the US Health Care Sector. *American Economic Review 106*(8), 2110–2144.

Chandra, A. and D. Staiger (2007). Productivity Spillovers in Health Care: Evidence from the Treatment of Heart Attacks. *Journal of Political Economy 115*(1), 103–140.

Chiuve, S. E., M. L. McCullough, F. M. Sacks, and E. B. Rimm (2006). Healthy Lifestyle Factors in the Primary Prevention of Coronary Heart Disease Among Men: Benefits Among Users and Nonusers of Lipid-Lowering and Antihypertensive Medications. *Circulation 114*(2), 160–167.

CMS (2015). Hospital Outpatient Regulations and Notices: Addendum E: Final HCPCS Codes That Are Paid Only as Inpatient Procedures for CY 2015. Technical Report CMS-1613-FC, Centers for Medicare & Medicaid Services.

CMS (2018). National Health Expenditure Data. Technical report, Office of the Actuary, Centers for Medicare & Medicaid Services.

CMS (2020a). CY 2021 Medicare Hospital Outpatient Prospective Payment System and Ambulatory Surgical Center Payment System Final Rule. Technical Report CMS-1736-FC, Centers for Medicare & Medicaid Services.

CMS (2020b). National Health Expenditures 2019 Highlights. Technical report, Centers for Medicare & Medicaid Services.

Cutler, D. M., R. S. Huckman, and J. T. Kolstad (2010). Input Constraints and the Efficiency of Entry: Lessons from Cardiac Surgery. *American Economic Journal: Economic Policy 2*(1), 51–76.

Datti, B. and M. W. Carter (2006). The effect of direct-to-consumer advertising on prescription drug use by older adults. *Drugs & Aging 23*(1), 71–81.

Dave, D. and H. Saffer (2012). Impact of Direct-to-Consumer Advertising on Pharmaceutical Prices and Demand. *Southern Economic Journal 79*(1), 97–126.

Deshpande, M. and Y. Li (2019). Who Is Screened Out? Application Costs and the Targeting of Disability Programs. *American Economic Journal: Economic Policy 11*(4), 213–248.

Dranove, D., M. Shanley, and C. Simon (1992). Is Hospital Competition Wasteful? *The RAND Journal of Economics 23*(2), 247.

D'Agostino, R. B., R. S. Vasan, M. J. Pencina, P. A. Wolf, M. Cobain, J. M. Massaro, and W. B. Kannel (2008). General Cardiovascular Risk Profile for Use in Primary Care: The Framingham Heart Study. *Circulation 117*(6), 743–753.

Erwteman, T. M., N. Nagelkerke, J. Lubsen, M. Koster, and A. J. Dunning (1984). Beta blockade, diuretics, and salt restriction for the management of mild hypertension: a randomised double blind trial. *BMJ 289*(6442), 406–409.

Fadlon, I. and T. H. Nielsen (2019). Family Health Behaviors. *American Economic Review 109*(9), 3162–3191.

FDA (2000). FDA Approves New Robotic Surgery Device.

FDA (2020). FDA Approved Drugs.

Finkelstein, J., E. Eckersberger, H. Sadri, S. Taneja, H. Lepor, and B. Djavan (2010). Open Versus Laparoscopic Versus Robot-Assisted Laparoscopic Prostatectomy: The European and US Experience. *Reviews in Urology 12*, 35–43.

Fischer, M. A. and J. Avorn (2003). Economic Consequences of Underuse of Generic Drugs: Evidence from Medicaid and Implications for Prescription Drug Benefit Plans: Economic Consequences of Underuse of Generic Drugs. *Health Services Research 38*(4), 1051–1064.

Galton, L. (1976). Encouraging Reports from hospitals here and abroad. *Boston Globe*, 18.

Gellad, Z. F. and K. W. Lyles (2007). Direct-to-Consumer Advertising of Pharmaceuticals. *The American Journal of Medicine 120*(6), 475–480.

Golub, S. A., W. Kowalczyk, C. L. Weinberger, and J. T. Parsons (2010). Preexposure Prophylaxis and Predicted Condom Use Among High-Risk Men Who Have Sex With Men. *JAIDS Journal of Acquired Immune Deficiency Syndromes 54*(5), 548–555.

Goodman-Bacon, A. (2021). Difference-in-differences with variation in treatment timing. *Journal of Econometrics*, 254–277.

Gourieroux, C., A. Monfort, and A. Trognon (1984, May). Pseudo Maximum Likelihood Methods: Applications to Poisson Models. *Econometrica 52*(3), 701.

Grabowski, H. G. and J. M. Vernon (1992). Brand Loyalty, Entry, and Price Competition in Pharmaceuticals after the 1984 Drug Act. *The Journal of Law and Economics 35*(2), 331–350.

Grossman, J. M. and D. A. Banks (1998). Unrestricted Entry and Nonprice Competition: The Case of Technological Adoption in Hospitals. *International Journal of the Economics of Business 5*(2), 223–245.

Gruber, J., P. Levine, and D. Staiger (1999, February). Abortion Legalization and Child Living Circumstances: Who is the "Marginal Child"? *The Quarterly Journal of Economics 114*(1), 263–291.

Grundy, S. M., J. I. Cleeman, C. N. B. Merz, H. B. Brewer, L. T. Clark, D. B. Hunninghake, R. C. Pasternak, S. C. Smith, and N. J. Stone (2004). Implications of Recent Clinical Trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. *Circulation 110*(2), 227–239.

Ha, S. K. (2014). Dietary Salt Intake and Hypertension. *Electrolytes & Blood Pressure 12*(1), 7.

Hajar, R. (2017). Coronary Heart Disease: From Mummies to 21st Century. *Heart Views: The Official Journal of the Gulf Heart Association 18*(2), 68–74.

Hausman, J., B. H. Hall, and Z. Griliches (1984, July). Econometric Models for Count Data with an Application to the Patents-R & D Relationship. *Econometrica 52*(4), 909.

Hoagland, A. (2021). An Ounce of Prevention or a Pound of Cure? The Value of Health Risk Information.

Hodgkin, D. (1996). Specialized service offerings and patients' choice of hospital: The case of cardiac catheterization. *Journal of Health Economics 15*(3), 305–332.

Hopkins, J. (2021). Transurethral Resection of the Prostate (TURP).

Horn, D. (2013). *Chronic Resilience: Sanity-Saving Strategies for Women Coping with the Stress of Illness*. Conari Press.

Hurwitz, M. A. and R. E. Caves (1988). Persuasion or Information? Promotion and the Shares of Brand Name and Generic Pharmaceuticals. *The Journal of Law and Economics 31*(2), 299–320.

Hyman, D. J. and V. N. Pavlik (2000). Self-reported Hypertension Treatment Practices Among Primary Care Physicians: Blood Pressure Thresholds, Drug Choices, and the Role of Guidelines and Evidence-Based Medicine. *Archives of Internal Medicine 160*(15), 2281.

Ilic, D., S. M. Evans, C. A. Allan, J. H. Jung, D. Murphy, and M. Frydenberg (2017). Laparoscopic and robotic-assisted versus open radical prostatectomy for the treatment of localised prostate cancer. *Cochrane Database of Systematic Reviews*.

Imbens, G. W. and J. M. Wooldridge (2009). Recent Developments in the Econometrics of Program Evaluation. *Journal of Economic Literature 47*(1), 5–86.

Jacobs, B. L., Y. Zhang, T. A. Skolarus, J. T. Wei, J. E. Montie, F. R. Schroeck, and B. K. Hollenbeck (2013). Certificate of Need Legislation and the Dissemination of Robotic Surgery for Prostate Cancer. *Journal of Urology 189*(1), 80–85.

Jorgenson, D. W. (2011). Innovation and Productivity Growth: T.W. Schultz Lecture. *American Journal of Agricultural Economics 93*(2), 276–296.

Kaestner, R., M. Darden, and D. Lakdawalla (2014). Are investments in disease prevention complements? The case of statins and health behaviors. *Journal of Health Economics 36*, 151–163.

Kasting, M. L., G. K. Shapiro, Z. Rosberger, J. A. Kahn, and G. D. Zimet (2016). Tempest in a teapot: A systematic review of HPV vaccination and risk compensation research. *Human Vaccines & Immunotherapeutics 12*(6), 1435–1450.

Kelleher (2018). By the numbers a comparison of Framingham's population to the United States. *MetroWest Daily News*.

Kempner, W. (1948). Treatment of hypertensive vascular disease with rice diet. *The American Journal of Medicine 4*(4), 545–577.

Kessler, D. P. and M. B. McClellan (2000). Is Hospital Competition Socially Wasteful? *The Quarterly Journal of Economics 115*(2), 577–615.

KFF (2018). Prescription Drugs Filled at Retail Pharmacies. Technical report, Henry J. Kaiser Family Foundation.

Khera, A. V., C. A. Emdin, I. Drake, P. Natarajan, A. G. Bick, N. R. Cook, D. I. Chasman, U. Baber, R. Mehran, D. J. Rader, V. Fuster, E. Boerwinkle, O. Melander, M. Orho-Melander, P. M. Ridker, and S. Kathiresan (2016). Genetic Risk, Adherence to a Healthy Lifestyle, and Coronary Disease. *New England Journal of Medicine 375*(24), 2349–2358.

Kim, H. B., S. A. Lee, and W. Lim (2019). Knowing is not half the battle: Impacts of information from the National Health Screening Program in Korea. *Journal of Health Economics 65*, 1–14.

Ko, H. and S. A. Glied (2021, March). Robotic Prostatectomy and Prostate Cancer–Related Medicaid Spending: Evidence from New York State. *Journal of General Internal Medicine*.

Kornfield, R., J. Donohue, E. R. Berndt, and G. C. Alexander (2013). Promotion of Prescription Drugs to Consumers and Providers, 2001–2010. *PLoS ONE 8*(3), e55504.

Krauss, R. M., R. J. Deckelbaum, N. Ernst, E. Fisher, B. V. Howard, R. H. Knopp, T. Kotchen, A. H. Lichtenstein, H. C. McGill, T. A. Pearson, T. E. Prewitt, N. J. Stone, L. Van Horn, and R. Weinberg (1996). Dietary Guidelines for Healthy American Adults: A Statement for Health Professionals From the Nutrition Committee, American Heart Association. *Circulation 94*(7), 1795–1800.

Königbauer, I. (2007). Advertising and generic market entry. *Journal of Health Economics 26*(2), 286–305.

La Berge, A. F. (2007). How the Ideology of Low Fat Conquered America. *Journal of the History of Medicine and Allied Sciences 63*(2), 139–177.

Leaverton, P. E., P. D. Sorlie, J. C. Kleinman, A. L. Dannenberg, L. Ingster-Moore, W. B. Kannel, and J. C. Cornoni-Huntley (1987). Representativeness of the Framingham risk model for coronary heart disease mortality: a comparison with a national cohort study. *Journal of Chronic Diseases 40*(8), 775–784.

Lepor, H. (2000). Selecting candidates for radical prostatectomy. *Reviews in Urology 2*(3), 182–189.

Luft, F. C. and M. H. Weinberger (1988). Review of salt restriction and the response to antihypertensive drugs. Satellite symposium on calcium antagonists. *Hypertension 11*(2_pt_2).

Mack, J. (2016). Annual Spending on Direct-to-Consumer Drug Advertising Ties an All-Time High.

Mack, M. J. (2001). Minimally Invasive and Robotic Surgery. *JAMA 285*(5), 568.

Mahmood, S. S., D. Levy, R. S. Vasan, and T. J. Wang (2014). The Framingham Heart

Study and the epidemiology of cardiovascular disease: a historical perspective. *The Lancet 383*(9921), 999–1008.

Mahoney, S. (2018). DTC Report 2018: Will more supersized campaigns follow Opdivo's and Keytruda's massive strikes? *Medical Marketing and Media*.

Mancino, L. and F. Kuchler (2009). Offsetting Behavior in Reducing High Cholesterol: Substitution of Medication for Diet and Lifestyle Changes. *Journal of Choice Modelling 2*(1), 51–64.

Mankiw, N. G. and M. D. Whinston (1986). Free Entry and Social Inefficiency. *The RAND Journal of Economics 17*(1), 48.

Morton, F. M. S. (2002). Horizontal Integration Between Brand and Generic Firms in the Pharmaceutical Industry. *Journal of Economics & Management Strategy 11*(1), 135–168.

NCSL (2019). Certificate of Need Laws. Technical report, National Conference of State Legislatures.

NHLBI (1984). The Lipid Research Clinics Coronary Primary Prevention Trial results. I. Reduction in incidence of coronary heart disease. *JAMA 251*(3), 351–364.

Ogden, C. L., M. D. Carroll, B. K. Kit, and K. M. Flegal (2014). Prevalence of Childhood and Adult Obesity in the United States, 2011-2012. *JAMA 311*(8), 806.

Oppenheimer, G. M. (2005). Becoming the Framingham Study 1947-1950. *American Journal of Public Health 95*(4), 602–610.

Oster, E. (2018). Diabetes and Diet: Purchasing Behavior Change in Response to Health Information. *American Economic Journal: Applied Economics 10*(4), 308–348.

Palumbo, F. B. and C. D. Mullins (2002). The development of direct-to-consumer prescription drug advertising regulation. *Food and Drug Law Journal 57*(3), 423–443.

Peltzman, S. (1975). The Effects of Automobile Safety Regulation. *Journal of Political Economy 83*(4), 677–725.

Prasad, V. and A. B. Jena (2014). The Peltzman effect and compensatory markers in medicine. *Healthcare 2*(3), 170–172.

Rosenthal, M. B., E. R. Berndt, J. M. Donohue, R. G. Frank, and A. M. Epstein (2002, February). Promotion of Prescription Drugs to Consumers. *New England Journal of Medicine 346*(7), 498–505.

Saklayen, M. G. and N. V. Deshpande (2016). Timeline of History of Hypertension Treatment. *Frontiers in Cardiovascular Medicine Volume 3*.

Sandoval Salinas, C., A. L. González Rangel, J. G. Cataño Cataño, J. C. Fuentes Pachón, and J. S. Castillo Londoño (2013, November). Efficacy of Robotic-Assisted Prostatectomy in Localized Prostate Cancer: A Systematic Review of Clinical Trials. *Advances in Urology 2013*, e105651. Publisher: Hindawi.

Savage, C. J. and A. J. Vickers (2009). Low Annual Caseloads of United States Surgeons Conducting Radical Prostatectomy. *Journal of Urology 182*(6), 2677–2681.

Schwartz, L. M. and S. Woloshin (2019). Medical Marketing in the United States, 1997-2016. *JAMA 321*(1), 80.

SEC (2003). Intuitive Surgical and Computer Motion Announce Merger Agreement. Technical report, Securities and Exchange Commission.

Sheetz, K. H., J. Claflin, and J. B. Dimick (2020). Trends in the Adoption of Robotic Surgery for Common Surgical Procedures. *JAMA Network Open 3*(1), e1918911.

Shimokawa, S. and S. Shimokawa (2015). Interaction between Dietary Knowledge and Exercise Knowledge in Leading to Healthier Diet after Hypertension Diagnosis: Evidence from China. Publisher: Unknown.

Shrank, W. H., E. R. Cox, M. A. Fischer, J. Mehta, and N. K. Choudhry (2009). Patients' Perceptions Of Generic Medications. *Health Affairs 28*(2), 546–556.

Shrank, W. H., J. N. Liberman, M. A. Fischer, C. Girdish, T. A. Brennan, and N. K. Choudhry (2011). Physician perceptions about generic drugs. *The Annals of Pharmacotherapy 45*(1), 31–38.

Skinner, J. (2011). Causes and Consequences of Regional Variations in Health Care. In *Handbook of Health Economics*, Volume 2, pp. 45–93. Elsevier.

Skinner, J. and D. Staiger (2007). Technology Adoption from Hybrid Corn to Beta-Blockers. In *Hard-to-Measure Goods and Services: Essays in Honor of Zvi Griliches*, pp. 545–570. University of Chicago Press.

Skinner, J. and D. Staiger (2015). Technology Diffusion and Productivity Growth in Health Care. *Review of Economics and Statistics 97*(5), 951–964.

Solon, G., S. J. Haider, and J. M. Wooldridge (2015). What Are We Weighting For? *Journal of Human Resources 50*(2), 301–316.

Srinivasan, A. V. (2019). Propranolol: A 50-Year Historical Perspective. *Annals of Indian Academy of Neurology 22*(1), 21–26.

Stevens, J. D., G. Binstok, J. F. Mullane, J. W. Woods, A. W. Pittman, F. del Greco, C. Huang, and J. H. Morledge (1983). Propranolol-hydralazine combination in essential hypertension. *Clinical Therapeutics 5*(5), 525–539.

Thomas, R. L. and E. Mentzakis (2020). The direct and spillover effects of diabetes diagnosis on behaviour. *University of Southampton Working Paper*.

Trap-Jensen, J. (1988). Effects of smoking on the heart and peripheral circulation. *American Heart Journal 115*(1), 263–267.

USPSTF (2008). Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine 149*, 185–191.

Virani, S. S., A. Alonso, E. J. Benjamin, M. S. Bittencourt, C. W. Callaway, A. P. Carson, A. M. Chamberlain, A. R. Chang, S. Cheng, F. N. Delling, L. Djousse, M. S. Elkind, J. F. Ferguson, M. Fornage, S. S. Khan, B. M. Kissela, K. L. Knutson, T. W. Kwan, D. T. Lackland, T. T. Lewis, J. H. Lichtman, C. T. Longenecker, M. S. Loop, P. L. Lutsey, S. S. Martin, K. Matsushita, A. E. Moran, M. E. Mussolino, A. M. Perak, W. D. Rosamond, G. A. Roth, U. K. Sampson, G. M. Satou, E. B. Schroeder, S. H. Shah, C. M. Shay, N. L. Spartano, A. Stokes, D. L. Tirschwell, L. B. VanWagner, C. W. Tsao, and On behalf of the American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee (2020). Heart Disease and Stroke Statistics—2020 Update: A Report From the American Heart Association. *Circulation 141*(9).

Weinmeyer, R. (2013). Direct-to-Consumer Advertising of Drugs. *AMA Journal of Ethics 15*(11), 954–958.

Wilson, P. W. F. (2021a). Atherosclerotic cardiovascular disease risk assessment for primary prevention in adults: Our approach. Technical Report Topic 1546 Version 47.0, UpToDate.

Wilson, P. W. F. (2021b). Cardiovascular disease risk assessment for primary prevention: Risk calculators. Technical Report Topic 114029 Version 20.0, UpToDate.

Wooldridge, J. M. (1999, May). Distribution-free estimation of some nonlinear panel data models. *Journal of Econometrics 90*(1), 77–97.

Wosinska, M. (2002). Just What the Patient Ordered? Direct-to-Consumer Advertising and the Demand for Pharmaceutical Products. *SSRN Electronic Journal*.

Yaxley, J. W., G. D. Coughlin, S. K. Chambers, S. Occhipinti, H. Samaratunga, L. Zajdlewicz, N. Dunglison, R. Carter, S. Williams, D. J. Payton, J. Perry-Keene, M. F. Lavin, and R. A. Gardiner (2016). Robot-assisted laparoscopic prostatectomy versus open

radical retropubic prostatectomy: early outcomes from a randomised controlled phase 3 study. *The Lancet 388*(10049), 1057–1066.

Zhao, M., Y. Konishi, and P. Glewwe (2013). Does information on health status lead to a healthier lifestyle? Evidence from China on the effect of hypertension diagnosis on food consumption. *Journal of Health Economics 32*(2), 367–385.

Zweifel, P. (2017). The Seven Myths of Health and Health Care. *Pharmacoeconomics: Open Access 02*(01).

Appendix A

Appendix to Chapter 1

A.1 Calculating the Framingham Risk Score

The Framingham Risk Score (FRS) is calculated from the 2008 formula published by the Adult Treatment Panel III from the National Heart Lung and Blood Institute (D'Agostino et al., 2008). The score is calculated separately for men and women. Each score has an associated probability of experiencing a cardiovascular event in the next 10 years. The calculation below excludes the score assignment for high-density lipoprotein (HDL) due to lack of consistent data collection with the original Framingham cohort. Excluding this measure introduces variability into the score of up to 3 points across the sample. However, total cholesterol was collected at each exam in the sample time period and is included in the FRS. The score assignment is as follows:

									On Hypertension Medication					Not on Hypertension Medication				
		Age	Total Cholesterol <160 mg/dL	Total Cholesterol 160-199 mg/dL	Total Cholesterol 200-239 mg/dL	Total Cholesterol 240-279 mg/dL	Total Cholesterol ≥280 mg/dL	Current Smoker	Systolic blood pressure <120 mm Hg	Systolic blood pressure 120-129 mm Hg	Systolic blood pressure 130-139 mm Hg	Systolic blood pressure 140-159 mm Hg	Systolic blood pressure ≥160 mm Hg	Systolic blood pressure <120 mm Hg	Systolic blood pressure 120-129 mm Hg	Systolic blood pressure 130-139 mm Hg	Systolic blood pressure 140-159 mm Hg	Systolic blood pressure ≥160 mm Hg
Female																		
Age Range	20 - 34	-7	0	4	8	11	13	9	0	3	4	5	6	0	1	2	3	4
	35 - 39	-3	0	4	8	11	13	9	0	3	4	5	6	0	1	2	3	4
	40 - 44	0	0	3	6	8	10	7	0	3	4	5	6	0	1	2	3	4
	45 - 49	3	0	3	6	8	10	7	0	3	4	5	6	0	1	2	3	4
	50 - 54	6	0	2	4	5	7	4	0	3	4	5	6	0	1	2	3	4
	55 - 59	8	0	2	4	5	7	4	0	3	4	5	6	0	1	2	3	4
	60 - 64	10	0	1	2	3	4	2	0	3	4	5	6	0	1	2	3	4
	65 - 69	12	0	1	2	3	4	2	0	3	4	5	6	0	1	2	3	4
	70 - 74	14	0	1	1	2	2	1	0	3	4	5	6	0	1	2	3	4
	75+	16	0	1	1	2	2	1	0	3	4	5	6	0	1	2	3	4
Male																		
Age Range	20 - 34	-9	0	4	7	9	11	8	0	1	2	2	3	0	0	1	1	2
	35 - 39	-4	0	4	7	9	11	8	0	1	2	2	3	0	0	1	1	2
	40 - 44	0	0	3	5	6	8	5	0	1	2	2	3	0	0	1	1	2
	45 - 49	3	0	3	5	6	8	5	0	1	2	2	3	0	0	1	1	2
	50 - 54	6	0	2	3	4	5	3	0	1	2	2	3	0	0	1	1	2
	55 - 59	8	0	2	3	4	5	3	0	1	2	2	3	0	0	1	1	2
	60 - 64	10	0	1	1	2	3	1	0	1	2	2	3	0	0	1	1	2
	65 - 69	11	0	1	1	2	3	1	0	1	2	2	3	0	0	1	1	2
	70 - 74	12	0	0	0	1	1	1	0	1	2	2	3	0	0	1	1	2
	75+	13	0	0	0	1	1	1	0	1	2	2	3	0	0	1	1	2

The score is translated into a prediction of 10-year risk of being diagnosed with CVD using the chart below:

	10-Year Risk	
FRS	Male	Female
<1	0.00	0.00
1	0.01	0.00
2	0.01	0.00
3	0.01	0.00
4	0.01	0.00
5	0.02	0.00
6	0.02	0.00
7	0.03	0.00
8	0.04	0.00
9	0.05	0.01
10	0.06	0.01
11	0.08	0.01
12	0.10	0.01
13	0.12	0.02
14	0.16	0.02
15	0.20	0.03
16	0.25	0.04
17	0.30	0.05
18	0.30	0.06
19	0.30	0.08
20	0.30	0.11
21	0.30	0.14
22	0.30	0.17
23	0.30	0.22
24	0.30	0.27
25+	0.30	0.30

A.2 Risk Score Matching

An alternative to matching on the timing of a CVD diagnosis to identify the control group for the main analysis presented in Section 1.4 is to match on Framingham risk score (FRS) – the 10-year risk of experiencing a CVD event. See Appendix A.1 for detail on how the FRS is calculated. Matching begins by determining the treatment group. This is defined the same way as it is in the main analysis, Section 1.4: treated individuals are those that will have a first diagnosis of CVD at one of six exams between exam 9 and 14. Additionally, they must attend the exam prior to diagnosis, the diagnosis exam and the two exams after diagnosis. The potential control group for each sub-sample of treated individuals are study participants who have not experienced a diagnosis of CVD prior to the exam that the treated individual is diagnosed and must attend each exam that the treated attends. At the exam prior to diagnosis, the calculated FRS is used to match treated individuals (by sex) with one, or more, control individuals. The FRS takes into account age, total cholesterol, smoking status, systolic blood pressure and usage of hypertension medication, see Section A.1. The control group is weighted by their relative representation within each match cell such that the total weight for all control individuals for each treated individual sums to 1. The results using this matching procedure are presented in Table 1.5.

A.3 Appendix Tables

Table A1: Hypertension and Hyperlipidemia Medication Timeline

Year	Hypertension Medications Introduced	Hyperlipidemia Medications Introduced
1953	Peripherally Acting Alpha-Adrenergic Blockers & Vasodilators	
1954	Rauwolfia Alkaloids	
...		
1958	Diuretics	
...		
1973	Beta Blockers	Bile Acid Sequestrants
...		
1980		
1981	Angiotension-Converting Enzyme (ACE) Inhibitors	Fibrates
...		
1984	Centrally-Acting Alpha Adrenergics	
1985		
1986	Calcium Channel Blockers	
1987		Statins
...		
1995	Angiotension II Antagonists	
1996		
1997		Niacin
1998	Combination Medications	
...		
2001		Cholesterol Absorption Inhibitors
2002		Combination Medications

Notes: Timeline of FDA medication approvals for the introduction of each drug class listed. (FDA, 2020)

Table A2: Comparison of the Mean Ten-Year Risk of Cardiovascular Disease for Sample Treatment and Control Individuals by Group

	Treatment	Control	T-Statistic
Group 9	0.113	0.115	0.146
	(0.064)	(0.069)	
Group 10	0.117	0.115	-0.292
	(0.068)	(0.064)	
Group 11	0.101	0.093	-0.997
	(0.064)	(0.064)	
Group 12	0.165	0.159	-0.662
	(0.078)	(0.075)	
Group 13	0.120	0.115	-0.729
	(0.058)	(0.059)	
Group 14	0.128	0.110	-2.171
	(0.061)	(0.060)	

Notes: The above table presents the mean Framingham Risk Score (the probability of being diagnosed with CVD in the next ten years) at the time treated individuals are diagnosed. This indicates that there is not a statistical difference between the risk score of treated and control individuals at the time CVD diagnosis occurs in each group. the exception is group 14 which shows that treated individuals have a 1.7 percentage point higher probability of being diagnosed with CVD in the next 10 years.

Table A3: Association of Ten-Year Risk of Cardiovascular Disease with the Probability of Being Diagnosed with Cardiovascular Disease

	Ten-Year Risk	
Group 9	-0.219	(0.288)
Group 10	0.147	(0.318)
Group 11	0.120	(0.339)
Group 12	0.503 **	(0.198)
Group 13	-0.990 ***	(0.163)
Group 14	0.159	(0.278)
Total	0.045	(0.034)

Notes: Estimation results demonstrating the association of ten-year risk of CVD with the probability of being diagnosed at the time treated individuals are diagnosed. Controls include age, age-squared, 5-year age group, marital status, over 64-years-old and under treatment for diabetes and/or cancer diagnosis, and individual-fixed effects. The regressions are for the exam periods prior to and including diagnosis. The results indicate that there is not a systematic association between ten-year risk and being diagnosed as a treated individual as opposed to a control individual who is diagnosed at three or four exams in the future. The only two significant estimates are of opposite sign. Robust standard errors clustered at the individual level are in parenthesis. * Significant at the 10% level, ** significant at the 5% level, *** significant at the 1% level.

Table A4: Comparison of Means: Framingham and National Health Interview Survey

	(1) Male		(2) Female	
Age - Framingham	63.021	(9.298)	64.711	(9.687)
Age - NHIS	56.378	(18.469)	57.573	(19.730)
Married - Framingham	0.753	(0.431)	0.464	(0.499)
Married - NHIS	0.778	(0.416)	0.481	(0.500)
Widowed-Divorced-Separated - Framingham	0.068	(0.253)	0.311	(0.463)
Widowed-Divorced-Separated - NHIS	0.115	(0.319)	0.407	(0.491)
Sample Percentage - Framingham	0.507		0.493	
Sample Percentage - NHIS	0.488		0.512	
N - Framingham	6,470		6,280	
N - NHIS	3,900		4,008	

Notes: The above table presents means for key characteristics for the Framingham sample used in this study compared to a nationally-representative sample from the National Health Interview Survey (NHIS). Both samples include only individuals that have been diagnosed with CVD. During the time frame of this study, NHIS only asked about CVD status in 1974 and 1976; hence, the NHIS values are from those two years only. The characteristics reports are the available measures from NHIS for the applicable years. The NHIS values are weighted to reflect a nationally-representative sample. Standard deviation is in parenthesis.

A.4 Medication as a Complement or Substitute for Healthy Behavior

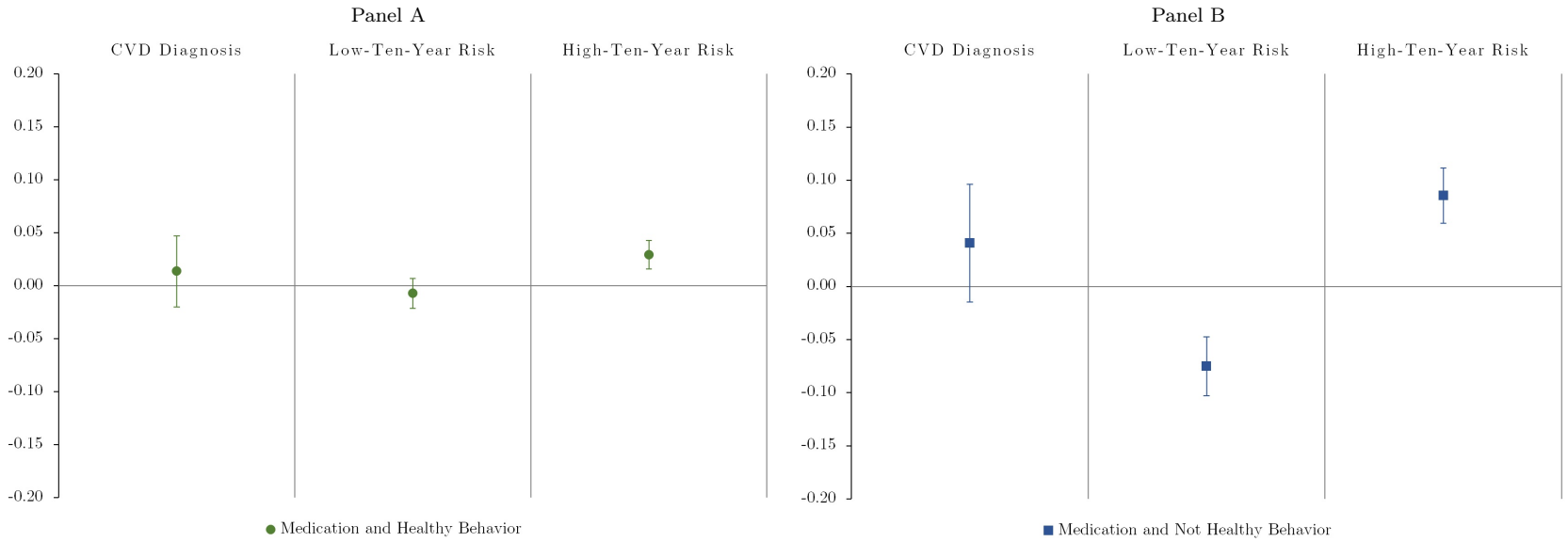
Table A5: Combination Treatment Choices After FDA Approval at Exam 12

	Current Smoker		Low-Salt Diet		Low-Fat Diet		BMI	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
	Rx & Non-Smoker	Rx & Smoker	RX & On Diet	RX & No Diet	RX & On Diet	RX & No Diet	Rx & BMI Decrease	Rx & BMI Increase
CVD Diagnosis	0.01 (0.02)	0.04 (0.03)	0.01 (0.01)	0.03 (0.03)	-0.0002 (0.01)	0.04 (0.03)	0.04 (0.02)	0.01 (0.03)
Low-Ten-Year Risk	-0.01 (0.01)	-0.08*** (0.01)	0.00 (0.01)	-0.08*** (0.02)	0.02** (0.01)	-0.10*** (0.02)	-0.03*** (0.01)	-0.05*** (0.01)
High-Ten-Year Risk	0.03*** (0.01)	0.09*** (0.01)	0.03*** (0.01)	0.10*** (0.02)	0.00 (0.01)	0.12*** (0.02)	0.03*** (0.01)	0.09*** (0.01)
N	8,161	8,161	6,948	6,948	6,948	6,948	8,161	8,161

Notes: This table presented the results from estimating equation 1.6 where the outcome is taking medication and engaging in healthy or unhealthy behavior as indicated in each column. Treated individuals are those who had a diagnosis of CVD at exam 12, 13 or 14 as compared to matched controls who will have a diagnosis of CVD two or three exams after the treated group; low-ten-year risk shows the association of low risk for CVD in the next 10 years (<10%) with each treatment choice as compared to those with intermediate risk, and high-ten-year risk shows the association of high risk of CVD in the next 10 years (20% or more) with each treatment choice as compared to those with intermediate risk. The time frame is exam 12 through exam 16 after the FDA approval of beta blockers and bile-acid sequestrants. Controls include age, age-squared, 5-year age group, marital status, over 64-years-old and under treatment for diabetes and/or cancer diagnosis plus individual-fixed effects. Robust standard errors clustered at the individual level are presented in parenthesis.

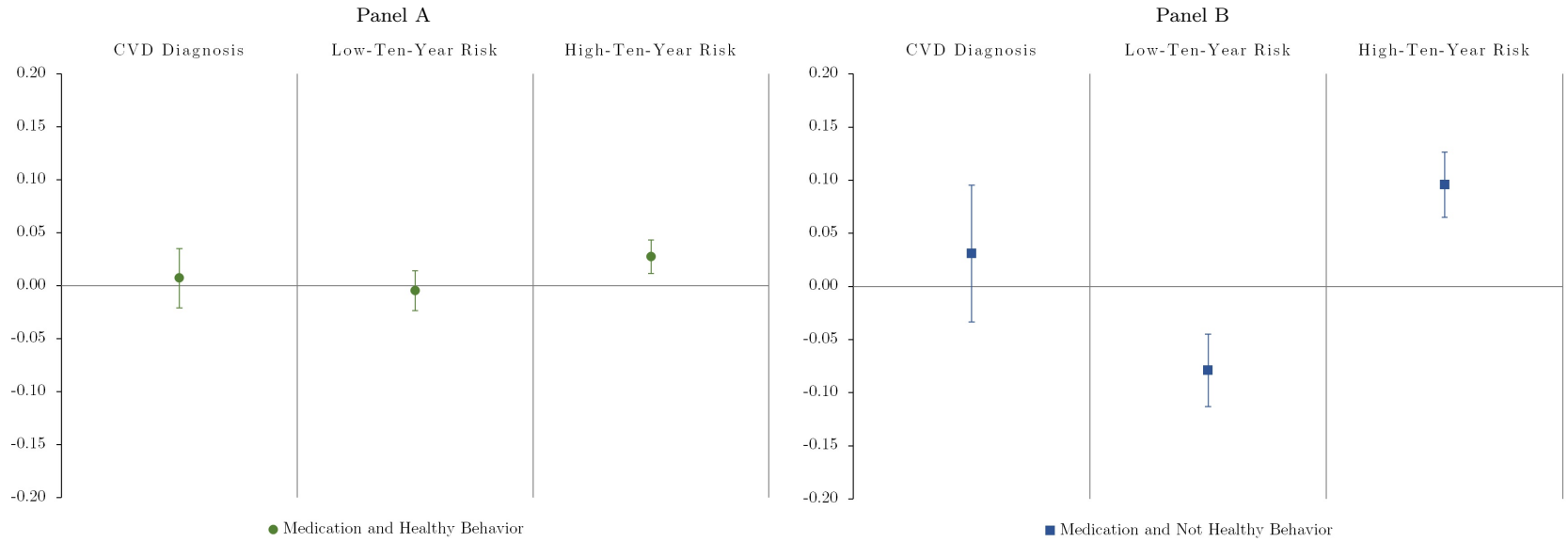
Figures A1, A2, A3 and A4 below provide a visual representation of the point estimates presented above.

Figure A1: Impact of Cardiovascular Disease Diagnosis and Risk Score on Choice of Treatment in Relation to Current Smoking Status



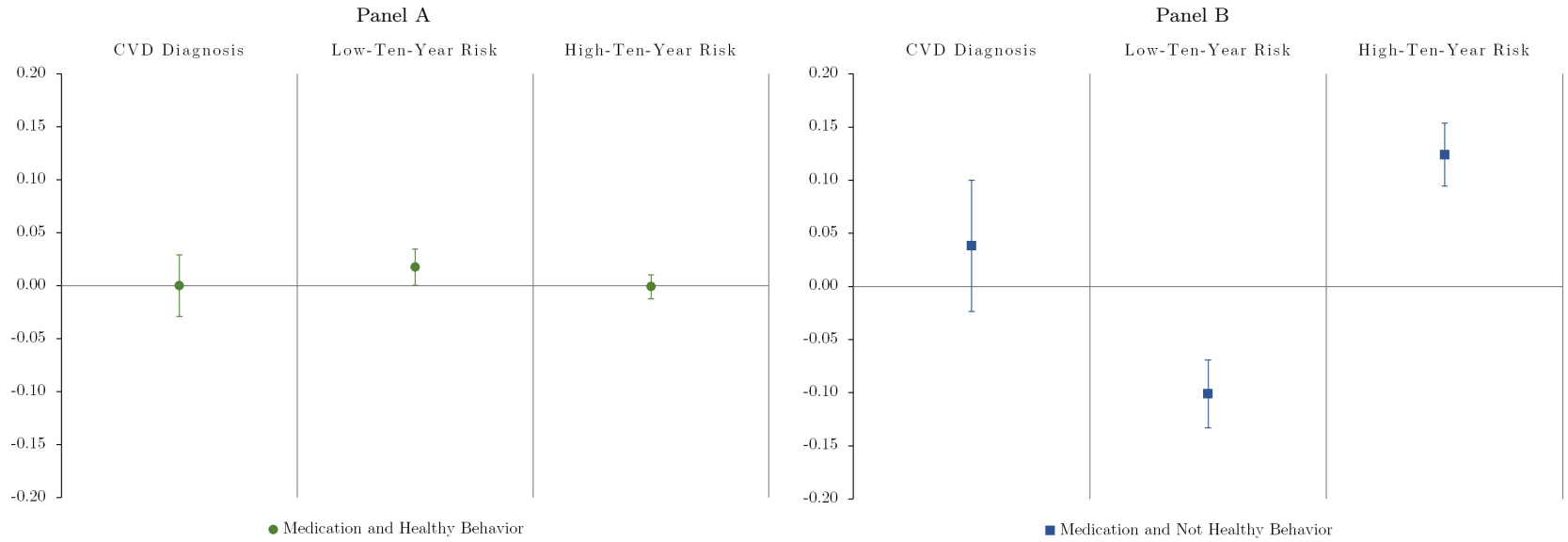
Notes: This figure plots the coefficients from estimating equation 1.6 where the outcome is taking medication and engaging in healthy (green bar) or unhealthy (blue bar) behavior. There are three variables plotted: CVD diagnosis indicates the impact of a CVD diagnosis for treated individuals (those who had a diagnosis of CVD at exam 12, 13 or 14) as compared to matched controls who will have a diagnosis of CVD two or three exams after the treated group; low-ten-year risk shows the association of low risk for CVD in the next 10 years (<10%) with each treatment choice, and high-ten-year risk shows the association of high risk of CVD in the next 10 years (20% or more) with each treatment choice. The time frame is exam 12 through exam 16 after the FDA approval of beta blockers and bile-acid sequestrants. Controls include age, age-squared, 5-year age group, marital status, over 64-years-old and under treatment for diabetes and/or cancer diagnosis plus individual-fixed effects. Error bars show 95% confidence intervals estimated with robust standard errors clustered at the individual level.

Figure A2: Impact of Cardiovascular Disease Diagnosis and Risk Score on Choice of Treatment in Relation to Following a Low-Salt Diet



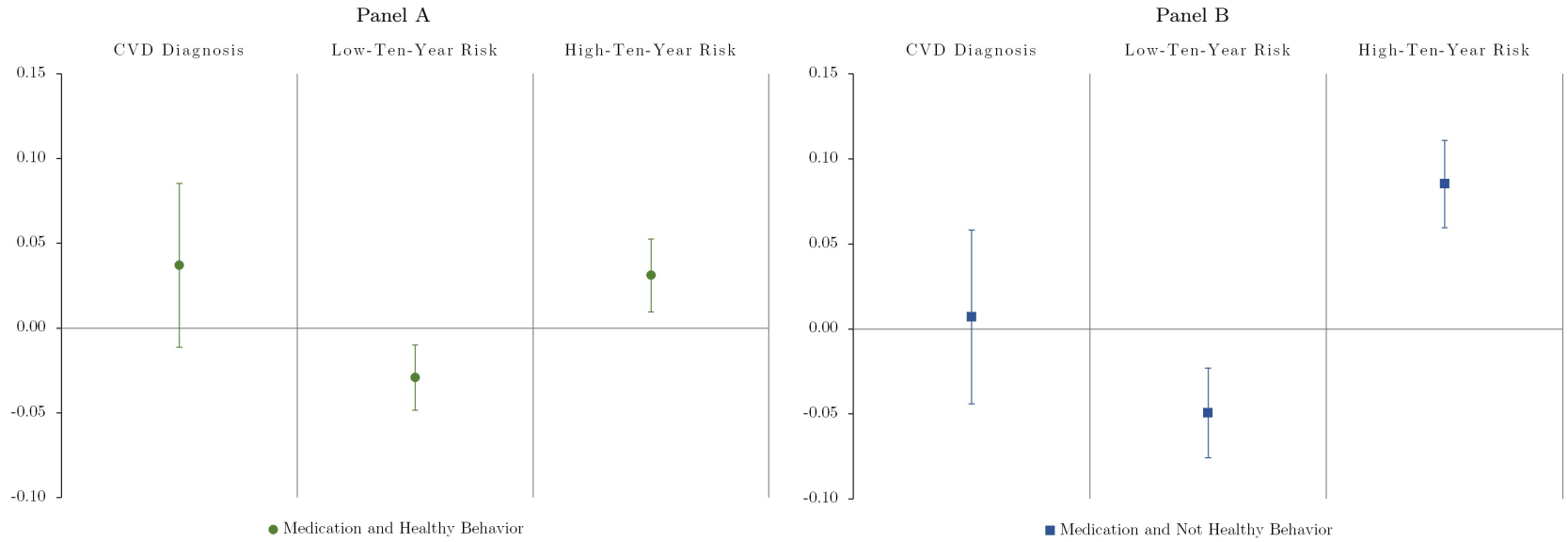
Notes: This figure plots the coefficients from estimating equation 1.6 where the outcome is taking medication and engaging in healthy (green bar) or unhealthy (blue bar) behavior. There are three variables plotted: CVD diagnosis indicates the impact of a CVD diagnosis for treated individuals (those who had a diagnosis of CVD at exam 12, 13 or 14) as compared to matched controls who will have a diagnosis of CVD two or three exams after the treated group; low-ten-year risk shows the association of low risk for CVD in the next 10 years (<10%) with each treatment choice, and high-ten-year risk shows the association of high risk of CVD in the next 10 years (20% or more) with each treatment choice. The time frame is exam 12 through exam 16 after the FDA approval of beta blockers and bile-acid sequestrants. Controls include age, age-squared, 5-year age group, marital status, over 64-years-old and under treatment for diabetes and/or cancer diagnosis plus individual-fixed effects. Error bars show 95% confidence intervals estimated with robust standard errors clustered at the individual level.

Figure A3: Impact of Cardiovascular Disease Diagnosis and Risk Score on Choice of Treatment in Relation to Following a Low-Fat Diet



Notes: This figure plots the coefficients from estimating equation 1.6 where the outcome is taking medication and engaging in healthy (green bar) or unhealthy (blue bar) behavior. There are three variables plotted: CVD diagnosis indicates the impact of a CVD diagnosis for treated individuals (those who had a diagnosis of CVD at exam 12, 13 or 14) as compared to matched controls who will have a diagnosis of CVD two or three exams after the treated group; low-ten-year risk shows the association of low risk for CVD in the next 10 years (<10%) with each treatment choice, and high-ten-year risk shows the association of high risk of CVD in the next 10 years (20% or more) with each treatment choice. The time frame is exam 12 through exam 16 after the FDA approval of beta blockers and bile-acid sequestrants. Controls include age, age-squared, 5-year age group, marital status, over 64-years-old and under treatment for diabetes and/or cancer diagnosis plus individual-fixed effects. Error bars show 95% confidence intervals estimated with robust standard errors clustered at the individual level.

Figure A4: Impact of Cardiovascular Disease Diagnosis and Risk Score on Choice of Treatment in Relation to Distance to Mean BMI by 5-Year Age Group



Notes: This figure plots the coefficients from estimating equation 1.6 where the outcome is taking medication and engaging in healthy (green bar) or unhealthy (blue bar) behavior. There are three variables plotted: CVD diagnosis indicates the impact of a CVD diagnosis for treated individuals (those who had a diagnosis of CVD at exam 12, 13 or 14) as compared to matched controls who will have a diagnosis of CVD two or three exams after the treated group; low-ten-year risk shows the association of low risk for CVD in the next 10 years (<10%) with each treatment choice, and high-ten-year risk shows the association of high risk of CVD in the next 10 years (20% or more) with each treatment choice. The time frame is exam 12 through exam 16 after the FDA approval of beta blockers and bile-acid sequestrants. Controls include age, age-squared, 5-year age group, marital status, over 64-years-old and under treatment for diabetes and/or cancer diagnosis plus individual-fixed effects. Error bars show 95% confidence intervals estimated with robust standard errors clustered at the individual level.

Appendix B

Appendix to Chapter 2

B.1 Estimating Effects of Adoption on the Characteristics of the Average and Marginal Patient

In Section 2.5.3 of the main text, we estimate the effect of robot adoption on the average characteristics of patients as well as the characteristics of the marginal patients induced to receive treatment. To develop this approach, we draw on Gruber et al. (1999) and construct the Poisson regression analog to their two-stage least squares approach. Here, the "first stage" repeats our main specification given by equation 2.1, which we use to estimate the effect of adoption on patient volume in the text:

$$N_{ht} = \exp\left(\alpha_t + \alpha_h + \beta \cdot interim_{ht} + \gamma \cdot post_{ht} + X_{ht}\Omega\right) + \epsilon_{ht}. \tag{B.1}$$

We also estimate a "reduced form" effect of robot adoption on the average characteristics of patients in the hospital (or market):

$$C_{ht} = \exp\left(\delta_t + \delta_h + \kappa \cdot interim_{ht} + \lambda \cdot post_{ht} + X_{ht}\Phi\right) + \upsilon_{ht}, \tag{B.2}$$

where C_{ht} is the average characteristic of patients treated at hospital h in year t.[1] In the Poisson model, γ can be interpreted as the log-point effect of adoption on patient volume while λ represents the log point effect of adoption on the average patient characteristic.

These estimates can be combined to yield an elasticity of average patient characteristics with respect to volume:

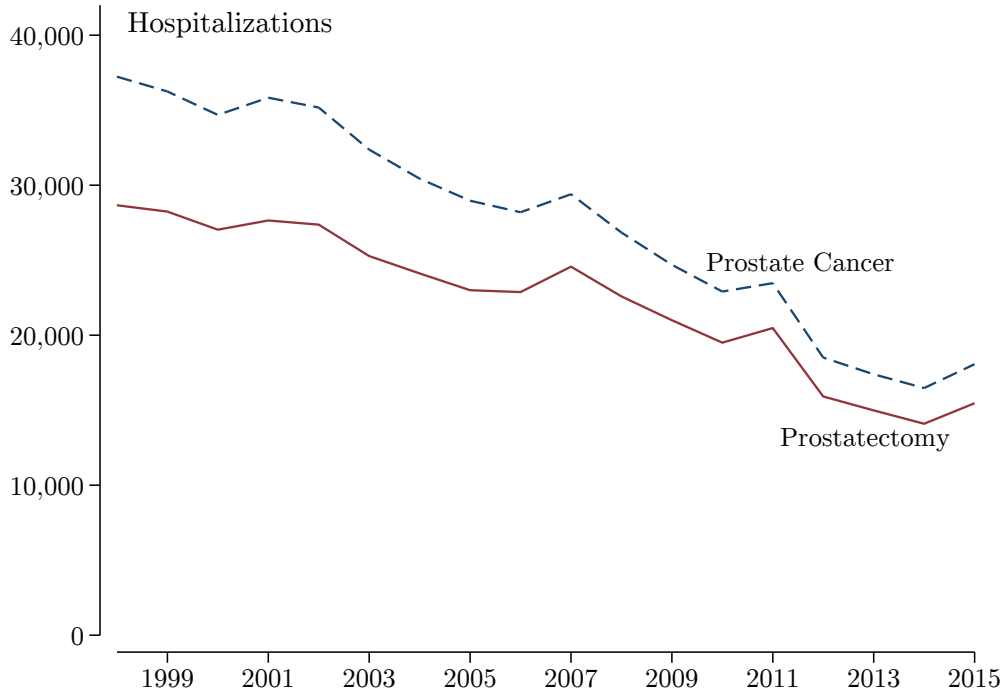
$$\eta = \frac{\lambda}{\gamma}. \tag{B.3}$$

Assuming there are no defiers — people who only come to the hospital if there is no robot, and do not come if there is one — this elasticity can also be interpreted as the log-point difference in average characteristics between the marginal patients and incumbent patients. We conduct inference on this object by estimating the "first stage" and "reduced form" as a stacked regression, an approach that is analogous to seemingly unrelated regression and is supported by the Stata command ppmlhdfe, and using the delta method. The market estimates follow the same methodology with a change in notation from h indexing hospitals to r indexing markets.

[1]This average is not defined for a hospital (or market) with no patients in the given year. Hence, observations with no patients must drop out from this regression. To ensure both regressions are run with the same sample, we omit any hospital-year or market-year with no patients from both.

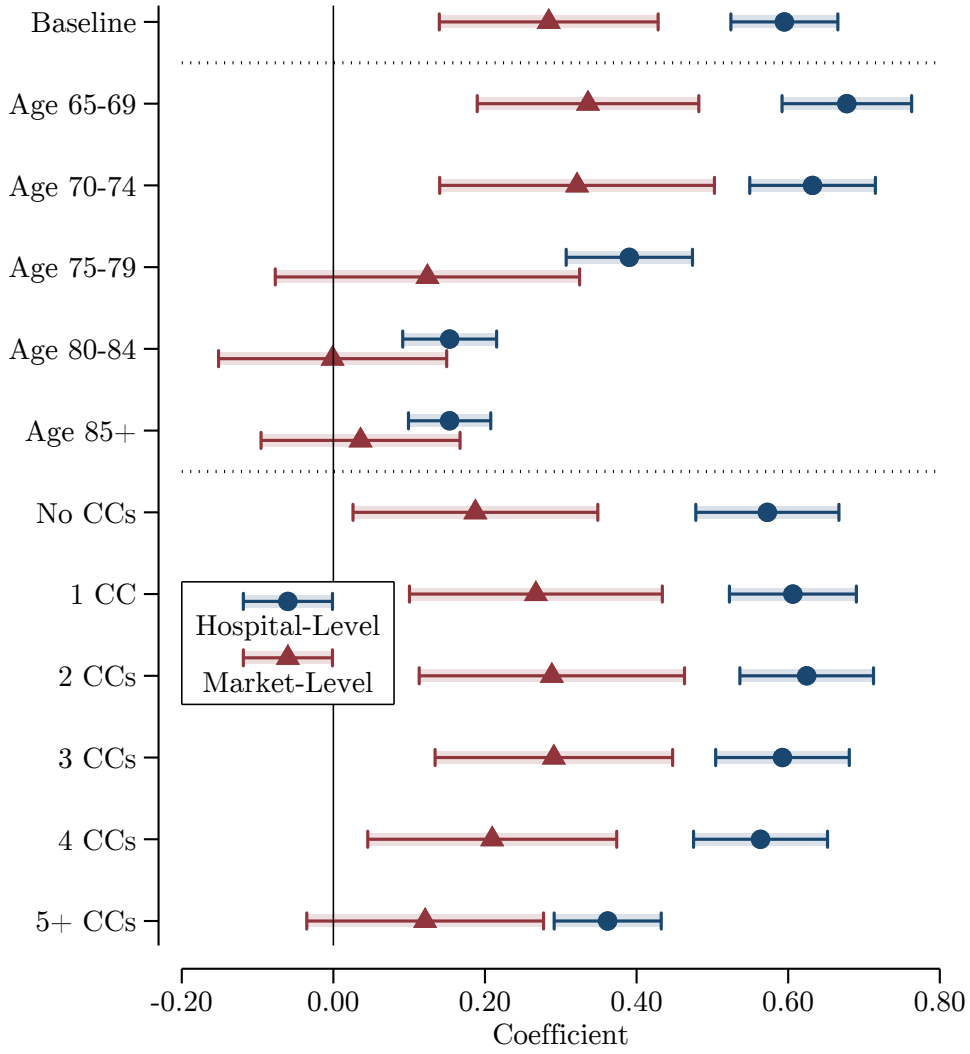
B.2 Appendix Figures

Figure B1: Trends in Prostate Cancer and Prostatectomy Hospitalizations, 1998 - 2015



Notes: This figure shows the total number of Original Medicare hospitalizations for prostate cancer and prostatectomy from 1998 - 2015.

Figure B2: Effect on Prostate Cancer Volume by Patient Age and Chronic Conditions



Notes: This figure plots estimates from equation 2.1 of the effect of adopting a robot on the volume of prostate cancer patients in the specified age and chronic condition (CC) bins. Hospital-level effects depicted with circles and market-level effects depicted with triangles. Estimates of effects on the total volume of patients reported at the top of the figure ("Baseline", repeated from Table 2.2). Coefficients have a log-point interpretation, e.g. a coefficient of 0.2 implies a 20 log point change. Error bars depict 95% confidence intervals based on robust standard errors clustered at the market level. Regressions control for year and level (hospital or market) fixed effects.

B.3 Appendix Tables

Table B1: Diagnosis and Procedure Codes Used to Identify Relevant Patients

	ICD-9	ICD-10
Prostate Cancer Diagnosis	CCS code 29 excluding V10.46	CCS code NEO039 excluding Z85.46
Prostatectomy Procedure	CCS codes 113, 114	CCS code MRS003 or 0Vx0yZZ (x $\in \{5, B\}$, y $\in \{0, 3, 4, 7, 8\}$) or XV508A4
Cancer (excluding skin) Diagnosis	CCS codes 11-21, 24-47	CCS codes NEO001-NEO024, NEO029-NEO074
Robot-assisted Procedure	17.4x	8E0WxCx
Prostatectomy, Non-Laparoscopic* (Physician Billing)	Open: CPT codes 55801, 55810, 55812,55815, 55821, 55831, 55840, 55842, 55845 TURP: CPT codes 52601, 52612, 52614, 52620, 52630	
Prostatectomy, Laparoscopic (Physician Billing)	CPT code 55866	

* We include trans-urethral resection of the prostate (TURP) procedures when identifying prostatectomies in physician billing.

Table B2: Robustness of Prostate Cancer Hospital-Level Results

		Controls				Sample		Model		Dynamics	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
	Baseline	Fixed Trends	Bed-Year FE	Market-Year FE	Market Adoption	Ever Adopters	All Hospitals	Log-Linear	asinh-Linear	Baseline	Ever Adopters
Interim	0.17	0.10	0.17	0.22	0.17	0.05	0.17	0.17	0.22	0.27	0.20
	(0.03)	(0.02)	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)	(0.02)	(0.02)	(0.02)	(0.02)
Post	0.59	0.36	0.57	0.72	0.59	0.37	0.62	0.49	0.62	0.53	0.44
	(0.04)	(0.04)	(0.04)	(0.03)	(0.04)	(0.04)	(0.03)	(0.03)	(0.03)	(0.04)	(0.04)
Interim (Rest of Market)					-0.08						
					(0.07)						
Post (Rest of Market)					-0.19						
					(0.09)						
Post *										0.09	0.08
Relative Adopt Year										(0.01)	(0.01)
DV Average	11.5	11.5	11.5	11.5	11.5	19.0	9.5	1.8	2.3	11.5	19.0
Hospitals	2,255	2,255	2,255	2,236	2,255	1,090	2,929	2,261	2,261	2,255	1,090
Observations	40,590	40,590	40,590	40,225	40,590	19,620	52,722	40,698	40,698	40,590	19,620

Notes: This table assess the robustness of the hospital-level results on prostate cancer patient volume. Column (1) repeats the baseline estimate from Table 2.2. Columns 2-5 add controls for hospital-specific linear trends, hospital bed size decile indicators interacted with years, market-year fixed effects, and rest-of-market robot adoption, respectively. Column 6 limits the sample to hospitals that adopted a robot, dropping never-adopters. Column 7 expands the sample to all hospitals that treated at least 1 patient annually during the analysis period, adding back hospitals that adopted a robot after 2012 or that failed to meet the minimum patient thresholds described in the main text. Columns 8 and 9 use linear regression instead of Poisson regression with the outcomes defined as $\ln(N_{ht}+1)$ and $\text{asinh}(N_{ht})$, respectively. Columns 10 and 11 add an interaction between Post and the hospital's relative adoption year (which starts at zero in the first year the hospital's Post indicator turns on) to the models previously estimated in columns 1 and 6, respectively. See text for more details. Robust standard errors clustered at the market level in parentheses. All regressions control for year and hospital fixed effects.

Table B3: Robustness of Prostatectomy Hospital-Level Results

		Controls				Sample		Model		Dynamics	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
	Baseline	Fixed Trends	Bed-Year FE	Market-Year FE	Market Adoption	Ever Adopters	All Hospitals	Log-Linear	asinh-Linear	Baseline	Ever Adopters
Interim	0.19	0.11	0.19	0.26	0.19	0.05	0.19	0.17	0.22	0.32	0.24
	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)	(0.04)	(0.03)	(0.02)	(0.03)	(0.02)	(0.03)
Post	0.69	0.43	0.66	0.85	0.69	0.43	0.72	0.54	0.67	0.64	0.53
	(0.04)	(0.04)	(0.04)	(0.04)	(0.04)	(0.05)	(0.04)	(0.03)	(0.04)	(0.04)	(0.04)
Interim (Rest of Market)					-0.09						
					(0.08)						
Post (Rest of Market)					-0.20						
					(0.10)						
Post *										0.11	0.09
Relative Adopt Year										(0.01)	(0.01)
DV Average	9.5	9.5	9.5	9.5	9.5	15.8	8.5	1.6	2.0	9.5	15.8
Hospitals	2,212	2,212	2,212	2,190	2,212	1,090	2,669	2,261	2,261	2,212	1,090
Observations	39,816	39,816	39,816	39,369	39,816	19,620	48,042	40,698	40,698	39,816	19,620

Notes: This table assess the robustness of the hospital-level results on prostatectomy patient volume. Column (1) repeats the baseline estimate from Table 2.2. Columns 2-5 add controls for hospital-specific linear trends, hospital bed size decile indicators interacted with years, market-year fixed effects, and rest-of-market robot adoption, respectively. Column 6 limits the sample to hospitals that adopted a robot, dropping never-adopters. Column 7 expands the sample to all hospitals that treated at least 1 patient annually during the analysis period, adding back hospitals that adopted a robot after 2012 or that failed to meet the minimum patient thresholds described in the main text. Columns 8 and 9 use linear regression instead of Poisson regression with the outcomes defined as $\ln(N_{ht}+1)$ and $\text{asinh}(N_{ht})$, respectively. Columns 10 and 11 add an interaction between Post and the hospital's relative adoption year (which starts at zero in the first year the hospital's Post indicator turns on) to the models previously estimated in columns 1 and 6, respectively. See text for more details. Robust standard errors clustered at the market level in parentheses. All regressions control for year and hospital fixed effects.

Table B4: Robustness of Prostate Cancer Market-Level Results

		Controls	Sample	Model	
	(1)	(2)	(3)	(4)	(5)
	Baseline	Fixed Trends	Broad Hosp. Sample	Log-Linear	asinh-Linear
Interim	-0.04	-0.00	-0.04	-0.03	-0.05
	(0.06)	(0.05)	(0.06)	(0.06)	(0.06)
Post	0.28	0.20	0.31	0.43	0.46
	(0.07)	(0.07)	(0.08)	(0.07)	(0.08)
DV Average	90.2	90.2	91.3	4.0	4.7
Markets	306	306	306	306	306
Observations	5,508	5,508	5,508	5,508	5,508

Notes: This table assess the robustness of the market-level results on prostate cancer patient volume. Column (1) repeats the baseline estimate from Table 2.2. Columns 2 adds controls for market-specific linear trends. Column 3 expands the sample of hospitals used to measure market-level adoption and patient volume to include hospitals that failed to meet the minimum patient thresholds described in the main text. Columns 4 and 5 use linear regression instead of Poisson regression with the outcomes defined as $\ln(N_{rt}+1)$ and $\text{asinh}(N_{rt})$, respectively. See text for more details. Robust standard errors clustered at the market level in parentheses. All regressions control for year and market fixed effects.

Table B5: Robustness of Prostatectomy Market-Level Results

		Controls	Sample	Model	
	(1)	(2)	(3)	(4)	(5)
	Baseline	Fixed Trends	Broad Hosp. Sample	Log-Linear	asinh-Linear
Interim	-0.05	0.02	-0.04	-0.01	-0.03
	(0.07)	(0.04)	(0.07)	(0.06)	(0.07)
Post	0.34	0.29	0.37	0.54	0.60
	(0.08)	(0.06)	(0.08)	(0.08)	(0.09)
DV Average	73.1	73.1	73.8	3.8	4.4
Markets	306	306	306	306	306
Observations	5,508	5,508	5,508	5,508	5,508

Notes: This table assess the robustness of the market-level results on prostatectomy patient volume. Column (1) repeats the baseline estimate from Table 2.2. Columns 2 adds controls for market-specific linear trends. Column 3 expands the sample of hospitals used to measure market-level adoption and patient volume to include hospitals that failed to meet the minimum patient thresholds described in the main text. Columns 4 and 5 use linear regression instead of Poisson regression with the outcomes defined as $\ln(N_{rt}+1)$ and $\text{asinh}(N_{rt})$, respectively. See text for more details. Robust standard errors clustered at the market level in parentheses. All regressions control for year and market fixed effects.

Table B6: Effect of Adoption on Characteristics of Prostate Cancer Patients

	Hospital-Level		Market-Level				
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Characteristic:	Age	Chronic Conditions	Age	Chronic Conditions	Beds (Baseline)	Volume (Baseline)	Teaching Hospital
A. First Stage: Outcome is Patient Volume							
Post	0.503	0.453	0.281	0.215	0.281	0.281	0.281
	(0.033)	(0.037)	(0.074)	(0.074)	(0.074)	(0.074)	(0.074)
B. Reduced Form: Outcome is Average Characteristic							
Post	-0.034	-0.128	-0.026	-0.071	0.019	0.016	0.054
	(0.002)	(0.013)	(0.005)	(0.029)	(0.020)	(0.022)	(0.050)
C. Ratio of Reduced Form to First Stage: Elasticity of Average Characteristic with Respect to Volume							
Elasticity	-0.068	-0.283	-0.091	-0.332	0.068	0.058	0.192
	(0.005)	(0.031)	(0.026)	(0.169)	(0.073)	(0.080)	(0.180)
Average Characteristic	74.74	3.01	73.32	2.74	407.63	26.73	0.46
Hospitals/Markets	2,249	2,244	306	306	306	306	306
Observations	68,770	60,190	11,000	9,778	11,000	10,984	8,954

Notes: This table reports results from estimating the impact of robotic adoption on the characteristics of prostate cancer patients. Panel A reports the "first stage" results from estimating equation 2.1 and differs only from Table 2.2 because it omits observations (hospital- or market-years) with no prostate cancer patients. Panel B reports the "reduced form" estimates of the same specification with the outcome redefined as the average characteristic of prostate cancer patients. Coefficients in Panels A and B have a log-point interpretation, e.g. a coefficient of 0.2 implies a 20 log point change in volume or the average characteristic. Panel C reports the ratio of the reduced form estimate to the first stage estimate. These coefficients have an elasticity interpretation, i.e. the elasticity of the average characteristic with respect to volume. In columns 5-7, the outcome is the average characteristic of the patients' hospitals. Columns 5 and 6 measure the hospital's beds and prostate cancer patient volume at baseline (1998) levels. See text for more details. Robust standard errors clustered at the market level in parentheses. Regressions control for year and level (hospital or market) fixed effects.