Essays on Innovation in the Medical Device Industry

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Abstract

This dissertation includes three empirical papers on the development and adoption of medical devices in the United States. Economists attribute as much as half of recent gains in life expectancy in the United States to the use of new medical technologies. When developing medical technologies, manufacturers must consider the "total product lifecycle" of devices, spanning from development costs to regulatory approval to insurer coverage and ultimately patient and physician adoption. The three chapters of this dissertation examine different stages of the total product lifecycle for medical devices.

In Chapter 1, I study how medical device firms change their investments in research and develop following external shocks to production costs. Using damage to device manufacturing facilities caused by Puerto Rican hurricanes as a natural experiment, I find that increases in storm exposure cause firms to spend less on research and development and bring fewer medical devices to market. I also find that devices brought to market following storms are cited in competitor regulatory submissions no more or less often than the average medical device. This suggests that device firms do not meaningfully target more or less scientifically innovative projects at the margin when reducing investments in research and development.

In Chapter 2, I describe the availability of cost-effectiveness analyses for medical devices in the United States. Cost-effectiveness analyses are not consistently used by insurers when making coverage decisions in the United States. I find that one of the barriers to using cost-effectiveness analyses is the timing of when analyses become available. Cost-effectiveness analyses are not available until several years after regulatory approval.

In Chapter 3, I examine the effect of industry payments on physicians' adoption of Medtronic's Micra leadless pacemaker in fee-for-service Medicare. Leadless pacemakers have lower complication rates but a higher cost compared to traditional leaded pacemakers. I find that physicians who receive more payments from pacemaker manufacturers are more likely to adopt leadless pacemakers. However, this relationship is not robust to either physician fixed effects or an instrumental variables analysis predicting receipt of manufacturer payments as a function of distance from Medtronic headquarters.

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CHAPTER 1: Financial Shocks and Innovation in the Medical Device Industry: Quasi-Experimental Evidence from Hurricanes

1.1 Introduction

The development of new health technologies has saved millions of lives and has the potential to save many more. Reductions in mortality both in the U.S. and globally over the past several decades are largely due to the development and adoption of new medical treatments.[1–8] Understanding what drives health technology innovation is crucial to designing reimbursement and regulatory mechanisms that incentivize the development of new and better lifesaving technologies. Accordingly, the determinants of innovation in health technology have long been a perennial topic in the health economics literature. The literature to date has primarily focused on how incentives such as changes in reimbursement[9] or regulatory mechanisms[10] affect firms' investments in innovation on the extensive margin, or whether firms choose to pursue developing new products. There is also a smaller but growing literature focused on how incentives affect investments in innovation on the intensive margin, or how firms modify the quality and composition of their research and development (R&D) portfolio following changes in incentives.[11,12] Studies examining overall investments in health technology innovation largely conclude that positive shocks (like increased reimbursement) encourage greater investments in R&D and negative shocks (like new taxes) discourage R&D investment[9,10,12–16] (although most of the causal evidence studying the drivers of health technology innovation focuses primarily on the pharmaceutical industry).There is much less agreement regarding changes in the quality and composition of R&D portfolios following financial shocks. In

this study, I explore the effects of negative shocks on both investments in innovation and the quality of innovation in a relatively understudied setting: the medical device industry.

The medical device industry as a setting is well-suited for studying the drivers of innovation in health technology. Medical devices comprise approximately 5% of total health care spending in the United States,[17,18] with millions of patients using medical devices every year.[19] The medical device industry also heavily invests in research and development and brings thousands of new devices to market every year.[20] Importantly, the industry has two unique institutional details that I leverage in this study to address prior limitations of the literature examining the determinants of medical device innovation. First, most medical devices in the U.S. reviewed by the U.S. Food and Drug Administration (FDA) enter the market through a regulatory mechanism wherein applicant devices identify one or more devices already on the market ("predicate" devices) that are similar in safety and effectiveness to the applicant device.[21] This creates the opportunity to create a new empirical measure of device quality based on whether devices facilitate more follow-on innovations; if a device goes on to be cited as a predicate in many future regulatory submissions, that product is more innovative than a device that is never cited as a predicate in a future regulatory submission.

Second, many medical device companies have manufacturing facilities on the island of Puerto Rico. Puerto Rico is the easternmost seaport in the United States, meaning locating manufacturing facilities on the island facilitates easier global distribution of medical devices. Additionally, locating in Puerto Rico offers numerous tax advantages relative to other areas of the U.S. Consequently, many medical device manufacturers have facilities on the island.[22] However, for all its advantages, the island

also regularly experiences hurricanes and tropical storms. These storms create a natural experiment where firms experience quasi-random negative shocks; firms have their manufacturing facilities spread across different parts of the island, and firms cannot control the trajectories of storms, meaning hurricanes in Puerto Rico damage some companies' production facilities more than others.

In this study, I exploit these unique institutional details to isolate the causal effect of negative shocks on investments in innovation and the quality of innovation in the medical device industry. I first combine several datasets, including a novel dataset previously unexplored in the economics and health policy literatures derived through natural language processing of public U.S. Food and Drug Administration (FDA) documents, to create firm-year measures of both investments in innovation and quality of innovation. These measures include R&D spending, counts of FDA approvals of new medical devices, and counts of FDA approvals weighted by the number of future competitor devices that cite a firm's devices as predicates in subsequent FDA submissions (i.e. a measure of whether the firms' devices are "scientifically valuable"[23] and facilitate follow-on innovations). I then use data describing the trajectory of hurricanes and tropical storms in Puerto Rico to create a firm-year measure of storm exposure. Given that storm exposure is effectively random from firms' perspectives, studying the effect of storm exposure on innovation outcomes allows me to isolate the causal relationship between negative financial shocks and innovation in the medical device industry.

I find that increases in storm exposure cause firms to decrease their investment in R&D, bring fewer devices to market, and have their portfolio of devices cited less often

in future submissions to the FDA. A one standard deviation increase in storm exposure causes a $37 million reduction in same-year R&D spending. These reductions in R&D spending persist for several years, and the magnitude of the finding is consistent with prior non-causal analyses of the determinants of innovation in the medical device industry. I also find a one standard deviation increase in storm exposure causes firms to bring roughly two fewer devices and five fewer citation-weighted devices to market in the year following a storm. Results from the citation-weighted analysis imply that on average firms bring less innovative devices to market following storms, although these results are too imprecise to rule out that devices entering the market following storms are no more or less innovative than the average device.

The results collectively suggest that financial shocks slow the development of future medical devices. My study adds to the literature by providing new causal estimates of the effect of negative financial shocks on both overall investments in innovation and the quality of future products in the medical device industry.

This paper proceeds as follows. In Section 1.2, I offer background, focusing on regulatory and reimbursement incentives that affect R&D investment decisions, findings from prior literature related to R&D investment decisions and innovation in the device industry, and the context for my natural experiment. In Section 1.3, I formally define my measures of storm exposure and innovation, describe the data used in generating these measures, and present my empirical strategy for isolating the causal effect of storm exposure on innovation outcomes. Section 1.4 summarizes the findings from my analysis, and Section 1.5 concludes by discussing the implications and limitations of my findings.

1.2 Background

1.2.1 Overview of the Medical Device Industry

A medical device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article…intended to affect the structure or any function of the body… which does not achieve its primary intended purposes through chemical action within or on the body…".[24] Medical devices include relatively simply technologies such as surgical trays and rubber gloves as well as complicated technologies such as cardiac defibrillators and neurostimulators. Researchers estimate that at least 3.6 million patients in the U.S. receive an implantable medical device every year,[19] and that medical devices represent approximately 5% of total U.S. health care spending.[17,18]

Before a medical device can enter the market, it must undergo regulatory review to demonstrate that it is safe and effective. In the U.S., the FDA determines safety and efficacy in the vast majority of devices through one of three mechanisms.[21] These mechanisms are the most onerous and uncertain for device manufacturers when they seek regulatory approval for truly novel devices, with effort and risk decreasing as the novelty of devices decreases. First, most analogous to the pharmaceutical approval pathway, high-risk medical devices such as cardiac pacemakers and insulin pumps are reviewed by the FDA through the Pre-Market Approval process (PMA). PMA devices demonstrate that they are safe and effective through evidence from human clinical trials.

Second, most medium-risk and some low-risk devices such as artificial hip replacements and power wheelchairs are approved through the Pre-Market Notification (PMN) process, usually through the 510(k) notification process. 510(k)-cleared devices

provide evidence of safety and efficacy by demonstrating "substantial equivalence" to one or more legally marketed "predicate" devices; firms can use either devices already approved by the FDA through the 510(k) process or devices that were on the market prior to the FDA's 1976 authority to regulate medical devices as predicates. Firms can demonstrate substantial equivalence through human clinical data, but more often do so through in vitro or bench testing. When establishing substantial equivalence, firms must demonstrate that their new product does not raise any new safety or efficacy concerns. As such, 510(k)-cleared devices can be identical to predicate devices or introduce new features so long as the new features do not raise new concerns. The 510(k) review process is the most common approval mechanism employed by the FDA.[21] Given the differences in the level of evidence required to submit a PMA application compared to a 510(k) application, firms report it costs $31 million on average to develop a 510(k) device compared to $94 million for a PMA device,[25] with a range between three to seven years to bring a product from concept to market.[21]

Third and finally, the FDA simply exempts most low-risk devices such as toothbrushes from review. There are several other approval mechanisms for medical devices, but these are relatively rare.[21] In summary, firms face greater regulatory risk as they pursue developing more novel medical devices. If a firm adds new features to a predicate device in a 510(k) submission, they face a greater risk of the FDA determining the firm's device raises new safety or efficacy concerns. Furthermore, human clinical trials are inherently uncertain, meaning seeking a PMA involves expending considerable time and money without any guarantee that a product will come to market.

After a medical device is determined to be safe and effective by the FDA, medical device manufacturers generally sell their products to hospitals or clinics, often after negotiating prices for their products through group purchasing organizations. These hospitals and clinics then make the purchased medical devices available to physicians.[18,26] While device firms do not sell directly to physicians, device firms must be aware of the extent to which providers will be reimbursed for the cost of purchasing and using a medical device in order to credibly market their devices to those providers; if a physician will not be paid for the costs associated with implanting a device, it is very unlikely that providers will purchase that device.

In the U.S., device manufacturers generally face more uncertainty in reimbursement for novel devices but with potential for greater reward if reimbursement is more directly tied to the price of their new products. Providers are largely reimbursed for the costs of medical devices on a capitated basis. The cost of a medical device is incorporated into the reimbursement associated with procedure codes in fee-for-service arrangements or diagnosis-related group (DRG) payments in prospective payment systems. These reimbursement mechanisms are for the most part not tied to specific brands or models of medical devices. For example, a provider will receive the same reimbursement for implanting a pacemaker regardless of whether the provider uses a pacemaker from Company A or Company B, even if the price of Company A's pacemaker is higher than the price of Company B's pacemaker.[18,27]

As such, if manufacturers develop more effective but more expensive technologies, they must either petition for new procedure coding for providers to use when billing for medical services,[28] request additional payment for DRGs associated with

their devices,[29] or simply wait for insurers to adjust reimbursement amounts based on the additional costs of performing the procedure with the new device. Applying for new coding or additional DRG payments are time-consuming and uncertain processes. As such, when manufacturers develop novel products, they face greater uncertainty as to whether current reimbursement systems will adequately reimburse providers for the cost of the manufacturers' devices. However, if manufacturers are granted new procedure codes or DRG adjustments exclusively for their products, reimbursement is more directly tied to the cost of the new device. This means that medical device manufacturers can potentially charge providers more for their devices, given that reimbursement is available to compensate for higher prices. Consequently, while medical device manufacturers face more uncertainty in reimbursement for novel devices, novel devices may also yield greater financial rewards.

Overall, from both a regulatory and reimbursement perspective, medical device firms face increasing risk and reward when they pursue developing increasingly novel devices. Given that incentives for developing new medical devices change as a function of product novelty, one might expect that firms could disproportionately target either innovation or unoriginal products on the margin when responding to financial shocks, depending on the expected risks and benefits for different types of products. For example, if the regulatory risks associated with novel products on average outweigh the financial benefits associated with new procedure coding, one might expect medical device firms to disproportionately remove innovative products from their product development pipeline following a decrease in their R&D budget. Conversely, if the financial benefits of new

coding outweigh the regulatory risks associated with novel products, then firms might target unoriginal products when forced to cut projects from their R&D budget.

1.2.2 R&D Investment Decisions Following Financial Shocks

Firms make R&D investment decisions based on the expected profitability of potential products in their R&D pipeline.[12,14,30] In the medical device industry, the expected profitability of a new device will be a function of the probability of whether the device receives regulatory approval, the cost of producing the device, the price at which the medical manufacturer can charge for the device, and the likelihood that providers will adopt the product. All of these dimensions are influenced by the device's regulatory environment, the device's reimbursement environment, whether the device improves upon the prior standard of care, and the availability of competitor devices in the market.

A negative financial shock could reduce a company's investments in R&D by causing a decrease in the expected profitability of future products due to an increase in the cost of financing a product.[31] For example, a financial shock could decrease the amount of cash a company has on hand. This means that the firm would be less able to finance their projects with cash on hand and would more likely need to finance their projects through debt (which is more expensive than financing a project with cash on hand due to the cost of interest) or stock issues. As such, financial shocks may lower the expected profitability of R&D products, such that firms no longer invest in those projects.

Financial shocks may also decrease R&D investments through a mechanism other than lowering expected profitability. R&D intensive firms often report greater degrees of financial "constraint", or an inability to find external funds to finance their projects. Such firms have difficulty convincing external investors of the value of new and scientifically-

complex devices and are thus unable to finance R&D projects, causing firms to forego developing a product even if they believe the product to have a positive expected profit.[31,32] Consistent with what one would expect of R&D intensive firms, medical device companies report higher levels of financial constraint in public financial documents compared to other publicly traded firms[33,34] (**Table A-1**, Appendix).

Overall, whether negative financial shocks decrease the expected profitability of future products or constrain firms' ability to finance R&D projects, negative financial shocks are expected to reduce investments in R&D. It is expected that firms will either forego developing products with negative expected profitability if a financial shock reduces the profitability of products in the R&D pipeline or forego developing products with the lowest (but potentially still positive) expected profitability if a financial shocks constraints firms' ability to finance new R&D.

The current empirical literature studying investments in innovation in the medical device industry following changes in financial status or financial shocks is largely consistent with the expectations described above: medical devices firms decrease their investments in R&D following financial shocks. However, these studies often raise endogeneity concerns. Santerre and Schmutz (2013) use multivariate regression models to estimate the cash flow elasticity of R&D spending using data from CompuStat Capital IQ describing the financial status of publicly traded medical device companies. They estimate that a 1% reduction in a medical device firm's cash flow is associated with a 0.58% reduction in R&D spending (i.e. a cash flow elasticity of R&D of 0.58).[13] However, the study only reports associations between the two variables and does not claim to make causal inference; management styles unobserved in the CompuStat

database may determine both a company's cash flow and its R&D investments. For example, Chatterji (2009) finds that when managers have prior experience in large medical device companies, their start-ups are more likely to bring successful products to market.[35] Prior experience could also be associated with overall management capability and thus affect a firm's cash flow as well, implying that the results from Santerre and Schmutz could be biased. While there are many potential confounders that could positively or negatively bias the results, the important takeaway is that descriptive methods such as multivariate regression without a causal inference framework are insufficient for drawing causal conclusions about the relationship between financial status and R&D investments.

Lee (2018) uses a difference-in-differences analysis comparing medical device firms to other R&D-intensive firms before and after the passage of the Affordable Care Act (ACA) as a means of assessing the effect of the medical device tax in the ACA. The tax is treated as effectively random, and accordingly the study concludes that the tax reduced R&D spending in the medical device industry by 20%.[16] A difference-in-differences analysis in this setting assumes that no events coincided with the device tax that differentially affected the device industry relative to other firms. However, the ACA included many measures, such as coverage expansions and changes in reimbursement, that differentially affected the medical device industry relative to other health care sectors.[36] This means the results presented in Lee's work, while consistent with what one would expect from financially constrained firms making investment decisions, is not able to isolate other confounding factors.

Ball, Macher, and Stern (2020) use accelerated failure time models to estimate the effect of a medical device firm experiencing a recall on the time it takes the firm to bring its next product to market. They find that firms delay their next regulatory submission for a new medical device by 43 days following recalls of their devices, after controlling for product, firm, and year fixed effects. They also find that firms' products that enter the market following their recalls are not higher or lower quality than the average device, as measured by the risk of future recalls.[37] While the study's use of various fixed effects and other robustness checks likely rule out most endogeneity concerns, the study is unable to completely rule out time variant endogeneity. For example, unobserved changes in management practices may increase the likelihood of product recalls as well as the speed in which firms are capable of bringing products to market.

In addition to endogeneity concerns, most of the current medical device innovation literature is limited in that it largely describes the quantity of innovative activity as opposed to the quality of subsequent innovation (with the exception of Ball, Macher, and Stern's analysis of recall risk among firms recently affected by recalls). Similar to the medical device literature, studies of the pharmaceutical industry consistently find that drug manufacturers decrease their spending on R&D in response to decreases in cash flow[38] and increase their R&D in response to positive demand shocks.[9,14,15] However, these studies reach conflicting conclusions about what types of potential innovations are targeted on the margin following changes in market conditions. For example, a study by Dranove, Garthwaite, and Hermosilla (2014) finds that the pharmaceutical industry's increased investments in clinical trials following the passage of Medicare Part D (a positive demand shock) were not directed toward the development of

drugs that were the first to treat a new condition,[39] while another study by Krieger, Li, and Papanikolau (2018) finds that Part D enabled firms to pursue projects that had greater clinical value but were riskier to the firm from a regulatory perspective compared to their pre-existing product pipeline.[40] Given the differences between the medical device industry and the pharmaceutical industry in terms of how its products are regulated and reimbursed, it is unclear whether one would expect medical device firms faced with a financial shock to adjust their investments in innovation by targeting risky but clinically innovative products or products that that will likely receive regulatory approval but offer little marginal clinical value.

Overall, the current literature describing innovation in the medical device industry following financial shocks needs additional evidence from a causal inference perspective with greater attention given to changes in the quality of innovation following shocks. Prior literature suggests that following a negative financial shock, medical device companies will invest less in innovation, but further analysis is needed to verify the direction, magnitude, and timing of this relationship, as well as assess whether firms target particular types of products when reducing their investments in R&D.

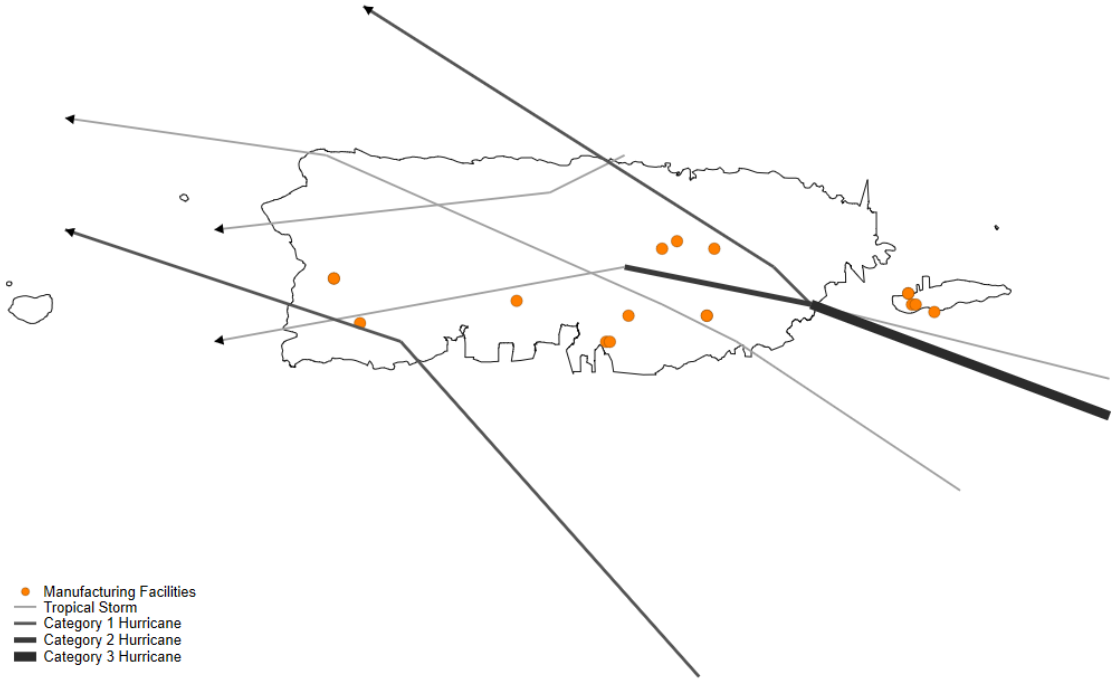
1.2.3 Setting of Natural Experiment: Hurricanes in Puerto Rico

This study treats damage to medical device production facilities from hurricanes and tropical storms in Puerto Rico as quasi-random financial shocks in order to isolate the causal effect of a financial shock on a medical device firm's subsequent innovation. Many medical device companies have production facilities spread across the islands of Puerto Rico (**Figure 1-1**).[41] Puerto Rico is the easternmost post of the United States, meaning the island is attractive to firms with global product distribution in mind.

Locating in Puerto Rico also has numerous tax advantages for businesses relative to other parts of the U.S. Consequently, many medical device companies currently operate on the island.[22]

However, hurricanes and tropical storms also affect Puerto Rico with some regularity, with 21 storms occurring between 1992 and 2016.[42] Since medical device manufacturers are spread across Puerto Rico, any given storm will affect some firms on the islands more than others, depending on the trajectory of the storm (**Figure 1-1**). For example, following the recent Hurricane Maria in 2017, Boston Scientific (whose main facility is in north-central Puerto Rico) reported less than $20 million in losses due to the storm.[43] Conversely, Medtronic (which has facilities in southeastern Puerto Rico) reported approximately $60 million in losses due to the storm.[44] This variation in damage due to the placement of production facilities creates natural variation where each storm, a random event from a company's perspective, results in different losses for each firm on the island. I exploit this variation to estimate the causal effect of a financial shock on investments in innovation and quality of innovation among a firm-year sample of medical device companies.

Figure 1- 1: Publicly traded medical device manufacturing facilities and trajectories of hurricanes and tropical storms in Puerto Rico, 1992 – 2016



Note: Author's analysis of NOAA historical hurricane tracker data of Puerto Rican storms between 1992-2016, U.S. Census shapefiles, and the FDA registry of medical device manufacturers for firms with one year of complete financial data in CompuStat Capital IQ between 1996 and 2012. Some borders in image include ocean (as opposed to shoreline) due to construction of shapefiles. Some segments of storm trajectories not presented for visual clarity.

1.3 Methods

1.3.1 Measuring Storm Exposure

I measure storm exposure, my treatment variable of interest, based on the wind speeds of Puerto Rican hurricanes and tropical storms and the location of those storms relative to device manufacturing facilities. I obtain information on wind speeds and storm trajectories from the National Oceanic and Atmospheric Administration's (NOAA) historical hurricane tracker.[42] NOAA maintains records for every hurricane and tropical

storm, including the latitude and longitude of storm centers and maximum wind speeds in six-hour increments; I extracted all data on hurricanes and tropical storms that affected Puerto Rico. I obtain information on FDA manufacturing facilities from the FDA medical device manufacturing registry, which reports the addresses of all U.S. medical device manufacturing facilities.[41] Combining these data sets, I am able to observe the distance between a medical device manufacturing facility and the center of a hurricane in six-hour increments, as well as the top wind speed associated with six-hour increments.

To create a firm-level measure of storm exposure, I calculate the smallest distance measured in kilometers between firm *i*'s manufacturing site *k* and the center of storm *j* out of all the six-hour increments of storm *j* ($DistanceToStorm_{i,j,k,t}$). I then sum the maximum wind speed measured in kilometers per hour associated with storm *j* in the six-hour increment where the storm was closest to firm *i*'s manufacturing site *k* ($WindSpeed_{i,j,k,t}$) weighted by the inverse of distance across the set of storms in year *t* (J_t) and across the manufacturing facilities operating by firm *i* (K_i) to create a firm-year level measure of storm exposure ($StormExposure_{i,t}$; **Equation 1-1**):

Equation 1-1: Firm-level measurement of storm exposure as a function of maximum wind speed and manufacturing facility distance from storm

$$StormExposure_{i,t} = \sum_{j \epsilon J_t} \sum_{k \epsilon K_i} WindSpeed_{i,j,k,t} * \left(DistanceToStorm_{i,j,k,t}\right)^{-1}$$

The units in this measure are not meaningful, but the measure increases as wind speed increases and as facility distance from the storm decreases. A storm exposure of 1.0 roughly corresponds to having one manufacturing facility 80 kilometers (slightly less than half the length of Puerto Rico) away from the center of a Category 1 hurricane, and a

storm exposure of 3.0 roughly corresponds to having one manufacturing facility 80 kilometers away from the center of a Category 4 hurricane.

1.3.2 Measuring Innovation

This study analyzes four main firm-year level outcomes of interest: R&D spending, the number of devices approved by the FDA through the PMA process, the number of devices approved by the FDA through the PMN process, and the number of devices approved by the FDA through the PMN process weighted by the number of times those devices are cited as predicates in future PMN submissions. R&D spending is the total dollars spent by firms "aimed at developing or significantly improving a product or service"[45] by firm *i* in year *t*. I obtain info on annual R&D spending from CompuStat Capital IQ, a commonly used finance database that aggregates financial documents from publicly traded firms into a firm-year panel.[13,16,38]

Counts of PMA devices are the number of firm *i*'s devices cleared by the FDA in year *t* through the Pre-Market Approval process. Counts of PMN devices are the number of firm *i*'s devices cleared by the FDA in year *t* through the Pre-Market Notification process. Counts of FDA PMA and PMN approvals come from FDA databases listing all approved medical devices.[46] FDA device approvals have been used as outcomes in prior studies.[35,37,47]

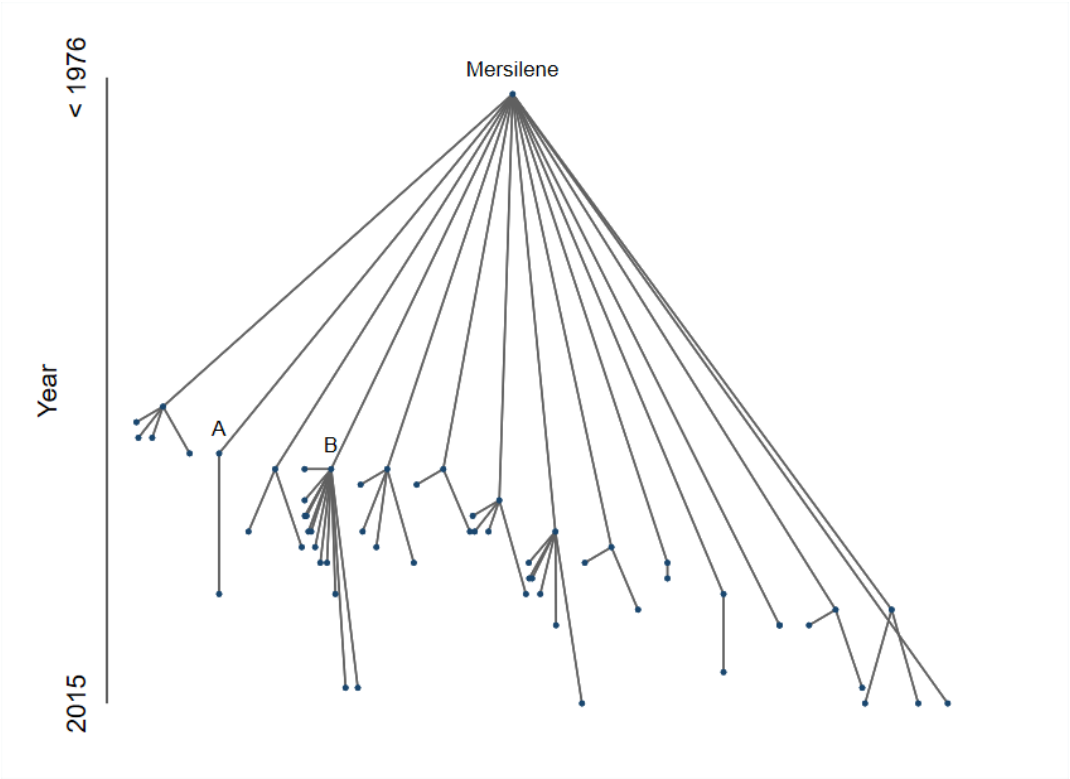
Citation-weighted PMN counts are the number of firm *i*'s devices cleared by the FDA in year *t* through the Pre-Market Notification process plus the number of times a competitor cites firm *i*'s devices from year *t* as a predicate in a 510(k) submission. Citation-weighted PMN counts will always be greater than or equal to unweighted PMN counts. For example, if Firm X has two PMN devices approved in 2010, and no

subsequent 510(k) submissions lists those two devices as predicates, then firm X has both a PMN approval count and a citation weighted PMN approval count of two in 2010. If Firm Y has two PMN devices approved in 2010, but a subsequent 510(k) submission cites one of the devices as a predicate, then Firm Y has a PMN approval count of two and a citation weighted PMN count of three. In cases where a firm uses its own device as a predicate, this is not added to the firm's citation count; firms often use the 510(k) process to make minor changes to the labeling of their products, and as such self-citations may not indicate that a new product was brought to market or that any additional innovation took place.

The citation weighted PMN count measure employed in this study is analogous to forward citation patent metrics used elsewhere in the broader economics of innovation literature.[48] The intuition behind both the forward citation weighted patent metric and the citation weighted PMN count used here is that devices that go on to be cited heavily offer some novel technological contribution compared to devices that are rarely or never cited. Forward citation metrics are often interpreted as reflecting the "scientific value" of an innovation.[49] **Figure 1-2** presents the first two "generations" of devices that cite Mersilene surgical mesh as a predicate in their 510(k) submission, previously reported in Zargar and Carr (2018),[50] and serves as an illustrative example. Mersilene mesh first entered the market prior to 1976, prior to the FDA's statutory authority to regulate medical devices. Node B, corresponding to Prolene Soft surgical mesh, cited Mersilene mesh as a predicate and was subsequently cited as a predicate in future 510(k) submissions over ten times. Node A, corresponding to Parietex surgical mesh, also cited Mersilene as a predicate but was subsequently cited as a predicate in a future 510(k)

submission just once. While both Prolene Soft and Parietex cited Mersilene mesh as a predicate, the two devices differed in important ways. Parietex was effectively a copy of Mersilene mesh and made no claim about the features of the product in its regulatory submission beyond the original Mersilene mesh.[51] Conversely, Prolene Soft claimed the mesh was "constructed of reduced diameter monofilament fibers, knitted into a unique design that results in a mesh that is 50 percent more flexible" than prior meshes.[52] Prolene Soft was accordingly cited as a predicate more often in subsequent 510(k) submissions.

Figure 1- 2: Two generations of 510(k) devices citing Mersilene mesh as a predicate or citing devices that cited Mersilene mesh as a predicate



Note: Author's analysis of data from Zargar and Carr (2018). Each node represents one medical device. A link indicates that a newer device cited the older device as a predicate in its 510(k) submission. In cases where a device cited multiple predicates, only the link to the most recent predicate link is plotted.

I obtain data on 510(k) submissions to construct citation weighted PMN approvals using a novel data set previously unexplored in the economics and health policy literatures. Currently, the FDA does not report the predicates used in 510(k) submissions in a research-ready format. However, predicates are often listed in individual summaries of 510(k) submissions posted as PDF files on the website. Zhu, Everhart, Karaca-Mandic, and Sen (2020) use a natural language processing algorithm to extract predicate identification numbers from 55,466 510(k) summary files from 2002 through 2019 found on the FDA website. They identify predicates in 81.41% of 510(k) submissions during the time period, with on-going work aimed at identifying the remaining predicates.[53] I use this data to identify predicates in 510(k) submissions and construct my citation weighted PMN count measure. The citation counts in this study most likely underestimate the true number of cases where a firm-year's devices are cited, as summary files are not consistently available from 1996 through 2002, and predicates were not identifiable in 18.59% of studied 510(k) submissions.

1.3.3 Sample Construction

My main analytic sample consists of medical device firm-years in CompuStat Capital IQ between 1996 and 2012. I identify medical device firms with the following North American Industry Classification system codes used in prior studies of the medical device industry[16]: 325413 "In-Vitro Diagnostic Substance Manufacturing", 334510 "Electromedical and Electrotherapeutic Apparatus Manufacturing", 334517 "Irradiation Apparatus Manufacturing", 339112 "Surgical and Medical Instrument Manufacturing", 339113 "Surgical Appliance and Supplies Manufacturing", and 339114 "Dental

Equipment and Supplies Manufacturing". I require that firms have at least one identifiable manufacturing facility in the FDA device manufacturer registry and limit my sample to observations with reported values for R&D spending, total earnings before interest and taxes, net cash flow, total debt, and number of employees. Relative to the sample size of all medical device firm-years in CompuStat between 1996 and 2012 (n=5,354), requiring an identifiable medical device manufacturing facility reduces my sample size by 71.22% (n=2,016), and requiring firm-years have reported values for the listed variables subsequently reduces my sample by an additional 23.56% (n=1,541). 21 unique storms were aggregated into aggregated into firm-year storm exposure measures.

1.3.4 Empirical Strategy

To isolate the causal effect of storm exposure on innovation, I employ two-way fixed effects difference-in-differences (DID) analyses (**Equation 1-2**) and model the firm-year outcome of interest ($y_{i,t}$) as a function of storm exposure ($StormExposure_{i,t}$) as well as firm fixed effects (α_i) and year fixed effects (γ_t), where the outcomes of interest are R&D spending, counts of PMA approvals, counts of PMN approvals, and citation weighted counts of PMN approvals (defined in Section 1.3.2). I estimate all models using untransformed versions of my outcome variables to estimate the linear effect of storm exposure on innovation (presented in Section 1.4.2), as well as inverse hyperbolic sine transformed outcome variables to derive semi-elasticities while retaining zero-valued observations without relying on arbitrary transformations (e.g. ln (y + 1) versus ln (y + 0.1))[54] (**Tables A-2 and A-3**, Appendix). The use of firm fixed effects controls for all time-invariant firm-level characteristics associated with the outcomes,

while year fixed effects control for common shocks that might affect outcomes for all firms in a given year. I cluster all standard errors at the firm level.

This is a somewhat unique DID context in that firms can "jump" between treatment statuses in different years. Firms without any manufacturing facilities in Puerto Rico will consistently serve as "control" observations, given that their value of $Storm\ Exposure_{i,t}$ will always equal zero. However, firms with manufacturing facilities in Puerto Rico will serve as "treatment" observations in years with storms and "control" observations in years without storms.

It is not immediately obvious when or for how long a financial shock to a medical device firm caused by a hurricane would affect the firm's innovative behavior. In order to allow for flexibility in the timing and duration of the effect of the financial shock, I forego standard DID specifications and instead exclusively use event study specifications to model the outcomes of interest as a function of lags and leads of storm exposure describing the four years proceeding and following a storm event. The year prior to the storm is omitted as a reference group.

Equation 1-2: Two-way fixed effects estimates of innovation outcomes as a function of storm exposure

$$y_{i,t} = \beta_c + \sum_{l=-4}^{-2} \beta_l * StormExposure_{i,t-l} + \sum_{l=0}^{4} \beta_l * StormExposure_{i,t-l} + \boldsymbol{\beta_i} * \boldsymbol{\alpha_i} + \boldsymbol{\beta_t} * \boldsymbol{\gamma_t} + \varepsilon_{i,t}\ ,$$

$$where\ StormExposure_{i,t-l} = \sum_{j \epsilon J_{t-l}} \sum_{k \epsilon K_i} WindSpeed_{i,j,k,t-l} * \left(DistanceToStorm_{i,j,k,t-l}\right)^{-1}$$

β_{-4} is interpreted as the difference between a.) the difference in outcome $y_{i,t}$ for firms who experience one unit of storm exposure compared to firms who do not experience a storm event four years prior to a storm event and b.) the difference in outcome $y_{i,t}$ for firms who experience one unit of storm exposure compared to firms who do not experience a storm event one year prior to a storm event. β_0 is interpreted as the difference between a.) the difference in outcome $y_{i,t}$ for firms who experience one unit of storm exposure compared to firms who do not experience a storm event in the year of a storm event and b.) the difference in outcome $y_{i,t}$ for firms who experience one unit of storm exposure compared to firms who do not experience a storm event one year prior to a storm event.

In order for a DID analysis to generate meaningful causal estimates of the effects of a financial shock to a firm's innovation, several things must be true.[55,56] First, the shock due to hurricanes must be relevant from a financial perspective, meaning there must be some demonstrable change in finances that follows a hurricane. Second, there cannot be time-variant firm-level characteristics that are associated both with storm exposure and innovation, other than intermediary characteristics through which storm exposure affects innovation. For example, if cash flow were correlated with both storm exposure and R&D spending, this would not invalidate the DID analysis, given that one expects storms to reduce R&D spending in part by reducing a firm's cash flow. Rather, such an association would be evidence in support of the first assumption. Third and finally, untreated firms (i.e. firm-years that did not experience Puerto Rican hurricanes) must have similar pre-treatment trends in outcomes spending prior to treated firm-years

experiencing hurricanes, such that the post-treatment trends in outcomes for control observations serve as an appropriate counterfactual for treated observations (commonly referred to as the "parallel trends" assumption). Under these assumptions, β_l can be interpreted as the causal effect of a one unit increase in storm exposure on the outcome of interest for affected firms *l* years after the storm.

To support the first assumption, I re-estimate the model specified in Equation 1 with common measures of financial status from CompuStat as outcomes. These measures include earnings before interest and taxes; net cash flow; total assets; total debt; and number of employees. Negative and statistically significant values of β_0 through β_4 in these models indicate that hurricanes represent meaningful financial shocks to medical device companies. The second assumption cannot be empirically supported or rejected within my data, but a violation of the assumption would require that firms adjust either their investments in innovation or the quality of their innovation in response to storms for a reason unrelated to the financial effects of storms. The validity of the third assumption can be assessed by observing the values of β_{-4} to β_{-2}. If any of these values are statistically different from zero, this is a violation of the parallel trends assumption and accordingly discredits the idea that trends in firms unaffected by storms serve as an appropriate counterfactual for firms affected by storms.

Finally, for the sake of making my results comparable to prior studies, I also calculate back-of-the-envelope elasticities of R&D spending with respect to my measures of financial status, based on the estimated coefficients and sample means. For example, the cash flow elasticity of R&D would be defined as the quotient of $\hat{\beta}_0$ from the R&D

model over the sample mean of R&D spending divided by the quotient of $\hat{\beta}_0$ from the cash flow model over the sample mean of cash flow.

1.4 Results

1.4.1 Characteristics of Analytic Sample

Table 1-1 reports measures of financial status, storm exposure, R&D spending, and counts of FDA approvals based on whether a firm had any manufacturing facilities in Puerto Rico. Overall, firms with manufacturing facilities in Puerto Rico are larger than firms without manufacturing facilities in Puerto Rico, as measured by the number of employees. Firms with Puerto Rican manufacturing facilities also report higher earnings, higher net cash flow, more debt, and more total assets (**Table 1-1**).

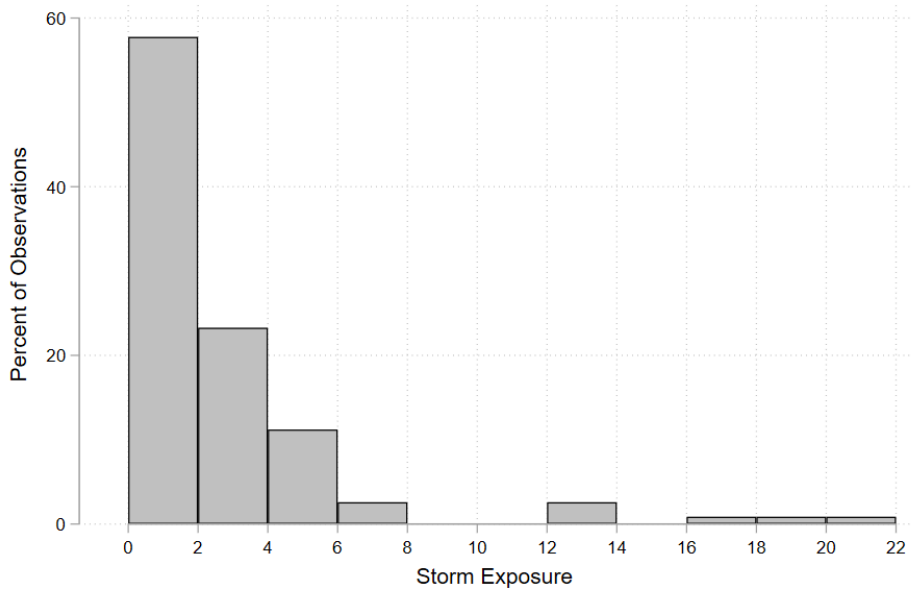
Table 1- 1: Characteristics of firms by presence of Puerto Rican manufacturing facilities

	Full Sample *Mean (SD)*	**Firms without Puerto Rican Facilities** *Mean (SD)*	**Firms with Puerto Rican Facilities** *Mean (SD)*
Storm exposure	0.204 (1.195)	0.000 (0.000)	1.697 (3.066)
Earnings before Income and Taxes	147.385 (516.607)	59.374 (298.463)	792.480 (1049.859)
Total Assets	1493.292 (5694.385)	916.490 (5159.159)	5721.096 (7413.362)
Net Cash Flow	139.555 (485.976)	64.693 (335.162)	688.269 (897.442)
Total Debt	262.466 (1067.409)	135.918 (709.556)	1190.024 (2201.203)
Employees	3923.617 (17105.681)	2944.724 (17610.896)	11098.638 (10305.831)
R&D Spending	81.156 (380.753)	51.943 (335.520)	295.278 (576.166)
PMA Approvals	0.066 (0.410)	0.021 (0.157)	0.395 (1.048)
PMN Approvals	3.300 (7.400)	1.832 (4.164)	14.065 (14.080)
PMN Approvals, Citation-weighted	6.459 (15.536)	3.518 (8.812)	28.011 (30.292)
Firm-year Observations	1,541	1,356	185
Distinct firms	168	154	14

Note: Author's calculations based on NOAA storm trajectory data, FDA medical device approval records, and CompuStat data on medical device firms from 1996 to 2012. Earnings, assets, cash flow, debt, and R&D reported in millions of 2012 USD dollars. Same-firm citations are not counted. R&D: research and development; PMN: pre-market notification; PMA: pre-market approval.

Among firm-years with non-zero storm exposure, the distribution of storm exposure is right skewed (skewness = 3.11; **Figure 1-3**). 32.76% of observations with non-zero storm exposures have values of storm exposure within one standard deviation of zero.

Figure 1- 3: Distribution of non-zero storm exposure

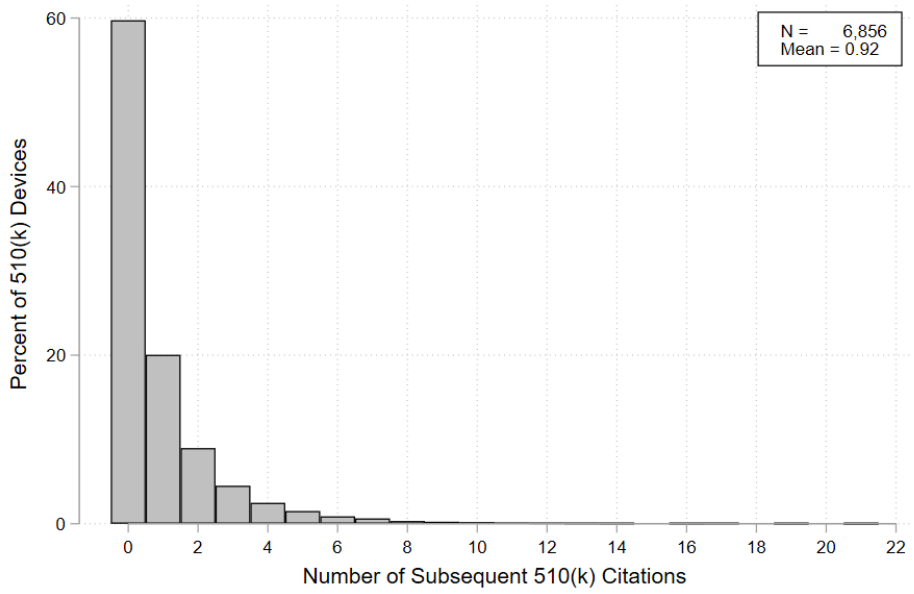


Note: Author's calculations based on NOAA storm trajectory data from 1996 to 2012 and locations of manufacturing facilities reported in FDA registry. Storm exposure is measured as wind speed weighted by the inverse of the distance between a storm center and a manufacturing facility, summed within firms and years.

The firm-years in the sample had a total of 101 devices cleared through the PMA process and 6,856 devices cleared through the PMN process between 1996 and 2012. Most devices (59.73%) cleared through the PMN process by firms in the sample were never cited as predicates in subsequent 510(k) submissions. However, a minority of devices were cited as predicates in future submissions, and some were cited many times;

the PMN devices in the sample had a median of 0 future citations and a mean of 0.92 future citations (**Figure 1-4**).

Figure 1- 4: Number of subsequent 510(k) citations among sample firms' devices cleared through the PMN process between 1996 and 2012



Note: Author's calculations based on data from natural language processing of PMN summary files. Same-firm citations are not counted. PMN: Pre-market notification.

Of note, while firms with manufacturing facilities in Puerto Rico tend to invest more in R&D and develop more medical devices, on average their devices do not appear to be more innovative than firms without manufacturing facilities in Puerto Rico. The ratio of the mean of citation weighted PMN approvals to the mean of PMN approvals is roughly equivalent for both firms without manufacturing facilities in Puerto Rico (3.518 / 1.832 = 1.92) and firms with manufacturing facilities in Puerto Rico (28.011 / 14.065 = 1.99) (**Table 1-1**); once they enter the market, the devices from treated firms are not cited in subsequent 510(k) submissions substantially more or less often than devices from control firms on average.

1.4.2 Effects of Storms on Financial Status and Innovation

Table 1-2 and **Figures 1-5a through 1-5e** report the impact of storm exposure on financial status as estimated by two-way fixed effects DID models. All results are reported as the effect of a one standard deviation increase in storm exposure (3.066) on either millions of 2012 US dollars or number of employees to facilitate interpretation. As context, a storm exposure of 3.066 roughly corresponds to having one manufacturing facility 65 kilometers away from the center of a Category 3 hurricane, suggesting that "devasting damage" will occur.[57]

Increases in storm exposure cause firms to report lower earnings, lower net cash flow, and fewer employees. A one standard deviation increase in storm exposure leads to same year declines of $137.53 million in earnings (95% CI: -241.08 to -33.98), $154.91 million in net cash flow (95% CI: -288.92 to -21.01), and 1,287.26 in employees (95% CI: -2,267.26 to -307.27). Results from inverse hyperbolic sine models are less precise and inclusive (**Table A-2**, Appendix). Overall, results from linear models suggest that Puerto Rican storms negatively affected firms' finances.

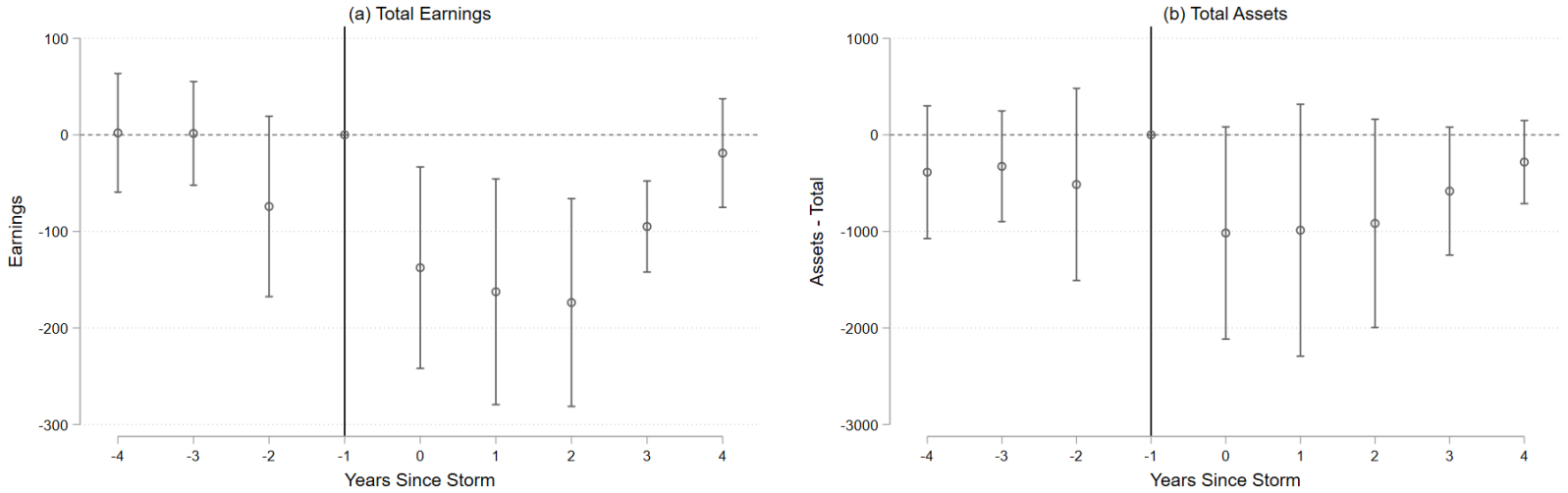
Table 1-3 and **Figures 1-6a through 1-6d** report the causal effect (under the assumptions described in Section 1.3.4) of storm exposure on innovation outcomes as estimated by two-way fixed effects models. All results are again reported as the effect of a one standard deviation increase in storm exposure (3.066). No individual leads of storm exposure (β_{-4}, β_{-3}, and β_{-2}) are statistically different from zero, providing evidence in support of the parallel trends assumption.

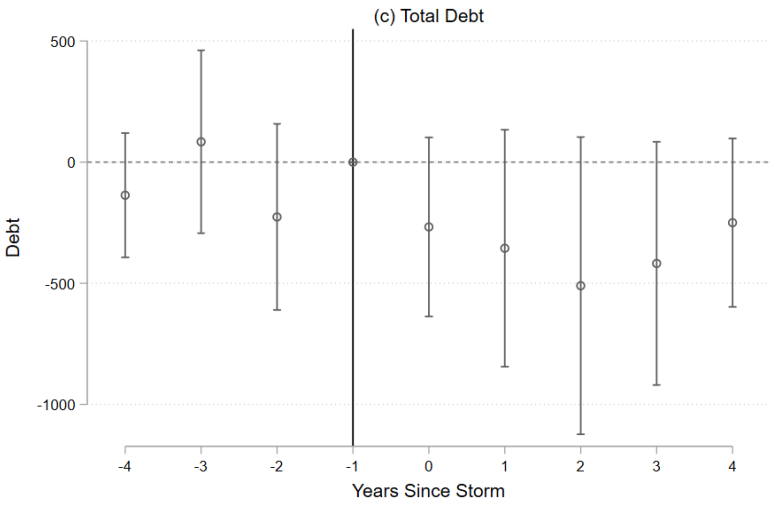
Table 1- 2: Estimates from Two-way Fixed Effects Models of a One Standard Deviation Change in Storm exposure on Financial Status

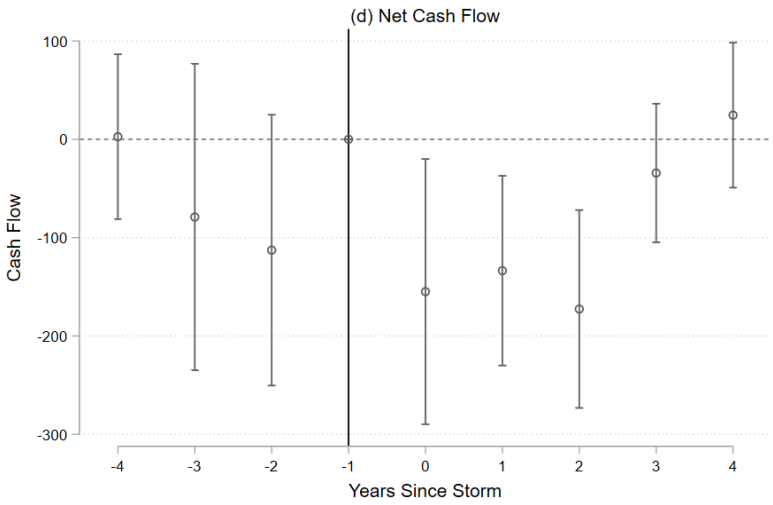
Years Since Storm	Earnings before Income and Taxes	Total Assets	Total Debt	Net Cash Flow	Employees
	Coefficient (95% CI)	*Coefficient (95% CI)*	*Coefficient (95% CI)*	*Coefficient (95% CI)*	*Coefficient (95% CI)*
-4	2.007 (-58.962, 62.976)	-386.863 (-1068.945, 295.219)	-136.530 (-391.194, 118.133)	2.641 (-80.579, 85.861)	-42.991 (-553.084, 467.102)
-3	1.470 (-51.789, 54.728)	-326.251 (-895.384, 242.882)	83.910 (-290.738, 458.558)	-79.029 (-233.708, 75.649)	-31.460 (-562.301, 499.380)
-2	-74.144 (-166.860, 18.572)	-513.981 (-1501.203, 473.241)	-226.362 (-607.520, 154.797)	-112.692 (-249.416, 24.033)	-618.638 (-1432.477, 195.201)
-1	Reference Period	Reference Period	Reference Period	Reference Period	Reference Period
0	-137.533 ** (-241.083, -33.982)	-1016.159 * (-2107.275, 74.956)	-267.459 (-634.326, 99.409)	-154.914 ** (-288.820, -21.008)	-1287.263 ** (-2267.256, -307.271)
1	-162.495 *** (-278.506, -46.485)	-987.477 (-2282.380, 307.425)	-355.407 (-840.822, 130.009)	-133.574 *** (-229.334, -37.814)	-1150.884 ** (-2126.336, -175.431)
2	-173.661 *** (-280.455, -66.867)	-917.005 * (-1987.073, 153.063)	-510.077 (-1118.986, 98.833)	-172.583 *** (-272.478, -72.687)	-1414.716 *** (-2447.144, -382.287)
3	-94.901 *** (-141.736, -48.067)	-582.759 * (-1240.201, 74.684)	-418.144 (-916.420, 80.132)	-34.274 (-104.240, 35.692)	-905.257 *** (-1449.061, -361.453)
4	-18.909 (-74.692, 36.874)	-281.978 (-708.832, 144.876)	-249.858 (-595.059, 95.343)	24.577 (-48.664, 97.818)	-445.846 *** (-765.407, -126.285)
N	1,541	1,541	1,541	1,541	1,541
R^2	0.916	0.943	0.751	0.892	0.937

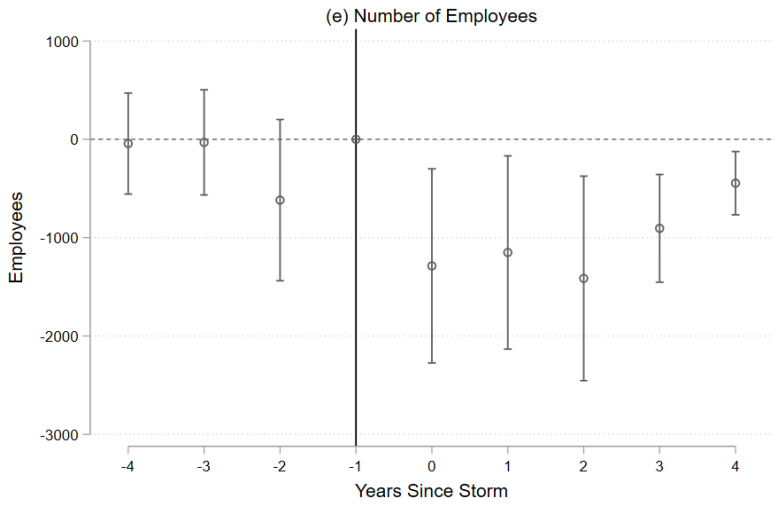
Note: Author's calculations based on NOAA storm trajectory data and CompuStat data on medical device firms from 1996 to 2012. Models regress financial outcomes in year *t* as a function of lags and leads of storm exposure, after adjusting for firm and year fixed effects. Standard errors are clustered at the firm-level. All outcomes except for employees are reported in millions of 2012 USD. *** p<0.01, ** p<0.05, * p<0.1

Figure 1- 5: Estimates from two-way fixed effects models of a one standard deviation change in storm exposure on financial status




(c) Total Debt
Debt
500
0
-500
-1000
-4
-3
-2
-1
0
1
2
3
4
Years Since Storm


(d) Net Cash Flow
Cash Flow
100
0
-100
-200
-300
-4
-3
-2
-1
0
1
2
3
4
Years Since Storm



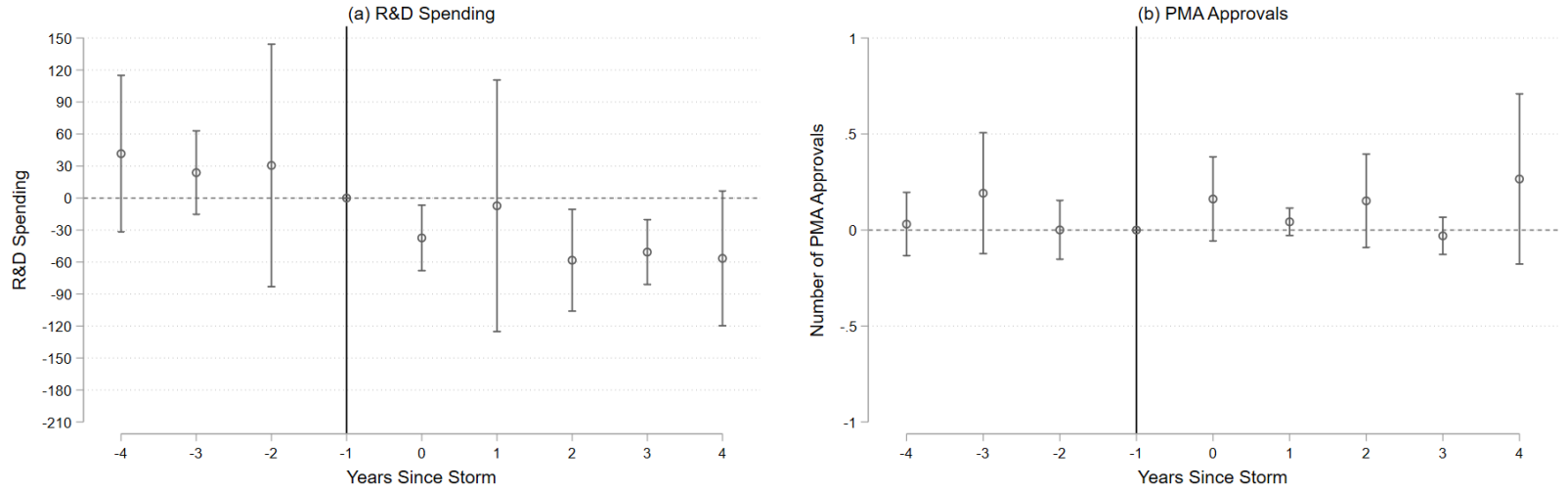
Note: Author's calculations based on NOAA storm trajectory data and CompuStat data on medical device firms from 1996 to 2012. Models regress financial outcomes in year *t* as a function of lags and leads of storm exposure, after adjusting for firm and year fixed effects. 95% confidence intervals are reported. Standard errors are clustered at the firm-level. Outcomes are (a) total earnings, (b) total assets, (c) total debt, (d) net cash flow, and (e) number of employees. All outcomes except for employees are reported in millions of 2012 USD.

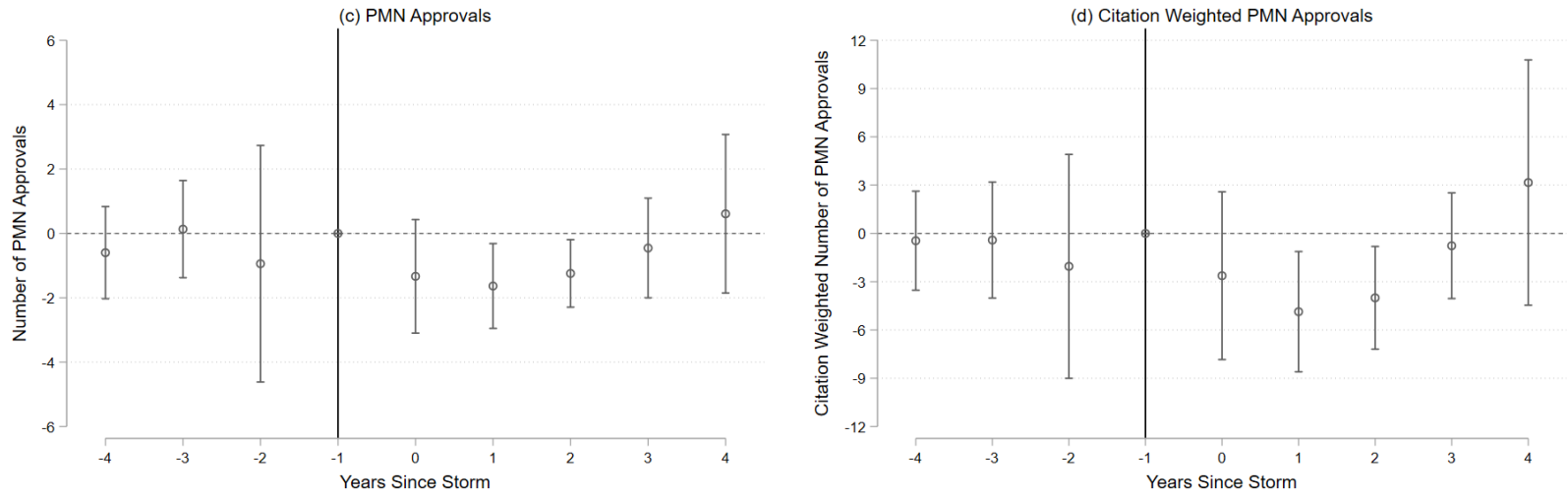
Table 1- 3: Estimates from two-way fixed effects models of a one standard deviation change in storm exposure on innovation outcomes

Years Since Storm	R&D Spending	PMA Devices	PMN Devices	PMN Devices, Citation Weighted
	Coefficient (95% CI)	*Coefficient (95% CI)*	*Coefficient (95% CI)*	*Coefficient (95% CI)*
-4	41.606 (-31.233, 114.445)	0.031 (-0.133, 0.195)	-0.597 (-2.018, 0.824)	-0.454 (-3.504, 2.597)
-3	23.806 (-15.029, 62.641)	0.192 (-0.120, 0.504)	0.133 (-1.366, 1.632)	-0.413 (-3.989, 3.164)
-2	30.567 (-82.266, 143.400)	0.001 (-0.151, 0.153)	-0.942 (-4.589, 2.706)	-2.047 (-8.950, 4.857)
-1	Reference Period	Reference Period	Reference Period	Reference Period
0	-37.381 ** (-67.878, -6.883)	0.162 (-0.056, 0.379)	-1.333 (-3.085, 0.419)	-2.627 (-7.799, 2.544)
1	-7.272 (-124.315, 109.771)	0.043 (-0.028, 0.113)	-1.633 ** (-2.941, -0.325)	-4.864 ** (-8.574, -1.153)
2	-58.282 ** (-105.639, -10.925)	0.152 (-0.089, 0.393)	-1.243 ** (-2.285, -0.201)	-4.002 ** (-7.169, -0.834)
3	-50.681 *** (-80.866, -20.496)	-0.030 (-0.126, 0.066)	-0.454 (-1.990, 1.082)	-0.766 (-4.023, 2.492)
4	-56.578 * (-119.262, 6.107)	0.266 (-0.174, 0.706)	0.609 (-1.836, 3.055)	3.161 (-4.402, 10.723)
N	1,541	1,541	1,541	1,541
R^2	0.857	0.618	0.840	0.800

Note: Author's calculations based on NOAA storm trajectory data, FDA device approval databases and natural language processing of FDA summary files, and CompuStat data on medical device firms from 1996 to 2012. Models regress outcomes in year *t* as a function of lags and leads of storm exposure, after adjusting for firm and year fixed effects. Standard errors are clustered at the firm level. R&D spending is reported in 2012 USD. Same-firm citations are not counted. R&D: research and development; PMA: pre-market approval; PMN: pre-market notification. *** p<0.01, ** p<0.05, * p<0.1

Figure 1- 6: Estimates from two-way fixed effects models of a one standard deviation change in storm exposure on innovation outcomes





Note: Author's calculations based on NOAA storm trajectory data, FDA device approval databases and natural language processing of FDA summary files, and CompuStat data on medical device firms from 1996 to 2012. Models regress outcomes in year *t* as a function of lags and leads of storm exposure, after adjusting for firm and year fixed effects. 95% confidence intervals are reported. Standard errors are clustered at the firm level. Outcomes are (a) R&D spending, (b) PMA approvals, (c) PMN approvals, and (d) citation weighted PMN approvals. R&D spending is reported in 2012 USD. Same-firm citations are not counted. R&D: research and development; PMA: pre-market approval; PMN: pre-market notification.

A one standard deviation increase in storm exposure leads to a same-year decrease in R&D spending of $37.38 million (95% CI: -67.88 to -6.88). This decrease in R&D persists and grows slightly throughout the four years of follow-up after storms, with the exception of the first year after the storm. Based on back-of-the-envelope calculations relating the estimated coefficients to sample means, R&D spending has a cash flow elasticity of 0.56.

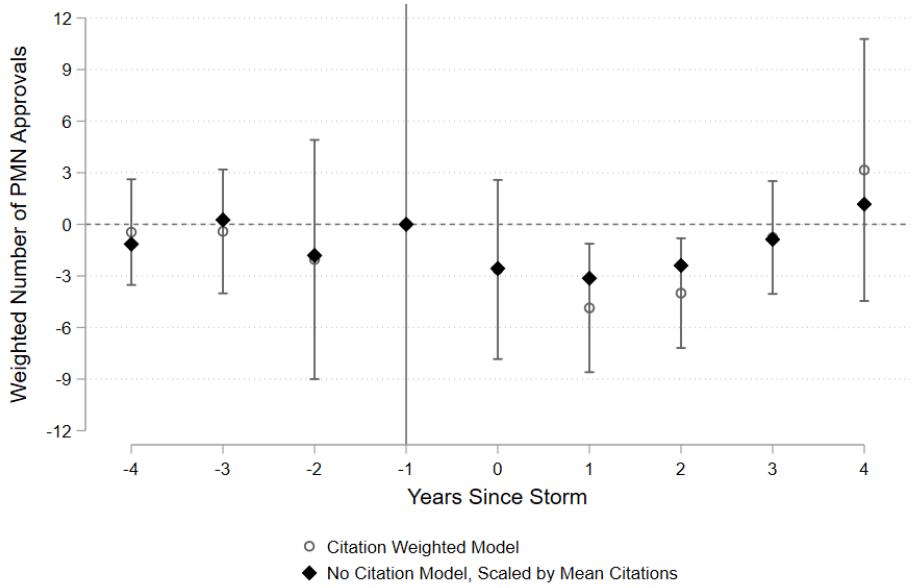
Storm exposure was not significantly associated with the number of devices cleared through the PMA process (devices approved based on data from human clinical trials). With respect to PMN devices (devices approved based on comparison to one or more predicate devices), a one standard deviation increase in storm exposure leads to a 1.63 decrease in the number of PMN devices cleared by the FDA in the following year (95% CI: -2.94 to -0.33). Put differently, it would require a storm exposure of 1.88 (roughly equivalent to having one manufacturing facility 100 kilometers away from the center of a Category 3 hurricane) to reduce the number of PMN devices a firm brings to market in the following year by one. Results from inverse hyperbolic sine models are qualitatively similar to the results described above, albeit with largely statistically insignificant coefficient estimates (**Table A-3**, Appendix).

Increases in storm exposure also lead to decreases in follow-on PMN devices. A one standard deviation increase in storm exposure leads to 4.86 fewer citation weighted PMN devices entering the market in the following year (95% CI: -8.57 to -1.15). This effect size is larger than what one would expect if the devices entering the market in the year after the storm yielded the average number of citations. The results from the model estimating unweighted PMN devices imply that if the devices entering the market the

year following a storm yielded the average number of citations (0.92), the coefficient corresponding to the next year reduction in citation weighted PMN approvals would be -3.14 (derived from the coefficient in the unweighted PMN model multiplied by one plus the mean number of citations, or -1.633 * (1 + 0.92)).

Taken at face value, this suggests that following storms, firms bring devices that yield fewer citations than an average device to market. However, the estimated coefficients in the citation weighted model are too imprecise to formally reject a null hypothesis that the true values of the coefficients in the weighted PMN model are equal to the estimated coefficients from the unweighted PMN model scaled by the mean number of citations for a PMN device. **Figure 1-7** plots the coefficients and confidence intervals from **Figure 1-6d** along with the coefficients from **Figure 1-6c** scaled by the mean number of citations (i.e. multiplied by 1.92). Statistical insignificance is demonstrated by the scaled coefficients from the unweighted PMN model being contained within the 95% confidence intervals of the weighted PMN model.

Figure 1- 7: Estimates from two-way fixed effects models of a one standard deviation change in citation weighted vs unweighted PMN approvals scaled by mean citations



Note: Author's calculations based on NOAA storm trajectory data, FDA device approval databases and natural language processing of FDA summary files, and CompuStat data on medical device firms from 1996 to 2012. Models regress outcomes in year *t* as a function of lags and leads of storm exposure, after adjusting for firm and year fixed effects. 95% confidence intervals are reported. Standard errors are clustered at the firm level. Same-firm citations are not counted. Coefficients from unweighted PMN model are scaled by the mean number of citations associated with PMN devices in the sample (i.e. coefficients are multiplied by 1.92). PMN: pre-market notification.

1.5 Discussion

The findings from this study align with both expectations of R&D intensive firms and prior empirical literature and demonstrate that the medical device industry reduces its investments in innovation following financial shocks. The results in **Table 1-2** demonstrate that following Puerto Rican storms, medical device firms report decreases in earnings, net cash flow, and employees. Hurricanes and tropical storms in Puerto Rico represent meaningful financial shocks to affected medical device firms, such that firms could hypothetically respond to storm events by changing their R&D investments. Indeed, following storm events, **Table 1-3** reports that firms decrease their same year R&D spending by approximately $37 million. This finding is consistent with prior non-causal studies of the relationship between financial status and investments in R&D in the medical device industry. Back-of-the-envelope elasticity calculations imply a cash flow elasticity of R&D of 0.56, similar to Santerre and Schmutz's finding of an elasticity of 0.58.[13] This study provides additional causal evidence supporting the finding of prior studies that following financial shocks, medical device firms decrease their investments in R&D.

This study also extends the previous literature by documenting changes in the development of new innovations following financial shocks. As reported in **Table 1-3**, firms experience minimal and statistically insignificant changes in the number of devices cleared through the PMA process following Puerto Rican storms. This is perhaps not surprising; this study's sample size may have been underpowered to detect changes in a rare outcome (firm-years only had 101 PMA devices cleared by the FDA during the sample period). It may also be that the financial shocks caused by storms are not large

enough to justify cancelling or delaying the nearly $100 million investment that often goes into developing a PMA device.[25]

While firms did not report any changes in PMA devices, firms received FDA clearance for fewer PMN devices following storms. Firms that experienced one standard deviation of storm exposure had 1.63 fewer PMN devices enter the market the following year. Put differently, a firm that had one manufacturing facility 100 kilometers away from the center of a Category 3 hurricane would produce one less PMN device in the year following the storm than they otherwise would have without experiencing the storm. The magnitude of this effect is intuitive, given that one standard deviation of storm exposure also causes a decrease in same year R&D spending slightly more than the estimated cost of bring a PMN device from concept to market.[25] Storms also inhibit the development of future medical devices. One standard deviation of storm exposure causes firms to clear 4.86 fewer citation weighted PMN devices for market entry in the following year.

There are two important implications to this set of findings. The first implication is that financial shocks inhibit innovation through negative spillover effects. The medical device industry relies heavily on iterative innovation, where medical devices improve on pre-existing technology.[18,27] Financial shocks due to storms decrease the number of devices entering the market, which in turn decreases the number of predicates available for future devices to improve upon, as evidenced by a reduction in citation weighted approvals. Thus, financial shocks can dampen innovation even among firms unaffected by those shocks.

As such, policies that increase the cost of developing a medical device may slow the development of future innovations in the medical device industry. For example,

consider on-going discussions related to the fifth iteration of the Medical Device User Fee Amendments (MDUFA V). Under the existing MDUFA regime, medical device companies pay user fees to have their devices reviewed by the FDA; these user fees allow the FDA to maintain staffing levels needed for timely regulatory reviews of new devices.[58] As the FDA prepares for the rollout of MDUFA V in 2022, it must decide whether to maintain current rates or increase user fees.[59] Discussions between the FDA and medical device manufacturers are still on-going, but commentators have suggested that changes could range anywhere from keeping fees at same rate to doubling them.[60,61] The results from this study suggest that an increase in user fees, and more generally policies that increase the cost of bring a device to market, may slow the development of future medical devices, both in the short-term and long-term by inhibiting iterative innovation in the industry.

However, it should be cautioned that a medical device firm's response to an unanticipated temporary shock caused by storms will likely differ from their response to an anticipated and enduring shock caused by a policy change. Firms can pre-emptively adapt to policy changes. As such, medical device firms may be more elastic in their response to policy shocks compared to shocks caused by hurricanes. Furthermore, firms have different options for responding to storms compared to policy interventions. In the case of storms, firms may potentially buy insurance to insulate themselves from the impact of storms, which is not a recourse available for policy interventions. However, surveys of business in Puerto Rico suggest many firms are underinsured,[62] and the empirical results in Section 4.2 imply insurance was not enough to prevent the decreases in earnings caused by storms. In the case of policies, firms have the option to lobby to

change policies that disadvantage them, although the current literature on the value of corporate lobbying currently suggests that on average lobbying costs more than the benefits it accrues.[63] This suggests firms are less able to mitigate the effects of policy shocks compared to storm shocks, again implying a potentially more elastic response to policy changes compared to storms. In short, the results from this study are likely underestimates of how responsive medical device firms would be to policy changes that increase the cost of bringing a device to market.

The second implication of this study's results comes from the observation that the reduction in citation weighted PMN devices is disproportionate to what one would expect if the devices entering the market following storms yielded the average number of citations; the observed reduction of 1.63 unweighted devices would correspond to a 3.14 reduction in citation weighted devices (as opposed to the observed 4.86 reduction in citation weighted devices) if the reduction in unweighted devices yielded a corresponding mean reduction in citations. Assuming that a device's number of citations corresponds to the scientific value of the device, the results from the citation weighted analysis suggest that medical devices that are brought to market following shocks are less innovative compared to the average device. However, it should be noted that the estimated coefficients from the citation weighted model are not precise enough to formally reject the null hypothesis that the true values of the coefficients correspond to the reduction in unweighted PMN devices scaled by the average number of citations.

While this study does not provide any formal evidence assessing this, these results are consistent with a pattern documented in prior work suggesting that the marginal products added/removed from an R&D pipeline following positive/negative shocks are

the products that are the riskiest from a regulatory perspective.[40] One would assume that the easiest way to receive a PMN approval from the FDA would be to create an exact duplicate of a pre-existing product. This product would not raise any new safety or efficacy concerns and thus likely receive FDA approval, but it would also be unlikely to garner many citations as another product already exists that could serve as an equally viable predicate device. Conversely, a new device that modifies a predicate in some substantial way will likely face greater regulatory scrutiny but also receive more citations in the future, given that the device is in some way novel relative to prior technology.

If it is true that higher cited products are risker from a regulatory perspective, the results from this study suggest there is room for change in the way medical devices are reimbursed. Ideally, increases in regulatory risk associated with pursuing new clinical innovations would be offset by greater reimbursement for clinical improvements, such that the expected value to a firm for products in the R&D pipeline stay relatively constant (or perhaps even increase) as regulatory risk increases. However, given the capitated payment model for many complicated medical devices, firms do not immediately yield financial rewards for marginally improving a pre-existing product. The results from this study are imprecise but consistent with the idea that pursuing novel PMN devices face brings on greater regulatory risk with little increase in expected profitability, and firms accordingly bring less novel PMN devices to market when faced with increased financial pressures. At the very least, this study does not find evidence supporting a hypothesis that medical device firms concentrate their R&D investments on devices that are *more* likely to be cited in future PMN submissions following financial shocks.

There are several limitations to this study. First, as noted earlier, this study documents how firms respond to an unexpected shock, which limits the study's ability to comment on how insurers or policymakers could modify the regulatory or reimbursement environment to better incentivize innovation. Given that firms can pre-emptively adapt to policy changes and use insurance to insulate themselves from the financial consequences of storms, medical device firms may be more elastic in their response to policy shocks compared to shocks caused by hurricanes.

Second, the exact mechanisms through which hurricanes affect R&D investments and subsequent innovation is unclear, which decreases the external validity of this study. One mechanism could be damage to production facilities raises the marginal cost of developing new devices, such that expected profitability decreases and new devices are no longer worth pursuing. Another mechanism could be that the disruption to the supply chain and revenue caused by limited production facilities reduces available cash and in turn constrains the financing of R&D. Hurricanes likely affect R&D investment decisions through both mechanisms, but some policy changes may work through one mechanism more than the other and consequently yield larger or smaller changes in innovation relative to what is observed in this study.

Third, the treated firms in this study are much larger than the control firms, which means we might not expect the same innovation responses if smaller firms were subjected to similar financial shocks; put differently, this study more likely provides an average treatment effect on the treated (ATT) than an average treatment effect (ATE).[55] On the one hand, a large financial impact such as one caused by a hurricane may simply not be sustainable for a smaller firm and cause the complete elimination of R&D budgets.

On the other hand, if smaller firms can endure similar financial impacts, smaller firms with a less diverse product portfolio and smaller market share may not have options for generating revenue beyond investing in new R&D, suggesting smaller firms would be more inelastic in their R&D response. Future research should exploit different natural experiments to understand how smaller firms respond to financial shocks.

Fourth, the primary measure of the quality of innovation used in this study, citation weighted PMN approvals, was derived from an imperfect natural language processing extraction of predicate identifiers from FDA summary documents. The natural language processing approach was unable to identify predicate devices in approximately 20% of the analyzed documents, and summary documents were not consistently available between 1996 and 2002.[53] However, given this study's use of difference-in-differences analysis, missing predicate information will only bias the presented results to the extent that missingness is correlated with treatment status. If both devices created by treated firms and devices created by control firms are missing one predicate citation on average, this missing predicate citation would difference out in the analysis. There is no current evidence to suggest that an inability to identify predicates is anything other than random, although work is still on-going to improve the natural language processing of 510(k) documents.

This study provides several directions for future research. Quality of innovation in this study is imprecisely measured through a newly developed count of predicate citations. Future work should explore what specific dimensions of quality are correlated with citations. For example, are highly cited devices more valuable from a clinical perspective? Or do they offer some form of cost savings that improve the bottom line on

a capitated payment? This work will likely require the development of new measures of innovation in the device industry that drill down into specific dimensions of quality. Additionally, more work is needed to better understand both the regulatory and financial risks and rewards associated with pursuing incremental innovations to pre-existing technologies. Researchers could explore whether PMN submissions for devices that differ substantially from predicates are more or less likely to receive FDA clearance. Researchers could also assess whether devices that improve on pre-existing technologies are rewarded with either greater reimbursement or greater market share, as well as when these potential benefits are accrued by medical device firms.

1.6 Conclusion

This study finds that medical device firms decrease their R&D investments and receive FDA clearance for fewer PMN devices in response to financial shocks caused by hurricanes and tropical storms in Puerto Rico. Results from an analysis of predicate citations provide suggestive but not definitive evidence that the PMN devices brought to market following storms are less innovative than the average medical device. While the study uses a novel quasi-experimental framework to assess the relationship between financial shocks and innovation in the device industry, the findings from this study are consistent with prior non-causal work. My findings suggest policymakers may need to realign reimbursement or regulatory incentives to encourage the development of more novel PMN devices, even in the face of financial shocks. Future research should further explore how firms change the composition and quality of their R&D portfolios in response to financial shocks.

CHAPTER 2: Characteristics of Cost-effectiveness Analyses of Medical Devices in the United States

2.1 Introduction

Academic researchers, physicians, and policymakers have called for greater use of cost-effectiveness analysis (CEA) to inform treatment and reimbursement decisions in the United States (US). However, in order for physicians or insurers to consider CEAs when making decisions, rigorous CEAs must be available. Prior work has documented a dearth of CEAs examining medical devices specifically,[64] despite the fact that medical devices comprise approximately 5% of total health care spending in the US.[17] In this descriptive study, I expand on prior work by documenting the number of published medical device CEAs in the US by regulatory review pathway, the average time between Food and Drug Administration (FDA) approval of medical devices and publication of CEAs, and the association between the cost-effectiveness of a medical device and its scientific value.

2.2 Background

CEAs play a limited in role in insurer coverage decisions for medical devices in the US. Most private insurers report considering cost when making coverage decisions,[65,66] but few rely on formal CEAs. Recent studies show that just considering cost can push private insurers to make coverage decisions at least roughly consistent with formal cost-effectiveness evidence. In a sample of employer-based private health plans, Brouwer and colleagues observe large declines in cost-sharing between 2010 and 2013 for drugs with small incremental cost-effectiveness ratios (ICERs) compared to declines in cost-sharing for drugs with larger ICERs. However, they find no relationship between

cost-sharing and cost-effectiveness for drugs with an ICER greater than $10,000 per quality-adjusted life year (QALY), suggesting formularies only use cost-sharing to promote use of the most cost-effective of treatments when not explicitly using CEAs in coverage decisions.[67]

In contrast to private insurers, the Centers for Medicare and Medicaid Services (CMS) is explicitly prohibited from considering CEAs or cost more generally when making Medicare coverage decisions (although Medicare does sometimes cite evidence from CEAs in national coverage determinations).[68] As such, it is not surprisingly that prior work by Chambers and colleagues finds that there is no obvious relationship between the cost-effectiveness of a medical device and outcomes of national coverage determinations by CMS.[68] Given the disparate considerations of cost between CMS and private insurers, CMS national coverage determinations only match with private payer decisions for medical device coverage approximately half of the time, with CMS not consistently being more or less restrictive in its coverage when not aligned with private payers.[69]

The lack of use of CEAs to inform medical device coverage decisions may be wasteful from a societal perspective. Insurers may cover medical devices that are not cost-effective relative to comparator devices or cover medical device-based interventions when surgical or pharmaceutical interventions may be more cost-effective.[64] Furthermore, the potential for waste caused by not considering CEAs in coverage decisions may be greater for medical devices compared to other types of interventions. Unlike pharmaceutical products, for example, most medical devices receive regulatory approval without demonstrating efficacy using human clinical data. Instead, the FDA

grants market access to most medical devices through the 510(k) notification process based on a device's "substantial equivalence" to a comparator "predicate" device already on the market. Substantial equivalence is often demonstrated through bioequivalence studies, bench testing, or in vitro analyses rather than clinical data.[21] Even among the subset of devices evaluated through the premarket authorization process (PMA) that require human clinical data prior to receiving regulatory approval, the quality of clinical evidence supporting medical device approvals tends to be lower compared to pharmaceutical products (e.g., more likely to be approved based on a single nonrandomized trial).[70,71] The relative opacity of incremental benefits for certain devices combined with insurers' inconsistent consideration of costs means that medical device-based interventions that do not meet convention thresholds of cost-effectiveness may be more likely to receive insurer coverage compared to other types of interventions. As such, society may benefit from more use of CEAs in insurer coverage decisions.

There are two primary barriers to greater adoption of CEA in coverage decisions for medical devices. First, there are very few published CEAs examining medical devices. The CEA literature disproportionately focuses on pharmaceutical interventions, while surgical and medical device-based interventions are underrepresented.[64] Second, some patient and physician groups do not believe that CEAs meaningfully capture the overall value of new medical technologies. These groups express concern that making coverage decisions based on CEAs will unduly inhibit patients from accessing innovative lifesaving treatments and lobby accordingly.[72]

This study aims to develop new evidence in relation to these two barriers. I first document the availability of medical device CEAs, both in terms of number of

publications as well as timing of publication relative to FDA approval. Unlike prior studies, I stratify analyses of CEA availability by the regulatory pathway in which the device was cleared for market access by the FDA. I then assess the extent to a device's cost-effectiveness is correlated with its scientific value. In short, I find that very few medical device CEAs are available, it takes an average of 3 to 5 years for a CEA to be published following FDA approval of a medical device, and measures of cost-effectiveness for 510(k) medical devices are correlated with a measure of scientific value.

2.3 Methods

2.3.1 Data sources

This study relies on three main data sources: the Tufts University Center for the Evaluation of Value and Risk in Health (CEVR) Cost-effectiveness Analysis Registry (Tufts CEAR), the FDA medical device approval database, and a 510(k) citation database. First, the Tufts CEAR is a repository of all peer-reviewed English-language CEAs identifiable in MEDLINE with incremental health benefits measured in QALYs. For each CEA, the Tufts CEAR catalogues bibliographic information such as date of publication and article authors, the identified intervention in the CEA, the disease treated by the intervention device (as defined by ICD-10 disease chapter), the ICER quadrant associated with the intervention, any funding sources for the CEA, and a reviewer score ranging from 1 to 7 assessing the methodological quality of the CEA (with 7 being the best). The CEAR catalogues CEAs published after 1976, but this study focuses on CEAs published between 2002 and 2017.[73]

Second, the FDA medical device approval database maintains records for all devices reviewed by the FDA through the Premarket Authorization process (PMA) and

the 510(k) notification process.[46] These records include a unique identification number for individual medical devices and the date in which medical devices were granted market access by the FDA.

Third and finally, the 510(k) citation database is a natural language processing-derived data set that identifies the predicates cited in individual 510(k) submissions. The natural language processing used to derive the data is imperfect and only identifies approximately 85% of all predicates.[53] The citation database can be used to identify a "forward citation count", or the number of times a given medical device is cited as a predicate in subsequent 510(k) submissions. Forward citation counts are used to measure the scientific or technological novelty associated with a new product.[48]

To construct my analytic sample, I identify all fully reviewed CEAs in the Tufts CEAR between 2002 and 2017 where the studied intervention was a medical device, and the patient population was based in the US. Within this sample, I read through each CEA to identify the specific make and model of the intervention device in order to manually match the CEA to a corresponding medical device in the FDA medical device approval database. Specific medical devices were not always identifiable. For example, a CEA might assess the average cost effectiveness of all implantable cardiac defibrillators on the market, rather than specifically identifying the cost effectiveness of a Boston Scientific defibrillator vs a Medtronic defibrillator.

2.3.2 Data analysis

I first assess whether the CEAs linked to the FDA device registration database are representative of the larger medical device CEA literature. I test whether CEAs linked to the FDA database are statistically different from CEAs not linked to the FDA database

with respect to disease treated, funding sources, reviewer scores, and ICER quadrants using either t-tests or chi-square tests as appropriate. Then for both PMA and 510(k) devices, I create histograms describing the time between FDA approval of devices and publication of CEAs. Among CEAs linked to a 510(k) device, I assess whether 510(k) devices with an above median forward citation count have a different distribution of ICER quadrants (more QALYS and more expensive, more QALYs and less expensive, fewer QALYs and more expensive, or fewer QALYs and less expensive) compared to devices with a median or below median citation count using a chi-square test.

2.4 Results

There were 455 CEAs of medical devices in the Tufts CEAR, of which 172 examined medical device use among US patients. Of the 172 US-based CEAs of medical devices, 69 (40.1%) identified the specific make and model of the studied intervention and could be linked to the FDA database. CEAs with devices linked to the FDA database were mostly similar to unlinked CEAs, with the exception that studies linked to the FDA database were more likely to have industry sponsorship (**Table 2-1**).

CEAs of PMA devices are on average published more quickly following FDA approval compared to 510(k) devices, although these differences are not statistically significant. On average, CEAs of PMA devices are published 4.86 years (median = 3 years) after receiving FDA approval (**Table 2-2** and **Figure 2-1**), while CEAs of PMN devices are published 6.07 years (median = 5 years) after receiving FDA approval (**Table 2-2** and **Figure 2-2**). Note that there are some instances where CEAs of PMA devices are published prior to those devices receiving in FDA approval (**Figure 2-1**). These are largely cases where CEAs were published based on Phase I or Phase II clinical trial

results, prior to FDA approval. Among 510(k) devices, there are marginally significant differences ($p < 0.1$) in ICER quadrants based on the forward citation counts. Devices that received an above median number of citations (>3) were more likely to be less costly and yield more QALYs than the comparator device compared to devices yielding a median or below median number of citations (<= 3).

Table 2- 1: Characteristics of Cost-effectiveness Analyses of Medical Devices by Linkage to US Food and Drug Administration Database

	Not Linked to FDA	Linked to FDA	Diff. p-value
n	103	69	
Cost-effectiveness Quadrant			
1 (More costly, more QALYs)	15.53%	10.14%	0.492
2 (More costly, fewer QALYs)	61.17%	60.87%	
4 (Less costly, more QALYs)	23.30%	28.99%	
Disease Category			
Circulatory System	38.83%	43.48%	0.607
Musculoskeletal	7.76%	11.59%	
Neoplasms	10.68%	11.59%	
Other	42.72%	33.33%	
Sponsorship			
Foundation	6.79%	4.34%	0.034
Government	24.27%	10.14%	
Industry	21.36%	40.58%	
None	37.86%	37.68%	
Other	9.70%	7.24%	
Rating			
1.0	0.00%	0.00%	0.863
1.5	0.97%	0.00%	
2.0	0.97%	1.44%	
2.5	1.94%	0.00%	
3.0	6.79%	4.34%	
3.5	6.79%	8.69%	
4.0	16.5%	18.8%	
4.5	15.53%	13.04%	
5.0	21.36%	21.74%	
5.5	14.56%	17.39%	
6.0	8.73%	13.04%	
6.5	3.88%	1.44%	
7.0	1.94%	0.00%	

Note: Author's analysis of cost-effectiveness analysis publications in the Tufts University Cost Effectiveness Analysis Registry (CEAR) studying a medical device intervention and published between 2002 and 2017. Cost-effectiveness quadrant, disease category, and sponsorship identified in CEAR. Ratings assigned by Tufts University reviews based on methodological quality of article, with 1 being the lowest quality and 7 being the highest quality. Linkage status based on whether model and manufacturer of the medical device used in the intervention were identifiable and linked to US Food and Drug Administration databases. Differences in proportions assessed with chi-squared tests.

Table 2- 2: Characteristics of Cost-effectiveness Analyses of Medical Devices by Regulatory Pathway

	510(k) Devices	PMA Devices	Diff. p-value
n	27	42	
Cost-effectiveness Quadrant			
1 (More costly, more QALYs)	14.81%	7.143%	0.21
2 (More costly, fewer QALYs)	48.15%	69.05%	
4 (Less costly, more QALYs)	37.04%	23.81%	
Disease Category			
Circulatory System	25.93%	54.76%	0.032
Musculoskeletal	7.40%	14.29%	
Neoplasms	14.81%	9.52%	
Other	51.85%	21.43%	
Sponsorship			
Foundation	3.70%	4.76%	0.317
Government	11.11%	9.52%	
Industry	37.04%	42.86%	
None	48.15%	30.95%	
Other	0.00%	11.90%	
Rating			
1.0	0.00%	0.00%	0.348
1.5	0.00%	0.00%	
2.0	3.70%	0.00%	
2.5	0.00%	0.00%	
3.0	7.40%	2.38%	
3.5	14.81%	4.76%	
4.0	14.81%	21.43%	
4.5	11.11%	14.29%	
5.0	25.93%	19.05%	
5.5	18.52%	16.67%	
6.0	3.70%	19.05%	
6.5	0.00%	2.38%	
7.0	0.00%	0.00%	
Mean Years to CEA Publication	6.07	4.86	0.388

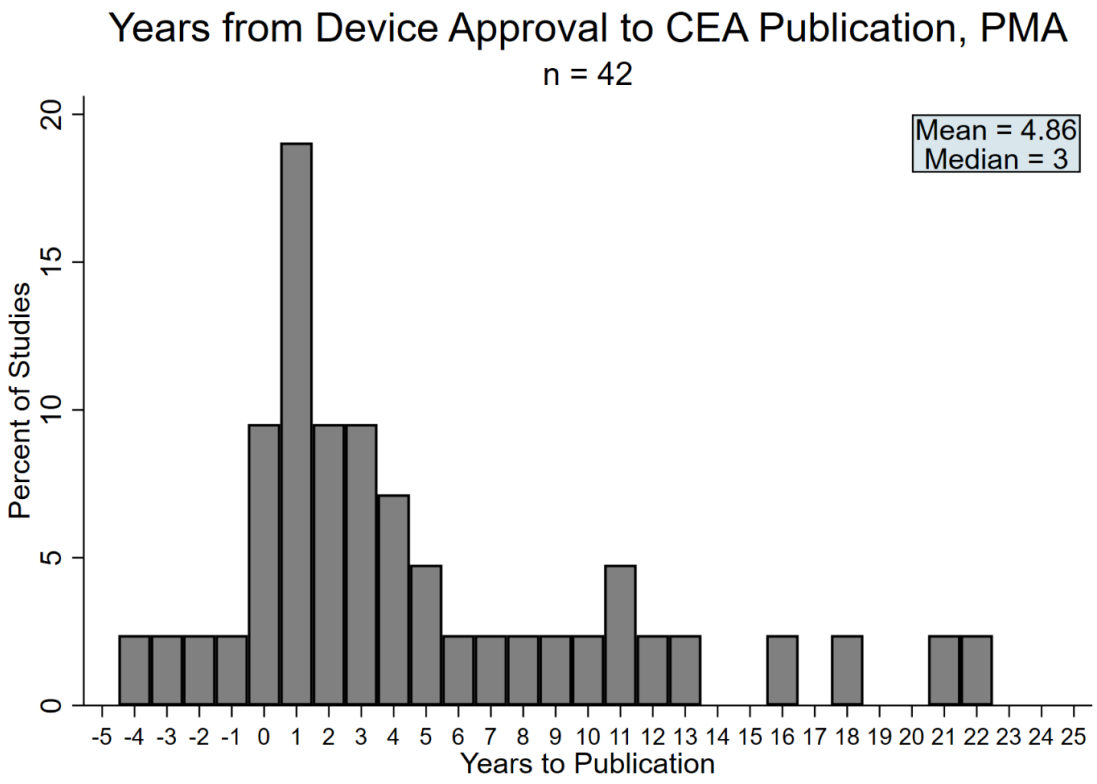
Note: Author's analysis of cost-effectiveness analysis (CEA) publications in the Tufts University Cost Effectiveness Analysis Registry (CEAR) studying a medical device intervention and published between 2002 and 2017. Sample limited to cost-effectiveness analyses where the model and manufacturer of the medical device used in the intervention were identifiable and linked to US Food and Drug Administration (FDA) databases. Cost-effectiveness quadrant, disease category, and sponsorship identified in CEAR. Ratings assigned by Tufts University reviews based on methodological quality of article, with 1 being the lowest quality and 7 being the highest quality. Years to CEA publication measured as difference between date of FDA approval of medical device and date of CEA publication. Differences in proportions assessed with chi-squared tests. Differences in means assessed with t-tests.

Table 2- 3: Characteristics of Cost-effectiveness Analyses of 510(k)-cleared Medical Devices by Number of Citations

	510(k) Devices with <=3 Citations	510(k) devices with >3 citations	Diff. p-value
n	15	12	
Cost-effectiveness Quadrant			
1 (More costly, more QALYs)	6.67%	25.00%	0.086
2 (More costly, fewer QALYs)	66.67%	25.00%	
4 (Less costly, more QALYs)	26.67%	50.00%	

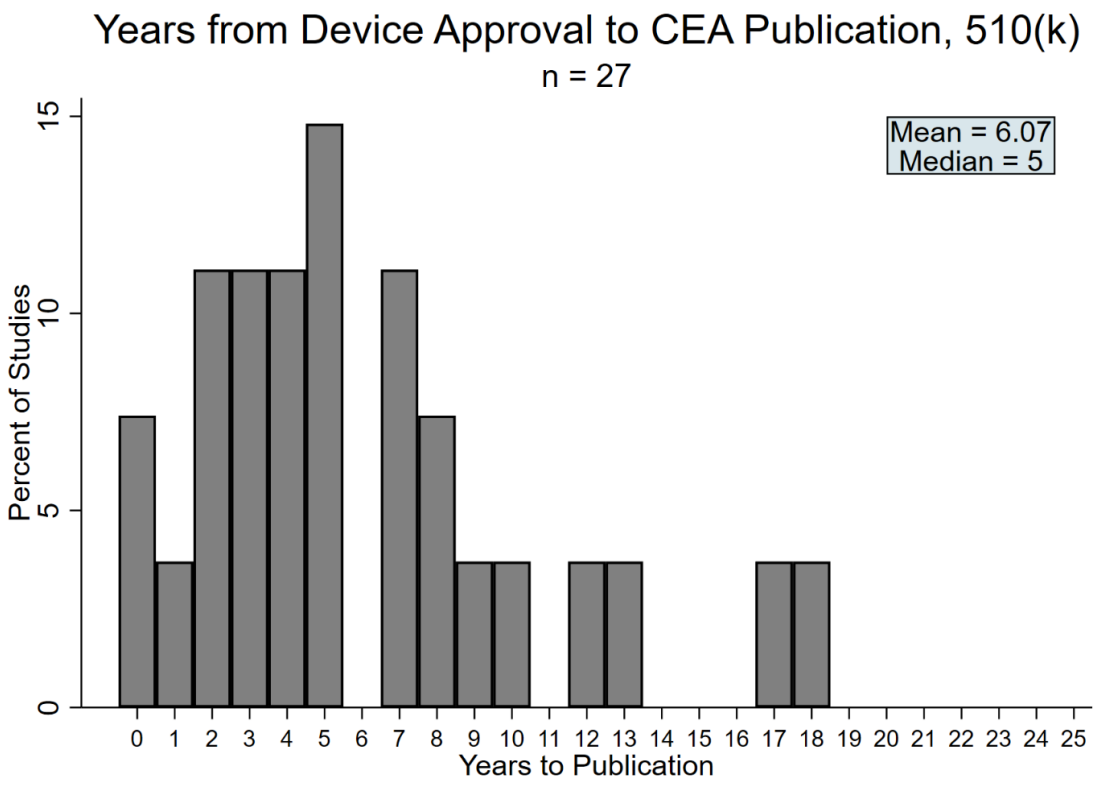
Note: Author's analysis of cost-effectiveness analysis (CEA) publications in the Tufts University Cost Effectiveness Analysis Registry (CEAR) studying a medical device intervention and published between 2002 and 2017. Sample limited to cost-effectiveness analyses where the model and manufacturer of the medical device used in the intervention were identifiable and cleared through the 510(k) process. Cost-effectiveness quadrant identified in CEAR. Differences in proportions assessed with chi-squared tests.

Figure 2- 1: Distribution of Years between PMA Approval and CEA Publication



Note: Author's analysis of cost-effectiveness analysis (CEA) publications in the Tufts University Cost Effectiveness Analysis Registry (CEAR) studying a medical device intervention and published between 2002 and 2017. Sample limited to cost-effectiveness analyses where the model and manufacturer of the medical device used in the intervention were identifiable and approved through the PMA process. Years to CEA publication measured as difference between date of US Food and Drug Administration approval of medical device and date of CEA publication.

Figure 2- 2: Distribution of Years between 510(k) Approval and CEA Publication



Note: Author's analysis of cost-effectiveness analysis (CEA) publications in the Tufts University Cost Effectiveness Analysis Registry (CEAR) studying a medical device intervention and published between 2002 and 2017. Sample limited to cost-effectiveness analyses where the model and manufacturer of the medical device used in the intervention were identifiable and approved through the 510(k) process. Years to CEA publication measured as difference between date of US Food and Drug Administration approval of medical device and date of CEA publication.

2.5 Discussion

There are very few CEAs of medical devices in the US. Of the limited studies available, most CEAs are not available until 3 years after FDA approval for PMA devices or 5 years after approval for 510(k) devices. Evidence of cost effectiveness, and in particular strict dominance of the comparator, is marginally correlated with the number of future citations 510(k) devices receive.

The small number of US-based medical device CEAs has been previously documented[64] and is not particularly surprising, given that Medicare is explicitly prohibited from considering cost when making coverage decisions[68] while many private insures do not consistently factor formal CEAs into coverage decisions.[65,66] However, the finding that most medical devices CEAs are not available until several years after FDA approval (a pattern also observed in CEAs of pharmaceutical products)[74] should inform how insurers might reasonably expect to increase their use of CEAs when making coverage decisions.

Insurers cannot expect CEAs to be consistently available immediately after FDA approval of new medical devices. This suggests that insurers wishing to incorporate CEAs into coverage decisions should instead consider conditional coverage strategies, where insurers initially cover new technologies but require manufacturers to develop evidence of cost-effectiveness in order to continue coverage beyond a set number of years. Medicare has employed this strategy in recent years by conditioning continued coverage of new products on developing new evidence of product effectiveness (without respect to cost).[75,76] Other insurers could apply this approach to requiring evidence of cost-effectiveness specifically.

This study also provides preliminary suggestive evidence that concerns that using CEA to make coverage decision will stifle access to innovative therapies may be somewhat misplaced. Bases on the limited sample of 510(k) devices included in this analysis, devices that receive more subsequent citations in 510(k) applications are more likely to strictly dominate their comparator in CEAs. Forward citations counts are often viewed as representing the scientific or technological value of a new product;[48] citations are evidence that a product offered something worth replicating. Taken at face value, the 510(k) citation results suggest that cost-effective devices are more innovative than devices that are not cost-effective, meaning covering cost-effective devices coincides with covering innovative devices.

However, there are numerous caveats to such a conclusion. First, the sample of 510(k) devices represented in this study is very small, and the relationship between cost-effectiveness and scientific innovation may not be generalizable beyond this sample. Second, the small sample size meant that including any control variables when assessing the relationship between cost-effectiveness and citations was not possible; the marginally significant association between the two may be confounded by unobservable variables. Third, the 510(k) pathway is only used to grant market access to medium complexity devices, the meaning inferred relationship between scientific value and cost-effectiveness for 510(k) devices may not be generalizable to high complexity PMA devices. Overall, the citation results presented here should be viewed as an early exploratory analysis, rather than definitive evidence of the relationship between cost-effectiveness and other dimensions of value.

There are several overall limitations to this study. This study only examined medical device CEAs based in the US. This was done to increase the likelihood that CEAs could be accurately matched to the FDA database. However, this also means that the results from this analysis may not be generalizable to medical device CEAs of populations outside of the US. This is a nontrivial limitation, as US insurers looking for evidence of cost-effectiveness might consider CEAs from other countries when making coverage decisions. Additionally, this study is limited in that the linkage between the Tufts CEAR and the FDA device approval database was performed manually. Errors in the linkage to the FDA database could potentially bias both the counts of devices with linked CEAs and average lag times between FDA approval and CEA publication.

2.6 Conclusion

In this exploratory analysis, I find that few medical devices in the US have an associated CEA examining the cost-effectiveness of the device in a US setting. The limited number of available CEAs are usually published 3 to 5 years after FDA approval, meaning insurers do not have evidence of cost-effectiveness when making initial coverage decisions for medical devices following FDA approval. Insurers may consider conditional coverage strategies for medical devices if they wish to incorporate CEAs into coverage decisions as CEAs are published.

CHAPTER 3: Manufacturer Payments and the Adoption of Leadless Pacemakers in Fee-for-Service Medicare

3.1 Introduction

Physicians' selection of medical devices affects both the cost and quality of health care in the United States. Medical devices represent 5% of total health care spending in the United States,[17] and researchers frequently attribute half of life expectancy gains in the United States to the development and adoption of new medical technologies.[77,78] Medical device manufacturers are highly involved in physicians' medical device selection. Medical device sales representatives are often present in surgical suites to advise physicians on medical device use,[79] and the industry pays approximately $900 million to physicians annually for things like speaking fees, royalties, and reimbursement for travel and lodging.[80] Critics argue that the device industry yields too much influence in physician decision making and that this influence erodes patients' belief that physicians are working in patients' best interest.[81] Accordingly, in this study I explore the influence of the medical device industry by examining the relationship between manufacturer payments to physicians and adoption of a new medical device, the Micra leadless pacemaker.

To date, the literature on the effects of industry payments on medical device selection is sparse. There is a large literature on the association between payment from pharmaceutical manufacturers and pharmaceutical prescribing that finds industry payments are associated with more expensive prescribing patterns and more clinically inappropriate prescribing.[82] These studies are largely associational studies. The limited studies using a causal inference framework tend to find smaller effect sizes compared to

associational studies with either ambiguous or modest positive effects on patient welfare.[83–85] However, studies of pharmaceutical prescribing may not be generalizable to studies of the medical device industry. To my knowledge, only one peer-reviewed has specifically examined the association between receipt of manufacturer payments and physicians' selection of medical devices.

This study adds to this sparse literature by using both physician fixed effects and instrumental variable regressions to estimate the effect of payments from pacemaker manufactures on physicians' adoption of the Micra leadless pacemaker when treating Medicare Fee-for-Service (FFS) between 2016 and 2018. The findings here suggest a relatively small causal effect of payments on Micra adoption and that payments do not affect behavior through a broad "brand loyalty" effect.

3.2 Background

3.2.1 Clinical and regulatory information on leadless pacemakers

Pacemakers are used to treat bradycardia, a condition where the heart beats too slowly. Traditional leaded pacemakers work by delivering electrical impulses to the heart to maintain a healthy heart rhythm. When implanting a pacemaker, a physician will cut a "pocket" in the patient's chest for a pulse generator (essentially a battery). From the pulse generator, "lead" wires are threaded through blood vessels to the heart. Both the creation of a pocket and the threading of lead wires pose infection risks to patients, and infections are one of the primary complications associated with leaded pacemakers.[86] Prior to the introduction of leadless pacemakers, physicians would have to choose between either a "single chamber" or "dual chamber" pacemaker that either placed leads on one or two chambers of the heart, based on the clinical needs of the patient. In practice,

approximately 85% of leaded pacemaker implants were performed with dual chamber pacemakers,[87] because in many patients there was little downside to implanting a dual chamber pacemaker, even when a single chamber pacemaker would be sufficient.

Unlike leaded pacemakers, leadless pacemakers do not require the creation of a pocket or lead wires. Instead, leadless pacemakers attach directly to the heart to delivery electrical impulses. During the sample period of this study, there was only one leadless pacemaker on the market: Medtronic's Micra leadless pacemaker. Micra received approval from the US Food and Drug Administration (FDA) in 2016 on the basis that patients implanted with Micra had fewer complications compared to patients implanted with traditional pacemakers.[76,86] A competitor product, the Nanostim leadless pacemaker from St. Jude Medical (which later merged with Abbott Laboratories), was developed around the same time as Micra but never received FDA approval due to safety concerns. In early 2017, Micra received a national coverage determination from Medicare, conditional on Medtronic using Medicare claims data to develop additional real-world evidence on the effectiveness of Micra.[76] In order for physicians to implant Micra when treating patients, physicians had to undergo training either in a lab environment (often a Medtronic training facility)[88–90] where physicians practiced implanting Micra in cadavers or animal models, or on-site at their hospital proctored by a physician who had undergone the lab environment training.[91]

Prior to 2020, leadless pacemakers were only able to perform single chamber pacing.[86] As such, physicians confronted a more complex trade-off when choosing between single chamber vs dual chamber pacemakers, where some physicians considered using a leadless (single chamber) pacemaker when previously they would have used a

leaded dual chamber pacemaker.[92] This means that while Micra was primarily a substitute for single chamber pacemakers during the study period, Micra could have also hypothetically replaced dual chamber pacemakers in certain circumstances.

3.2.2 Influence of industry payments on physician decision making

Discussions about the appropriateness of industry payments to physicians have persisted for decades. A 2009 report from the Institute of Medicine describes a fundamental tension wherein physician interactions with drug and device manufacturers further the development and adoption of new medical technologies, but those same interactions can also improperly influence physician decision making to the detriment of patients' care.[93] Accordingly, many studies explore potential improper influence by examining the relationship between receipt of payments from drug and medical device manufacturers and physician decision making.

Almost all of the literature studying the relationship between payments and physician decision making focuses on the prescribing of pharmaceutical products. Generally, these studies find that industry payments to physicians are associated with greater prescribing of the paying manufacturers' drugs, increased brand-name prescribing, and decreased quality of prescribing.[82] However, most of these studies are associational and do not employ a causal inference framework. The limited studies with causal inference strategies primarily rely on event study approaches that use physician fixed effects to control for time invariant physician characteristics. These studies generally find smaller effect sizes compared to associational studies and that industry interactions have a null or modestly positive effect on prescribing quality.[83,84] One exception to this trend is a study by Grennan and colleagues, which uses variation in

academic medical centers conflict of interest policies in an instrumental variables analysis to find that meal payments increased promoted statin prescribing by 41%, with the effect primarily concentrated among physicians who were under-prescribing statins.[94]

Studies of pharmaceutical prescribing are likely not generalizable to medical device selection. The nature of payments related to medical devices differs from pharmaceuticals,[80] and education related to medical devices is more likely to require hands-on training compared to medical devices. Unfortunately, the techniques used to study the relationship between industry payments and pharmaceutical prescribing cannot be readily applied to medical devices. Most studies examining pharmaceutical prescribing tend to measure prescribing in administrative claims data with National Drug Codes and then merge the claims data with physician payment data.[82] Similar analyses are not typically possible when examining physicians' medical device selection, as administrative claims do not include device identifiers that enable researchers to identify specific medical devices.

As such, only one study has examined the association between industry payments and device selection. Annapureddy and colleagues use data from a patient registry of implantable cardiac defibrillator implants and find that over 95% of implantable cardiac defibrillator implants were performed by physicians who received payments from device manufacturers, physicians were more likely to use the brand of implantable cardiac defibrillator from the manufacturer that paid them the most, and physicians who received larger payments were more likely to use combination pacemaker-defibrillators when indicated.[95] The study relies on cross-sectional variation and the authors specifically note

that their study does not identify a temporal or causal relationship between payments and device selection.

This study addresses this gap in the literature by using causal inference techniques to identify the relationship between pacemaker manufacturer payments to physicians and adoption of a new medical device.

3.3 Methods

3.3.1 Data and Cohort Construction

This study uses two primary data sources: the 2016 – 2018 Medicare Physician and Other Supplier Public Use Files (PUFs) from CMS, and the 2014 – 2018 Dollars for Docs Database from ProPublica. The Medicare Physician and Other Supplier PUFs are free and publicly available datasets derived from Medicare FFS claims data. The PUFs annually identify the number of Healthcare Common Procedure Common Coding System (HCPCS) procedures performed by providers, as identified by National Provider Identifiers (NPIs), whenever the provider performed the procedure for more than 10 Medicare FFS recipients. NPI-HCPCS combinations for procedures performed for fewer than 10 Medicare FFS recipients are not reported. Provider characteristics, including physician name, gender, specialty, and provider address are also included in the PUFs.[96]

The ProPublica Dollars for Docs database reports all information from the publicly available OpenPayments database from CMS, with the addition of physician NPIs. The Dollars for Docs database (as well as OpenPayments) identifies all payments or transfers of value (hereafter referred to as payments for simplicity) greater than $10 from pharmaceutical and medical device manufacturers to physicians and teaching hospitals The database identifies the name of the manufacturer, the name of the specific

drug or device associated with the payment, the date of payment, the payment amount, the nature of the payment (e.g., royalties, speaking fees, food and beverage, travel and lodging), the name of the physician or hospital receiving the payment, and provider information including address, specialty, and gender. The legislation that created OpenPayments specifically banned the inclusion of NPIs in the database; Dollars for Docs circumvented this issue by using the identifiable physician information in OpenPayments to merge the payment data with NPIs in the National Plan and Provider Enumeration System (NPPES) NPI registry. ProPublica reports a 99% match rate between Dollars for Docs and the NPPES NPI registry.[97]

This study analyzes a cohort of physician-year observations from 2016 through 2018 that performed more than 10 leaded pacemaker implants (HCPCS codes: 33206, 33207, 33208, 33212, 33213, 33214, 33227, 33228) in a given year. I excluded observations that did not merge with the Dollars for Docs database or whose practice address was located outside of the contiguous United States (in order to facilitate calculating travel distances for instrumental variables analysis, see "Data Analysis" section for details) from the analysis.

3.3.2 Outcome of Interest: Proportion of leadless pacemaker implants

The primary outcome of interest is the proportion of all pacemaker implants that physician *i* performed using a leadless pacemaker in in year *t*:

Equation 3-1: Proportion of pacemaker implants performed with a leadless pacemaker

$$y_{it} = \frac{A}{(A + B)}$$

A is the number of pacemaker implants performed with Medtronic's Micra leadless pacemaker. In most instances, specific makes and models of medical devices cannot be identified in administrative claims-based data sources. However, given that Micra was the only leadless pacemaker on the market at the time, procedure codes (HCPCS code: 0387T) can be used in this context to identify Micra implants.[76] *B* is the number of pacemaker implants performed with a leaded pacemaker.

y_{it} is not always directly observed in the Physician and Other Supplier PUFs, as *A* is only reported when more than 10 leadless pacemaker implants were performed (*B* is always greater than 10 in this study, by definition of the cohort). As such, the observed proportion of the pacemaker implants performed with a leadless pacemaker, $\widetilde{y_{it}}$, is interval censored, where $y_{it} = \widetilde{y_{it}}$ if $\widetilde{y_{it}} > 0$, and $y_{it} \in [0, \frac{10}{10+B}]$ if $\widetilde{y_{it}} = 0$.

Supplemental analyses also consider the proportion of single chamber pacemaker implants (HCPCS: 33206, 33207, 33212, 33227) performed with a leadless pacemaker (as opposed to all pacemaker implants performed with a leadless pacemaker). Using all pacemaker implants as the denominator was the preferred specification, as clinicians could hypothetically use leadless pacemakers in cases where previously they would have used a dual chamber pacemaker;[92] results from analyses using single chamber pacemaker implants as the denominator are reported in **Tables B-1** through **B-4**, Appendix.

3.3.3 Independent variables of interest: payments from pacemaker manufacturers

The main independent variables of interest document receipt of payments from pacemaker manufacturers. The largest manufacturers (based on 2014 global sales) of

cardiac implantable electronic devices were identified. These manufacturers include: Abbott Laboratories, Biotronik, Boston Scientific, Cook Medical, Edwards Lifesciences, Medtronic, and St. Jude Medical.[98]

I calculate the total amount of payments (converted to 2018 USD) from all listed pacemaker manufacturers for each physician-year observation in the sample. I also break total payments out into six mutually exclusive categories based on the nature of the payment: consulting; education; food and beverage; royalty, licensing, and investment; speaking fee; and other.[80] For travel and lodging payments, I identify the destination city of travel. In addition to same-year payments, I calculate a three-year rolling sum of payments (e.g., an observation's 2016 rolling sum would include payments for 2014, 2015, and 2016). All payment variables (including total payments and payments for different natures of payment) are broken out into three mutually exclusive bins: payments from Medtronic related to the Micra leadless pacemaker, payments from Medtronic unrelated to the Micra leadless pacemaker, and payments from all other pacemaker manufacturers.

3.3.4 Data Analysis

I calculate sample means and proportions of demographic information and receipt of payment by usage of leadless pacemakers for all physician-year observations in the sample. I create bar charts to identify the most common natures of payments for payments from Medtronic related to Micra, payments from Medtronic unrelated to Micra, and payments from all other pacemaker manufacturers.

To describe the association between receipt of payments and usage of leadless pacemakers, I use ordinary least squares models to regress the proportion of leadless

pacemaker implants on total payments; total payments from Medtronic related to Micra; total payments from Medtronic unrelated to Micra; total payments from all other pacemaker manufacturers; or all three mutually exclusive bins of total payments. I estimate models using either same-year payments or a three-year rolling sum of payments. I also estimate additional models using inverse hyperbolic sine-transformed payment variables to express results as semi-elasticities without relying on arbitrary adjustments to log transform zero-valued payments (e.g., $\log(x + 1)$ vs $\log(x + 0.1)$).[54] All models include year fixed effects, as well as either physician fixed effects or controls for physician gender, physician specialty, and Census division of physician's practice. All standard errors are clustered at the physician level. Additional results estimating linear probability models predicting a binary outcome of whether a physician performed any pacemaker implants with leadless pacemakers are presented in **Tables B-5** through **B-9**, Appendix.

In addition to ordinary least squares models, I estimate interval regression models to account for the interval censoring that occurs when using the Medicare PUFs to calculate the proportion of pacemaker implants performed with a leadless pacemaker. Interval regressions are generalizations of Tobit models that allow for observations to have unobserved outcomes that are known to fall within some interval. Interval regressions model conditional means linearly, meaning the coefficients from interval censored models are interpreted the same way as ordinary least squares coefficients.[99,100] I only estimate interval regressions with controls for year fixed effects, physician gender, specialty, and Census region; physician fixed effects models were not estimated due to

computational limitations with maximum likelihood estimation. Standard errors are clustered at the physician level.

Finally, I estimate two-stage least squares instrumental variables models to account for potential endogeneity. Ordinary least squares models may not estimate the causal relationship between a physician's receipt of payment and their use of leadless pacemakers. Receipt of payment may be correlated with other unobserved physician characteristics. A reverse causal relationship may also exist, where a physician's desire to perform Micra implantations causes physicians to seek out training opportunities and accordingly receive more payments from manufacturers to reimburse for the costs associated with attending those trainings.[82]

To account for both of these concerns, I use the driving distance between a physician's practice and the Minneapolis International Airport (calculated using the "georoute" package in STATA 16.1)[101] as an instrument for payment receipt. An important detail about Medtronic and the Micra pacemaker is that during the sample period, Medtronic's operational headquarters was located in Minneapolis. As such, the majority of payments made by Medtronic related to Micra to reimburse for travel and lodging during the sample period are for travel to Minneapolis (**Table 3-1**).

Table 3- 1: Destinations for "travel and lodging" payments

City of Travel	% of Payments
Minneapolis	51.74%
Orlando	38.11%
San Diego	2.60%
Tampa	3.35%
Other	4.50%

Note: Author's analysis of ProPublica Dollars for Docs payment-level data from Medtronic related to Micra from 2016 through 2018 for all physicians who performed more than 10 leaded pacemaker implants for Medicare FFS recipients. City of travel identified from all payments with "travel and lodging" nature.

The intuition behind travel distance to Minneapolis International Airport as an instrument is that physicians who live farther away from Minneapolis are more likely to receive any travel and lodging reimbursement for attending a training session at a Medtronic facility. The size of those payments are also likely to increase as flight costs and the need for overnight lodging increase for physicians flying to Minneapolis from further away locations.

Two assumptions must hold for travel distance to be a valid instrument for receipt of payment. First, the correlation between travel distance and receipt of payment must be sufficiently strong. I assess the strength of the relationship empirically using both the traditional Cragg-Donald first-stage F-statistic as well as the non-homoskedasticity-robust Montiel Olea and Pflueger effective first-stage F-statistic.[102,103] I also estimate identification-robust Anderson-Rubin confidence sets for second-stage results, which are efficient in single instrument settings even in the presence of a weak instrument,[103–105] as opposed to traditional Wald confidence intervals.

Second, travel distance must not affect physicians' decision to use leadless pacemakers through any mechanism other than by altering the amount of payment they

receive from pacemaker manufacturers (exclusion restriction). Given that Boston Scientific, St. Jude, and Abbott also had operational facilities in Minneapolis during the sample period, travel distance to Minneapolis also likely affects whether physicians received payments from these companies, meaning travel distance to Minneapolis cannot be used to instrument for any Medtronic-specific payments. Instead, all instrumental variable models only analyze total dollars received from all pacemaker manufacturers as an outcome.

Another potential exclusion restriction violation could be that certain geographic areas are faster adopters of new technologies. For example, the diffusion of arthroscopic rotator cuff repair (as opposed to open arthroscopic rotator cuff surgery) varied substantially across hospital referral regions (HRRs), comprising anywhere from 35% to 96% of all rotator cuff repairs in different HRRs for Medicare recipients in 2014.[106] If a similar extent of geographic variation existed in the adoption of leadless pacemakers, and the areas that adopted Micra more rapidly were either disproportionately close to or far away from Minneapolis, this would violate the exclusion restriction. Accordingly, I calculate an interclass correlation coefficient (ICC)[107] derived from a random effects model predicting the proportion of pacemaker implants performed with a leadless pacemaker as a function of a constant and an HRR-year random intercept (subscripted as *ht*):

Equation 3-2: Random intercept model and calculation of interclass correlation coefficient

$$y_{iht} = \beta_0 + u_{0ht} + \varepsilon_{iht}$$

Where:

$$u_{0ht} \sim Normal(0, \sigma^2_{0ht})$$

$$\varepsilon_{iht} \sim Normal(0, \sigma^2)$$

$$ICC = \frac{\sigma^2_{0ht}}{\sigma^2_{0ht} + \sigma^2}$$

The ICC is interpreted as the proportion of variance in leadless pacemaker implants attributable to between-HRR-year variation. A high ICC near 1 indicates that there is very little within-HRR variation, while a low ICC near 0 indicates that there is substantial within-HRR variation. A low ICC would also suggest that an exclusion restriction violation in this instrumental variable setting is unlikely, as location is not predictive of leadless pacemaker adoption.

As in previous models, instrumental variable models use all permutations of same-year payments vs three-year cumulative sum payments and untransformed payments vs inverse hyperbolic sine-transformed payments. All instrumental variable models control for year fixed effects, physician gender, and specialty. Physician fixed effects and geographic controls are omitted from instrumental variable models, as these are expected to be largely collinear with travel distance from Minneapolis. Standard errors are clustered at the physician level.

3.4 Results

3.4.1 Physician Characteristics and Patient Types

The analytic sample includes 9,862 physician-year observations, 108 (1.1%) of which performed more than 10 leadless pacemaker implants. Physicians who performed leadless pacemaker implants disproportionately identified as cardiac electrophysiologists as opposed to other cardiology specialties. Physicians who performed leadless pacemaker implants largely practiced in the same Census divisions as physicians who did not perform leadless pacemaker implants. Physicians who performed leadless pacemaker implants received larger payments from pacemaker manufactures, but over 90% of all physician-year observations in the sample received some payment from a pacemaker manufacturer (**Table 3-1**).

Table 3-2 presents counts of physician-year observations' use of leadless pacemakers based on whether they received any payment related to Micra in year *t* or the preceding two years (i.e., whether the three-year rolling sum of Micra payments was greater than zero). While most physicians who performed Micra implants received payments, receiving a payment related to Micra is neither a necessary nor sufficient condition for implanting a leadless pacemaker (**Table 3-2**).

Figure 1 presents the annual distribution of different natures of payment, separated into three mutually exclusive bins: payments from Medtronic related to Micra, payments from Medtronic unrelated to Micra, and payments from all other pacemaker manufacturers. Total payments from Medtronic unrelated to Micra and total payments from other pacemaker manufacturers are largely dominated by consulting and speaking

fee payments. Conversely, payments from Medtronic related to Micra are almost entirely dedicated to either food and beverage or travel and lodging payments.

Table 3- 2: Characteristics of physician-year sample

	<= 10 leadless implants	> 10 leadless implants
N	9,754	108
Unique physicians	4,133	95
Physician characteristics		
% Female	5.59%	5.56%
% Cardiac electrophysiologist	45.98%	76.85%
% Other cardiologist	48.96%	19.44%
% Other specialty	5.05%	3.70%
% East North Central	16.45%	14.81%
% East South Central	7.24%	9.26%
% Middle Atlantic	12.28%	11.11%
% Mountain	6.39%	6.48%
% New England	5.42%	6.48%
% Pacific	11.45%	7.41%
% South Atlantic	20.86%	25.93%
% West North Central	8.24%	7.41%
% West South Central	11.66%	11.11%
Payment information		
% Receiving any industry payment	92.28%	96.30%
Mean total industry payment	$4,511.70	$11,013.98
% Receiving payment from Medtronic related to Micra	28.72%	64.81%
Mean payment from Medtronic related to Micra	$159.86	$765.67
% Receiving payment from Medtronic unrelated to Micra	73.29%	85.19%
Mean payment from Medtronic unrelated to Micra	$1,359.26	$3,787.82
% Receiving payment from other pacemaker manufacturers	85.18%	90.74%
Mean payment from other pacemaker manufacturers	$2,992.58	$6,460.49

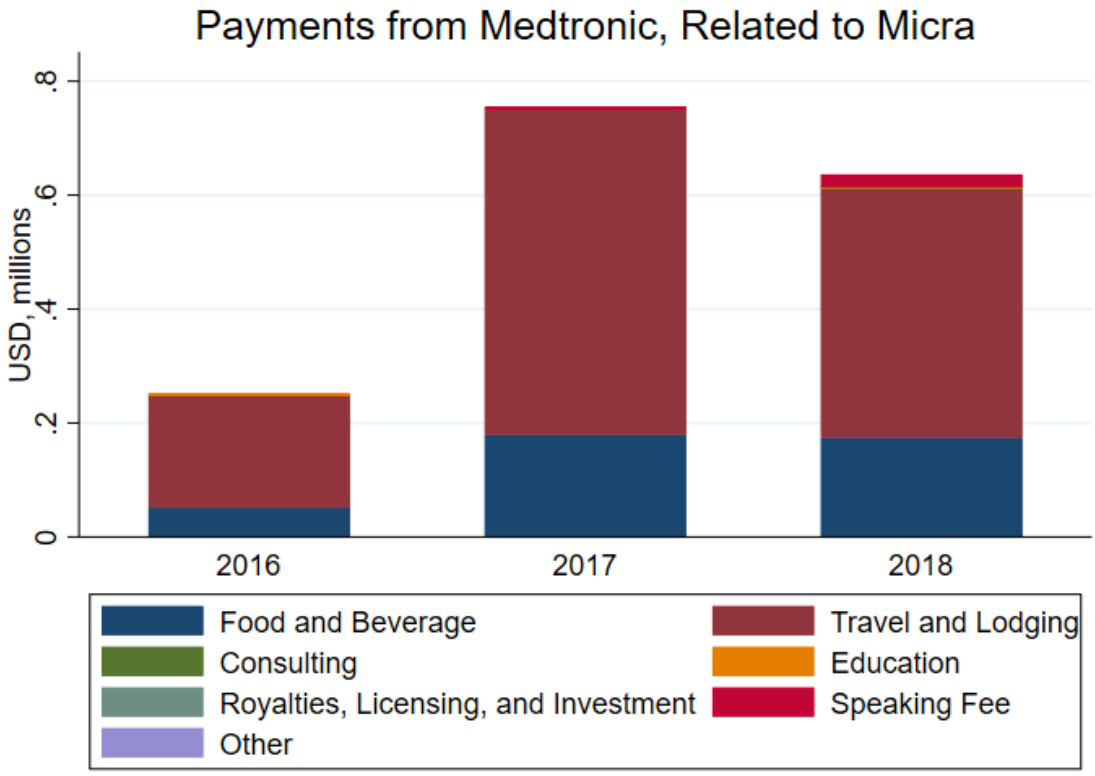
Note: Author's analysis of physician-year observations from Medicare Provider and Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients.

Table 3- 3: Physician-year use of leadless pacemakers by receipt of Micra payment

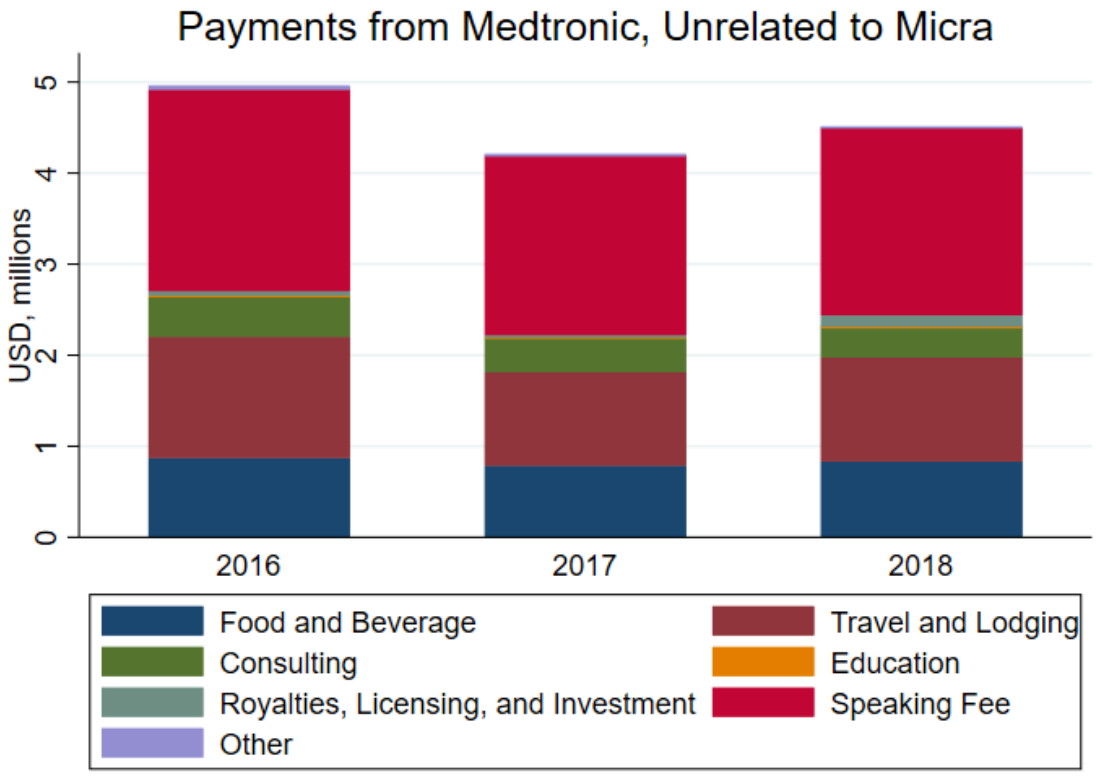
	<= 10 leadless implants	> 10 leadless implants
No receipt of Micra payment in past three years	6,326 (64.15%)	9 (0.09%)
Receipt of Micra payment in past three years	3,428 (34.76%)	99 (1.00%)

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Payment measured as binary outcome of whether physician-year received any Micra payment in current year or preceding two years.

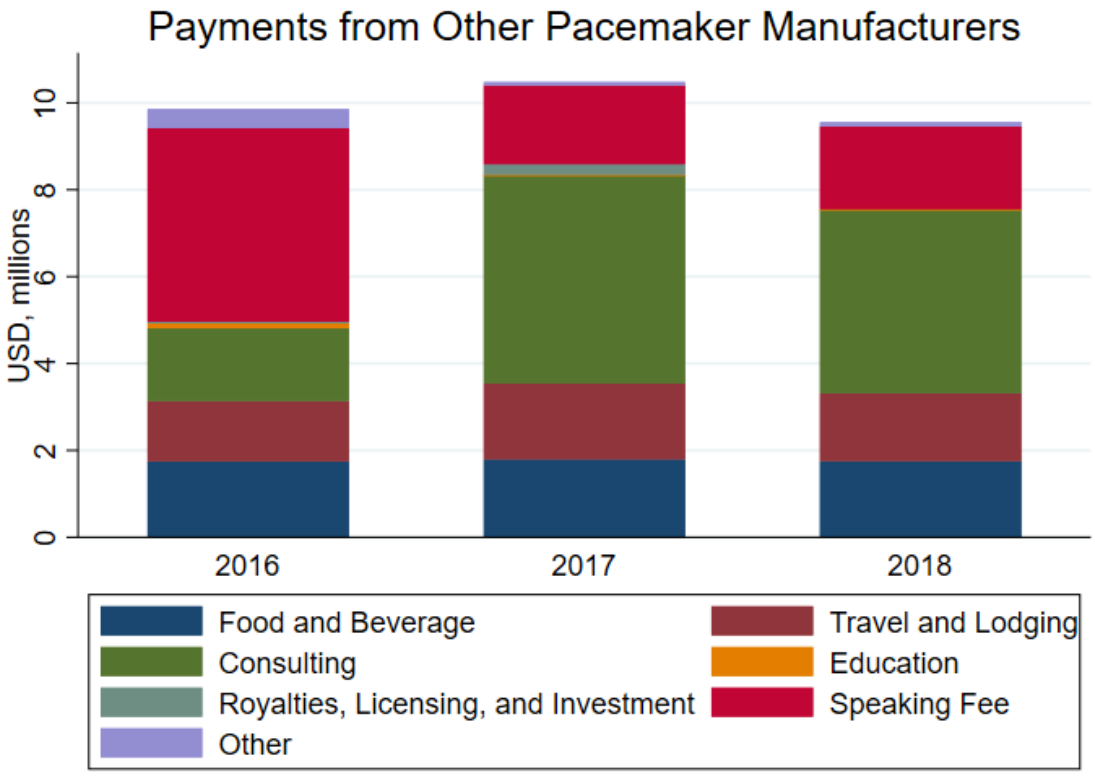
Figure 3- 1: Distributions of nature of payments



Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Same year payments to physicians from Medtronic related to Micra are reported in seven mutually exclusive bins. Results reported in millions of 2018 USD.



Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Same year payments to physicians from Medtronic unrelated to Micra are reported in seven mutually exclusive bins. Results reported in millions of 2018 USD.

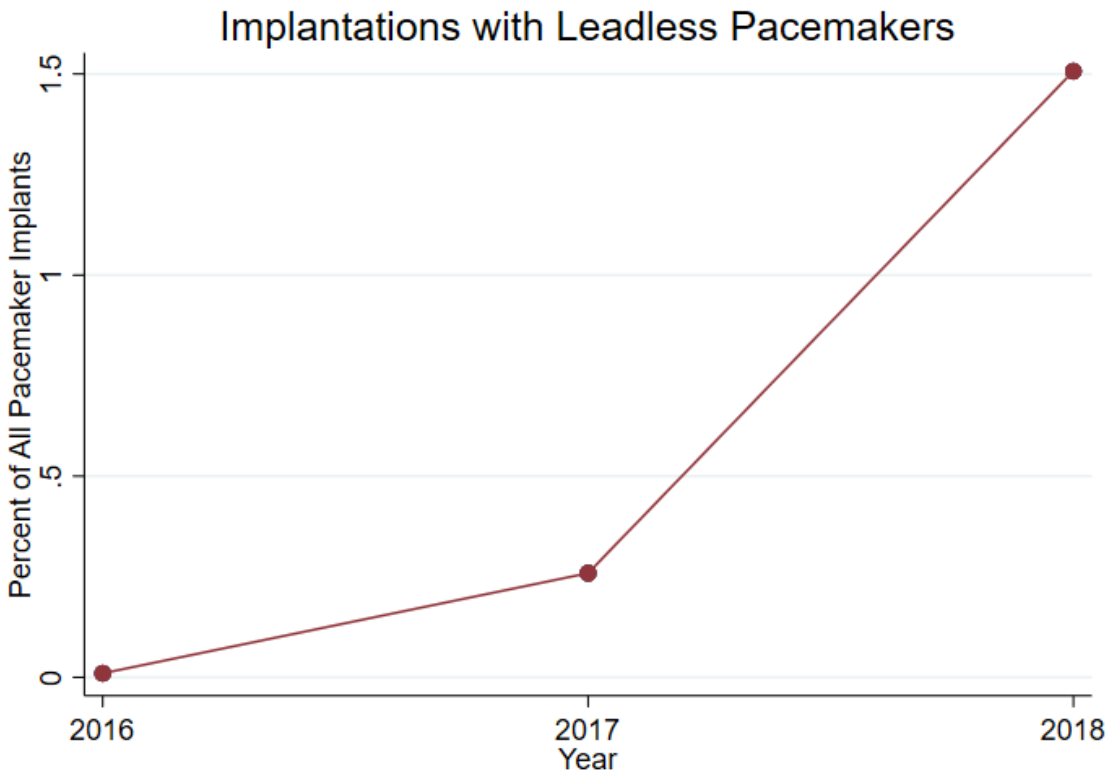


Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Same year payments to physicians from pacemaker manufacturers other than Medtronic are reported in seven mutually exclusive bins. Results reported in millions of 2018 USD.

3.4.2 Relationship between Industry Payments and Use of Leadless Pacemakers

Leadless pacemakers made up effectively 0% of pacemaker implants in the sample in 2016, increasing to 1.5% of all pacemaker implants in the sample in 2018 (**Figure 3-2**).

Figure 3- 2: Percentage of all pacemaker implants performed with leadless pacemakers



Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Numerator defined as total number of leadless pacemaker implants performed in year (HCPCS Current Procedural Terminology code: 0387T). Denominator defined as total number of leadless pacemaker implants plus total leaded pacemaker implants performed in year (HCPCS code: 33206, 33207, 33208, 33212, 33213, 33214, 33227, 33228).

Linear models suggest that total payments from pacemaker manufacturers are associated with greater physician adoption of Micra leadless pacemakers. In OLS estimates, a $1,000 increase in total payments is associated with a 0.010 percentage point increase in the proportion of implants performed with a leadless pacemaker. However, this effect seems to be primarily driven by payments for Micra specifically. A $1,000 increase in Micra payments is associated with a 0.769 percentage point increase in the proportion of implants performed with a leadless pacemaker (**Table 3-4, Panel A**), or a 1 percent increase in Micra payments is associated with a 0.06 percentage point increase in the proportion of implants performed with a leadless pacemaker (**Table 3-5, Panel A**). Payments from Medtronic unrelated to Micra and payments from other pacemaker manufacturers are not associated with Micra adoption, after controlling for Micra payments. Interval regression models suggest a slightly larger linear effect size but slightly smaller and statistically insignificant semi-elasticity effective size for Micra payments (**Table 3-4, Panel B; Table 3-5, Panel B**). However, the effects of same-year total payments and same-year Micra payments were not robust to controlling for physician fixed effects (**Table 3-4, Panel A; Table 3-5, Panel A**).

Table 3- 4: Adjusted associations between untransformed same year payments and leadless pacemaker use

MODEL TYPE	VARIABLES										
Panel A - Ordinary Least Squares	Total Payments from Pacemaker Manufacturers	0.00010**					0.00005				
		(0.00004)					(0.00015)				
	Payments from Medtronic Related to Micra		0.00790***			0.00769***		0.00261			0.00261
			(0.00225)			(0.00222)		(0.00308)			(0.00307)
	Payments from Medtronic Unrelated to Micra			0.00018**		0.00009*			0.00000		-0.00002
				(0.00008)		(0.00005)			(0.00032)		(0.00032)
	Payments from Other Pacemaker Manufacturers				0.00006	0.00003				0.00005	0.00005
					(0.00004)	(0.00003)				(0.00014)	(0.00014)
	Observations	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862
Panel B - Interval Regression	Total Payments from Pacemaker Manufacturers	-0.00002									
		(0.00010)									
	Payments from Medtronic Related to Micra		0.01185***			0.01134***					
			(0.00333)			(0.00321)					
	Payments from Medtronic Unrelated to Micra			0.00053*		0.00038					
				(0.00029)		(0.00024)					
	Payments from Other Pacemaker Manufacturers				-0.00017*	-0.00022***					
					(0.00009)	(0.00008)					
	Observations	9,862	9,862	9,862	9,862	9,862					
	Controls for Observable Physician Characteristics	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No
	Physician Fixed Effects	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes

Robust standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Regression models predict a physician-year's proportion of pacemaker implants performed with a leadless pacemaker as a function of same year payments received from pacemaker manufacturers. Models control for year fixed effects and either physicians fixed effects or a physician's gender, specialty, and Census division. Coefficients are reported as $1,000 change in payment. Interval regressions models with physician fixed effects could not be estimated. Standard errors are clustered at the physician level.

Table 3- 5: Adjusted associations between inverse hyperbolic sine-transformed same year payments and leadless pacemaker use

MODEL TYPE	VARIABLES										
Panel A - Ordinary Least Squares	Total Payments from Pacemaker Manufacturers	0.00049***					0.00031				
		(0.00015)					(0.00036)				
	Payments from Medtronic Related to Micra		0.00073***			0.00062***		-0.00022			-0.00025
			(0.00019)			(0.00018)		(0.00023)			(0.00024)
	Payments from Medtronic Unrelated to Micra			0.00048***		0.00031**			0.00028		0.00028
				(0.00014)		(0.00014)			(0.00027)		(0.00027)
	Payments from Other Pacemaker Manufacturers				0.00019	0.00000				0.00044	0.00044
					(0.00014)	(0.00015)				(0.00037)	(0.00037)
	Observations	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862
Panel B - Interval Regression	Total Payments from Pacemaker Manufacturers	-0.00055									
		(0.00052)									
	Payments from Medtronic Related to Micra		0.00046			0.00042					
			(0.00046)			(0.00044)					
	Payments from Medtronic Unrelated to Micra			0.00035		0.00050					
				(0.00045)		(0.00045)					
	Payments from Other Pacemaker Manufacturers				-0.00077	-0.00099**					
					(0.00049)	(0.00050)					
	Observations	9,862	9,862	9,862	9,862	9,862					
	Controls for Observable Physician Characteristics	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No
	Physician Fixed Effects	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes

Robust standard errors in parentheses
*** p<0.01, ** p<0.05, * p<0.1

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Regression models predict a physician-year's proportion of pacemaker implants performed with a leadless pacemaker as a function of same year inverse hyperbolic sine-transformed payments received from pacemaker manufacturers. Models control for year fixed effects and either physicians fixed effects or a physician's gender, specialty, and Census division. Coefficients are reported as $1,000 change in payment. Interval regressions models with physician fixed effects could not be estimated. Standard errors are clustered at the physician level.

A three-year rolling sum of total payments as well as a rolling sum of payments from Medtronic related to Micra (which can also be interpreted as cumulative Micra payments, as marketing for Micra began in 2016 and the sample period ends in 2018) are more consistently associated with leadless pacemaker adoption compared to single-year payments. In OLS estimates, a $1,000 increase in the three-year rolling sum of total payments is associated with a 0.003 percentage point increase in the proportion of pacemaker implants performed with Micra (**Table 3-6, Panel A**).

Again, the effect of total payments appeared to be driven primarily by Micra payments. A $1,000 increase in cumulative Micra payments is associated with a 0.721 percentage point increase in the proportion of implants performed with a leadless pacemaker, even after controlling for physician fixed effects, while payments from Medtronic unrelated to Micra and payments from other manufacturers are not significantly associated with Micra adoption after controlling for Micra payments. (**Table 3-6, Panel A).** Expressed as a semi-elasticity, a 1 percent increase in cumulative Micra payments is associated with a 0.06 percentage point increase in the proportion of implants performed with a leadless pacemaker (**Table 3-7, Panel A**), after controlling for physician fixed effects. Interval regression models estimate larger effect sizes associated with cumulative Micra payments compared to the linear models, as well as a negative relationship between the three-year rolling sum of payments from other pacemaker manufacturers and Micra usage (**Table 3-6, Panel B; Table 3-7, Panel B**).

Table 3- 6: Adjusted associations between untransformed sums of payments and leadless pacemaker use

MODEL TYPE	VARIABLES										
Panel A - Ordinary Least Squares	Total Payments from Pacemaker Manufacturers	0.00003**					0.00006				
		(0.00001)					(0.00005)				
	Payments from Medtronic Related to Micra		0.00641***			0.00638***		0.00723***			0.00721***
			(0.00141)			(0.00140)		(0.00231)			(0.00228)
	Payments from Medtronic Unrelated to Micra			0.00005**		0.00001			0.00005		0.00002
				(0.00002)		(0.00001)			(0.00007)		(0.00006)
	Payments from Other Pacemaker Manufacturers				0.00002	0.00000				0.00004	0.00003
					(0.00001)	(0.00001)				(0.00005)	(0.00004)
	Observations	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862
Panel B - Interval Regression	Total Payments from Pacemaker Manufacturers	-0.00001									
		(0.00004)									
	Payments from Medtronic Related to Micra		0.00915***			0.00908***					
			(0.00149)			(0.00152)					
	Payments from Medtronic Unrelated to Micra			0.00018*		0.00006					
				(0.00010)		(0.00006)					
	Payments from Other Pacemaker Manufacturers				-0.00007*	-0.00009***					
					(0.00004)	(0.00003)					
	Observations	9,862	9,862	9,862	9,862	9,862					
	Controls for Observable Physician Characteristics	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No
	Physician Fixed Effects	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes

Robust standard errors in parentheses
*** p<0.01, ** p<0.05, * p<0.1

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Regression models predict a physician-year's proportion of pacemaker implants performed with a leadless pacemaker as a function of a three-year rolling sum of payments (e.g., the rolling sum for 2016 includes payments for 2014, 2015, and 2016) received from pacemaker manufacturers. Models control for year fixed effects and either physicians fixed effects or a physician's gender, specialty, and Census division. Coefficients are reported as $1,000 change in payment. Interval regressions models with physician fixed effects could not be estimated. Standard errors are clustered at the physician level.

Table 3- 7: Adjusted associations between inverse hyperbolic sine-transformed sums of payments and leadless pacemaker use

MODEL TYPE	VARIABLES										
Panel A - Ordinary Least Squares	Total Payments from Pacemaker Manufacturers	0.00039***					0.00013				
		(0.00014)					(0.00034)				
	Payments from Medtronic Related to Micra		0.00121***			0.00123***		0.00064**			0.00063**
			(0.00018)			(0.00018)		(0.00030)			(0.00029)
	Payments from Medtronic Unrelated to Micra			0.00035**		0.00001			0.00005		-0.00011
				(0.00014)		(0.00015)			(0.00035)		(0.00039)
	Payments from Other Pacemaker Manufacturers				0.00013	-0.00014				0.00030	0.00023
					(0.00016)	(0.00017)				(0.00043)	(0.00047)
	Observations	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862
Panel B - Interval Regression	Total Payments from Pacemaker Manufacturers	-0.00065									
		(0.00049)									
	Payments from Medtronic Related to Micra		0.00158***			0.00181***					
			(0.00039)			(0.00038)					
	Payments from Medtronic Unrelated to Micra			0.00004		-0.00003					
				(0.00048)		(0.00052)					
	Payments from Other Pacemaker Manufacturers				-0.00100*	-0.00134**					
					(0.00055)	(0.00059)					
	Observations	9,862	9,862	9,862	9,862	9,862					
	Controls for Observable Physician Characteristics	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No
	Physician Fixed Effects	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes

Robust standard errors in parentheses
*** p<0.01, ** p<0.05, * p<0.1

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Regression models predict a physician-year's proportion of pacemaker implants performed with a leadless pacemaker as a function of an inverse hyperbolic sine-transformed three-year rolling sum of payments (e.g., the rolling sum for 2016 includes payments for 2014, 2015, and 2016) received from pacemaker manufacturers. Models control for year fixed effects and either physicians fixed effects or a physician's gender, specialty, and Census division. Coefficients are reported as $1,000 change in payment. Interval regressions models with physician fixed effects could not be estimated. Standard errors are clustered at the physician level.

When considering the use of travel distance as an instrument and potential exclusion restriction violations where location affects leadless pacemaker adoption through a mechanism other than industry payments, the ICC on a random effects model predicting Micra adoption as a function of HRR-year random effects is 0.049 (not reported in tables). This means that approximately 5% of total variation in leadless pacemaker usage is attributable to between-HRR-year variation, or that location is not predictive of leadless pacemaker usage.

Unlike the linear models (without fixed effects) which found that total payments from all pacemaker manufacturers were consistently associated with leadless pacemaker adoption, the estimated instrumental variable models found that total payments are not associated with Micra adoption (**Table 3-8**). While all model specifications find null results, only models regressing leadless implants as a function of inverse hyperbolic sine-transformed payments should be considered. Models using untransformed payments do not have effective first-stage F statistics greater than the critical value needed to ensure that any bias due to weak instruments is no more than 10% of the "worst-case situation when instruments are completely uninformative and when first-stage and second-stage errors are perfectly correlated"[108] and are only reported for transparency.

Table 3-8: Instrumental variable estimates of effect of total pacemaker manufacturer payments on use of leadless pacemakers

VARIABLES				
Total Payments from Pacemaker Manufacturers	-0.00086 [-0.002718, 0.000317]	-0.00191 [-0.004990, 0.000872]	-0.00028 [-0.000875, 0.000099]	-0.00191 [-0.004994, 0.000875]
Observations	9,862	9,862	9,862	9,862
Cragg-Donald F	37.45	174.10	39.97	150.93
Montiel Olea & Pflueger F	14.79	82.43	16.24	70.05
Critical Value, $\tau = 5\%$	37.42	37.42	37.42	37.42
Critical Value, $\tau = 10\%$	23.11	23.11	23.11	23.11
Payment Type	Same Year	Rolling Sum	Same Year	Rolling Sum
Payment Transformation	Untransformed	Untransformed	Inverse Hyperbolic Sine	Inverse Hyperbolic Sine

Anderson-Rubin confidence sets in brackets

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Two stage least squares instrumental variable models first predict total payments from pacemaker manufacturers as a function of physician's practice's distance from Minneapolis International Airport. Second stage predicts proportion of pacemaker implants performed with a leadless pacemaker as a function of predicted total payments. Total payments calculated as either same year payments or three-year rolling sum of payments and either untransformed or inverse hyperbolic sine-transformed. Three-year rolling sum refers to current year and preceding two years (e.g., the rolling sum for 2016 includes payments for 2014, 2015, and 2016). Critical values denote necessary Montiel Olea and Pflueger effective first stage F statistic in order for bias to be no worse than 5% or 10% of worst-case bias at confidence level of 5%. Models control for year fixed effects, physician's gender, and physician's specialty. Anderson-Rubin 95% confidence sets, as opposed to traditional Wald confidence intervals, are reported. Standard errors are clustered at the physician-level.

3.5 Discussion

I find that over 90% of physicians who performed pacemaker implants for Medicare FFS recipients between 2016 and 2018 received some payment or transfer of value from a pacemaker manufacturer. However, these payments appear to have a relatively small impact on physicians' adoption of the Micra leadless pacemaker. In associational analyses, a $1,000 increase in total payments from pacemaker manufacturers is associated with a 0.010 percentage point increase in the proportion of pacemaker implants performed with a Micra leadless pacemaker. However, this finding is not robust to either the inclusion of physician fixed effects or instrumental variables analysis. Furthermore, decomposing payments into distinct bins based on relevance to Micra usage demonstrates that the relationship between manufacturer payments and leadless pacemaker adoption is driven almost entirely by payments from Medtronic specifically related to Micra. A $1,000 increase in cumulative Micra payments is associated with a 0.721 percentage point increase in the proportion of pacemaker implants performed with a leadless pacemaker, after controlling for physician fixed effects; the same model finds no effect for payments from Medtronic unrelated to Micra or payments from other manufacturers after controlling for Micra payments.

This study's findings inform an on-going discussion about the role of industry payments to physicians. Critics of the practice argue that payments sometimes amount to improper inducement wherein physicians choose medical devices based on whether companies paid for their dinners rather than the quality of evidence for certain devices. Conversely, proponents of the practice argue that industry relationships with physicians are essential for training and educating physicians about new medical technologies.[81]

In the context of Micra adoption in Medicare FFS, this study does not find evidence consistent with payments causing improper inducement. In every model specification controlling for Micra-specific payments, payments from Medtronic unrelated to Micra are not associated with leadless pacemaker adoption. If physicians were choosing to adopt Micra out of a sense of obligation to Medtronic because the company had previously paid them, one would expect that any Medtronic payments would be associated with pacemaker adoption. Instead, only Micra-specific payments are associated with Micra adoption, and with a relatively small effect size; results from **Table 3-5, Panel A** suggest it would take a $1386.96 increase in Micra payments (almost twice the mean annual Micra payment among Micra users) to increase a physician's proportion of pacemaker implants performed with Micra by 1 percentage point.

Consideration of the local average treatment effect and the driving variation in the instrumental variables analyses in **Table 3-7** is also suggestive that increasing payments in this context did not improperly induce physicians to alter treatment decisions. The relationship between travel distance to Minneapolis and industry payments is almost mechanical. As physicians practiced farther away from Minneapolis, it cost more to fly to Minneapolis and was more likely that they needed overnight lodging. However, it is not obvious that physicians who practiced farther from Minneapolis would perceive themselves as receiving anything of greater "value" than physicians who live closer to Minneapolis if the increased payments simply offset greater costs associated with traveling to educational opportunities.

As such, it is perhaps not surprising that an instrumental variable analysis exploiting variation in payments amount without obvious variation in "value" does not

find that increasing payment amounts changed physician behavior. In this study, increasing the size of total payments to physicians did not have a causal effect on Micra adoption. This is in contrast to prior observational studies that have presented "dosing response" relationships (where larger payments are associated with larger changes in physician behavior) as suggestive evidence of a causal relationship between payments and physician decision making.[82]

Overall, this study makes several contributions to the literature on industry payments and physician decision-making. First, to my knowledge, this is one of only a few studies[94] to use instrumental variables to examine the causal relationship between industry payments and physician decision making. Most prior analysis studies that employed a causal inference framework relied on physician fixed effects or event study approaches.[83–85] However, event study analyses do not circumvent concerns of reverse causality, wherein physicians who are the most motivated to change how they practice medicine are the most targeted by industry payments or the most likely to seek out industry payment. Using travel distance to Minneapolis as an instrument for receipt of payment avoids concerns of reverse causality, so long as physicians' unobservable motivation to adopt leadless pacemakers was uncorrelated with their proximity from Minneapolis.

Second, in this study I disaggregate the effect of payments from a manufacturer related to the studied product from payments from the manufacturer unrelated to the studied product. This distinction allowed me more precisely disentangle inducement effects from education effects caused by industry payments.

Third, this is only the second study to examine the effects of industry payments on medical device selection specifically[95] (as opposed to pharmaceutical prescribing) and the first to study these effects through a causal inference framework. The nature of payments from medical device manufacturers differs from payments in the pharmaceutical industry. Physicians are more likely to need hands-on training to effectively use a new medical device compared to a new pharmaceutical product, and industry payments for medical devices are disproportionately spent on royalties and licensing agreements,[80] meaning results from studies of the pharmaceutical industry are not necessarily generalizable to the medical device industry.

Having distinct empirical evidence from both pharmaceutical and medical device contexts can enable policymakers to understand the nuanced relationship between industry payments and physician decision making as they consider changing regulations to manage conflicts of interest in medicine. For example, the results from this study suggest that policymakers could potentially restrict or ban certain types of industry payments related to medical devices, such as those related to food and lodging or travel and budget, without a large impact on the adoption of new technologies. The effect of industry payments on the adoption of Micra were relatively small, and both the average annual Micra payment per physician ($766) and average annual total Micra payments (less than $1 million annually) are small enough that feasibly hospitals or physicians could have paid for these costs directly, rather than having a medical device company reimburse physicians.

However, it should be cautioned that these results are not necessarily generalizable to other medical devices, one of the main limitations of this study. This

study examined use of the only leadless pacemaker available on the US market, a device that was both more expensive[109] and more effective[86] than the previous generation of single chamber pacemakers. Additionally, Micra is somewhat unique in that it was developed almost entirely as an internal Medtronic product, rather than relying on external physician inventors or licensing agreements with start-up companies as is common in the medical device industry.[110] Industry payments may have more or less pronounced effects on the development and adoption of technologies where competitor devices are available, technologies where the relative costs and benefits of those technologies are less obvious, technologies where the cost differential is less substantial between generations of a technology, or technologies developed with external physician collaborators or start-ups. Future research should explore the effect of industry payments on the adoption of other types of medical devices.

There were also several methodological limitations of this study. First, travel distance to Minneapolis could not be used to specifically instrument for Micra payments due to exclusion restriction concerns, meaning causal estimates could only be generated for the effect of total industry payments on Micra usage. However, in associational analyses, the relationship between Micra payments and Micra usage is the strongest of all payment variables analyzed, suggesting that only focusing on the causal effect of total payments potentially misses an important nuance in the relationship between industry payments and technology adoption. Additional research that can identify the causal relationship between product-specific payments and adoption of specific products would make a substantial contribution to the broader literature on industry payments and physician decision making.

Second, results from models that accounted for interval censoring in the data could be misleading if the underlying distributional assumptions are incorrect. Interval regression models best approximate results from uncensored data when outcomes over the censored region are normally distributed. Future research could avoid the challenges associated with these distributional assumptions by instead using non-censored data, such as a HCPCS-based extract of Medicare FFS claims, rather than the Physician and Other Supplier PUFs.

Third, this study was unable to comment on whether industry payments are associated with clinically appropriate use of leadless pacemakers. During the sample period, leadless pacemakers were only indicated for patients with atrioventricular block and atrial fibrillation or patients without atrial fibrillation with either atrioventricular block or sinus node dysfunction who were not good candidates for dual-chamber pacing.[76] This study could not identify whether patients that received leadless pacemakers met these requirements, as diagnosis information associated with procedures is not reported in the Physician and Other Supplier PUFs. This could again be circumvented by analyzing the same research question with a HCPCS-based extract of Medicare FFS claims.

Fourth and finally, the instrumental variable analyses in this study are only valid as long as physicians' distance from Minneapolis only affect their usage of Micra leadless pacemakers through distance's effect on receipt of payment. If location affects Micra adoption through some other channel, this would generate inconsistent instrumental variable results (though the lack of location's ability to explain variation in Micra adoption makes such an exclusion restriction unlikely).

3.6 Conclusion

I find that most physicians who performed pacemaker implants for Medicare FFS recipients between 2016 and 2018 received payments or transfers of value from pacemaker manufacturers. Total industry payments are associated with greater adoption of Medtronic's Micra leadless pacemaker, but this finding is not robust to physician fixed effects or instrumental variable analyses. Decomposing total payments into payments from Medtronic related to Micra vs payments from Medtronic unrelated to Micra demonstrates that only Micra-specific payments are associated with Micra adoption, suggesting industry payments in this setting do not develop a sense of brand loyalty that influenced adoption. These findings collectively suggest that the causal effect of industry payments to physicians on adoption of leadless pacemakers when treating Medicare FFS patients between 2016 and 2018 was minor and that payments more likely facilitated physician education rather than improperly induced physician adoption.

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APPENDIX A, Chapter 1 Appendices

Financial shocks may prevent medical device firms from bringing products to market, even if those products have a positive expected profit. If firms have difficulty acquiring external financing to fund their projects, then financial shocks may cause a disruption in cash flow and prevent firms from financing R&D projects internally. One would expect that R&D intensive firms are more financially "constrained" in their ability to acquire external financing; they may have difficulty explained the value of complicated scientific projects to external investors,[31] an information symmetry that can lead to adverse selection.[32]

While one might expect R&D intensive firms to be constrained, the empirical finance literature has often struggled to express financial constraint in a reliable manner. Studies generating measures of constraint tend to follow two main approaches, either using structural modeling to calculate measures of constraint based on financial data or by looking at proxy measures of constraint, such as credit ratings or sentiment in 10-K filings.[111] To demonstrate that medical device firms are financial constrained and would accordingly be more likely to reduce R&D investments in response to negative shocks, I characterize the level of constraint in the industry using the Hoberg-Maksimovic constraint index. Hoberg and Maksimovic (2015) use natural language processing to assess the sentiment in over 70,000 firm-years' Liquidity and Capitalization Resource subsections with their 10-K reports, specifically examining sentiment related to issues of liquidity and intended sources of capital.[33] While previous measures of constraint have generally fared poorly in predicting how firms make investments in response to financial

shocks,[111] Hoberg and Maksimovic find that their constraint index predicts whether firms will reduce R&D investments following exogeneous negative financial shocks.[33]

When comparing firms in the medical device industry (based on NAICS codes) to other firms in the Hoberg-Maksimovic sample from 1997 to 2012,[34] I find that medical device firms are significantly more constrained than other firms in the sample ($t = 8.673$, $p < 0.001$). An additional unit on the Hoberg-Maksimovic constraint index does not have a meaningful interpretation, but the data is centered such that zero is the average level of measured constraint across the study's larger 1997 to 2015 sample. Given that the mean constraint of the medical device industry is positive, this is another way of saying that the industry has an above average level of financial constraint. This is what one would expect of R&D intensive firms.[31]

Table A- 1: Differences in the Hoberg-Maksimovic Constraint Index Between Medical Device Firms and Non-Medical Device Firms

Group	Observations	Mean (95% CI)
Non-Medical Device Firms	74,589	-0.0011 (-0.0019, -0.0005)
Medical Device Firms	789	0.0304 (0.0232, 0.0376)
Difference		-0.0316 *** (-0.0388, -0.0243)

Note: Author's calculations based on data from Hoberg & Maksimovic (2015) and CompuStat data from 1997 to 2012. The constraint index is mean-centered at zero, with higher levels of the index indicated greater levels of constraint reported in Liquidity and Capitalization Resource subsections of public 10-K reports. *** p<0.01, ** p<0.05, * p<0.1

Table A- 2: Estimates from two-way fixed effects models of storm exposure semi-elasticities of financial outcomes

Years Since Storm	Earnings before Income and Taxes	Total Assets	Total Debt	Net Cash Flow	Employees
	Coefficient (95% CI)	*Coefficient (95% CI)*	*Coefficient (95% CI)*	*Coefficient (95% CI)*	*Coefficient (95% CI)*
-4	0.205 (-0.150, 0.560)	-0.019 (-0.155, 0.118)	0.091 (-0.245, 0.428)	0.052 (-0.183, 0.287)	0.008 (-0.051, 0.067)
-3	0.224 (-0.134, 0.582)	-0.010 (-0.137, 0.117)	0.172 (-0.205, 0.550)	0.128 (-0.163, 0.420)	0.016 (-0.051, 0.084)
-2	0.121 (-0.153, 0.396)	-0.028 (-0.142, 0.086)	-0.123 (-0.589, 0.343)	-0.005 (-0.187, 0.178)	0.005 (-0.056, 0.066)
-1	Reference Period	Reference Period	Reference Period	Reference Period	Reference Period
0	0.076 (-0.126, 0.277)	-0.019 (-0.101, 0.063)	-0.282 (-0.727, 0.164)	0.159 * (-0.006, 0.324)	0.004 (-0.044, 0.053)
1	0.048 (-0.123, 0.219)	-0.061 (-0.151, 0.028)	-0.343 ** (-0.675, -0.011)	0.121 (-0.040, 0.281)	-0.008 (-0.053, 0.036)
2	0.015 (-0.295, 0.325)	-0.048 (-0.188, 0.092)	-0.570 ** (-1.041, -0.099)	0.123 (-0.104, 0.351)	-0.016 (-0.093, 0.061)
3	-0.030 (-0.325, 0.265)	-0.015 (-0.139, 0.108)	-0.289 * (-0.600, 0.022)	0.027 (-0.242, 0.295)	-0.009 (-0.079, 0.061)
4	0.044 (-0.106, 0.195)	0.035 (-0.066, 0.137)	-0.234 (-0.633, 0.165)	0.106 (-0.036, 0.247)	0.002 (-0.062, 0.066)
N	1,541	1,541	1,541	1,541	1,541
R^2	0.837	0.946	0.824	0.822	0.962

Note: Author's calculations based on NOAA storm trajectory data and CompuStat data on medical device firms from 1996 to 2012. Models regress outcomes in year *t* as a function of lags and leads of storm exposure, after adjusting for firm and year fixed effects. Outcome are inverse hyperbolic sine transformed; coefficients are interpreted as semi-elasticities (percent change in outcome caused by one-unit change in storm exposure). Standard errors are clustered at the firm level. All outcomes except for employees are reported in millions of 2012 USD. *** p<0.01, ** p<0.05, * p<0.1

Table A- 3: Estimates from two-way fixed effects models of storm exposure semi-elasticities of innovation outcomes

Years Since Storm	R&D Spending	PMA Devices	PMN Devices	PMN Devices, Citation Weighted
	Coefficient (95% CI)	*Coefficient (95% CI)*	*Coefficient (95% CI)*	*Coefficient (95% CI)*
-4	0.028 (-0.064, 0.121)	0.063 (-0.027, 0.152)	-0.005 (-0.139, 0.129)	0.021 (-0.141, 0.183)
-3	0.028 (-0.045, 0.101)	0.097 (-0.031, 0.225)	-0.026 (-0.125, 0.073)	-0.048 (-0.180, 0.085)
-2	0.017 (-0.062, 0.096)	0.025 (-0.064, 0.114)	-0.017 (-0.171, 0.136)	-0.011 (-0.182, 0.160)
-1	Reference Period	Reference Period	Reference Period	Reference Period
0	-0.026 (-0.070, 0.018)	0.077 (-0.029, 0.183)	-0.034 (-0.113, 0.045)	-0.033 (-0.152, 0.087)
1	-0.032 (-0.086, 0.022)	0.020 (-0.018, 0.057)	-0.048 * (-0.104, 0.007)	-0.062 (-0.137, 0.013)
2	-0.068 (-0.165, 0.028)	0.073 (-0.050, 0.197)	-0.095 (-0.252, 0.063)	-0.115 (-0.291, 0.061)
3	-0.055 (-0.126, 0.016)	-0.014 (-0.083, 0.056)	-0.008 (-0.119, 0.103)	0.024 (-0.100, 0.149)
4	-0.031 (-0.113, 0.050)	0.093 (-0.076, 0.263)	-0.016 (-0.142, 0.110)	-0.001 (-0.162, 0.160)
N	1,541	1,541	1,541	1,541
R^2	0.953	0.567	0.802	0.790

Note: Author's calculations based on NOAA storm trajectory data, FDA device approval databases and natural language processing of FDA summary files, and CompuStat data on medical device firms from 1996 to 2012. Models regress outcomes in year *t* as a function of lags and leads of storm exposure, after adjusting for firm and year fixed effects. Outcomes are inverse hyperbolic sine transformed; coefficients are interpreted as semi-elasticities (percent change in outcome caused by one-unit change in storm exposure). Standard errors are clustered at the firm level. R&D spending is reported in millions of 2012 USD. Same-firm citations are not counted. R&D: research and development; PMA: pre-market approval; PMN: pre-market notification. *** p<0.01, ** p<0.05, * p<0.1

APPENDIX B, Chapter 3 Appendices

Table B- 1: Adjusted associations between untransformed same year payments and use of leadless pacemakers

VARIABLES										
Total Payments from Pacemaker Manufacturers	0.00142					0.00133				
	(0.00087)					(0.00189)				
Payments from Medtronic Related to Micra		0.09529***			0.08484***		0.03110			0.04114
		(0.01537)			(0.01593)		(0.07293)			(0.07912)
Payments from Medtronic Unrelated to Micra			0.00943**		0.00548*			-0.00307		-0.00323
			(0.00374)		(0.00310)			(0.00602)		(0.00548)
Payments from Other Pacemaker Manufacturers				0.00033	-0.00026				0.00209	0.00239
				(0.00075)	(0.00067)				(0.00246)	(0.00275)
Observations	660	660	660	660	660	660	660	660	660	660
Controls for Observable Physician Characteristics	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No
Physician Fixed Effects	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes

Robust standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Regression models predict a physician-year's proportion of single pacemaker implants performed with a leadless pacemaker as a function of same year payments received from pacemaker manufacturers. Models control for year fixed effects and either physicians fixed effects or a physician's gender, specialty, and Census division. Coefficients are reported as $1,000 change in payment. Standard errors are clustered at the physician level.

Table B- 2: Adjusted associations between inverse hyperbolic sine-transformed same year payments and use of leadless pacemakers

VARIABLES										
Total Payments from Pacemaker Manufacturers	0.01603***					0.01308				
	(0.00533)					(0.01812)				
Payments from Medtronic Related to Micra		0.02142***			0.01641***		0.00349			0.00445
		(0.00508)			(0.00517)		(0.01104)			(0.01101)
Payments from Medtronic Unrelated to Micra			0.01873***		0.01317***			0.00080		0.00123
			(0.00437)		(0.00459)			(0.01671)		(0.01673)
Payments from Other Pacemaker Manufacturers				0.00486	-0.00066				0.01124	0.01228
				(0.00463)	(0.00459)				(0.01656)	(0.01639)
Observations	660	660	660	660	660	660	660	660	660	660
Controls for Observable Physician Characteristics	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No
Physician Fixed Effects	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes

Robust standard errors in parentheses
*** p<0.01, ** p<0.05, * p<0.1

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Regression models predict a physician-year's proportion of single chamber pacemaker implants performed with a leadless pacemaker as a function of same year inverse hyperbolic sine-transformed payments received from pacemaker manufacturers. Models control for year fixed effects and either physicians fixed effects or a physician's gender, specialty, and Census division. Coefficients are reported as $1,000 change in payment. Standard errors are clustered at the physician level.

Table B- 3: Adjusted associations between untransformed rolling sums of payments and use of leadless pacemakers

VARIABLES										
Total Payments from Pacemaker Manufacturers	0.00041					0.00046				
	(0.00031)					(0.00151)				
Payments from Medtronic Related to Micra		0.07262***			0.07011***		0.02700			0.02692
		(0.01230)			(0.01275)		(0.05211)			(0.05233)
Payments from Medtronic Unrelated to Micra			0.00382***		0.00087			-0.00003		-0.00031
			(0.00144)		(0.00092)			(0.00196)		(0.00214)
Payments from Other Pacemaker Manufacturers				0.00001	-0.00031				0.00052	0.00042
				(0.00029)	(0.00022)				(0.00166)	(0.00159)
Observations	660	660	660	660	660	660	660	660	660	660
Controls for Observable Physician Characteristics	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No
Physician Fixed Effects	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes

Robust standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Regression models predict a physician-year's proportion of single chamber pacemaker implants performed with a leadless pacemaker as a function of a three-year rolling sum of payments (e.g., the rolling sum for 2016 includes payments for 2014, 2015, and 2016) received from pacemaker manufacturers. Models control for year fixed effects and either physicians fixed effects or a physician's gender, specialty, and Census division. Coefficients are reported as $1,000 change in payment. Standard errors are clustered at the physician level.

Table B- 4: Adjusted associations between inverse hyperbolic sine-transformed rolling sums of payments and use of leadless pacemakers

VARIABLES										
Total Payments from Pacemaker Manufacturers	0.01385***					0.00174				
	(0.00503)					(0.01136)				
Payments from Medtronic Related to Micra		0.03414***			0.03377***		0.00556			0.00556
		(0.00447)			(0.00457)		(0.01277)			(0.01218)
Payments from Medtronic Unrelated to Micra			0.01519***		0.00128			0.00063		-0.00338
			(0.00431)		(0.00414)			(0.02462)		(0.02473)
Payments from Other Pacemaker Manufacturers				0.00491	-0.00114				0.00766	0.00758
				(0.00471)	(0.00459)				(0.01327)	(0.01392)
Observations	660	660	660	660	660	660	660	660	660	660
Controls for Observable Physician Characteristics	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No
Physician Fixed Effects	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes

Robust standard errors in parentheses
*** p<0.01, ** p<0.05, * p<0.1

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Regression models predict a physician-year's proportion of single chamber pacemaker implants performed with a leadless pacemaker as a function of an inverse hyperbolic sine-transformed three-year rolling sum of payments (e.g., the rolling sum for 2016 includes payments for 2014, 2015, and 2016) received from pacemaker manufacturers. Models control for year fixed effects and either physicians fixed effects or a physician's gender, specialty, and Census division. Coefficients are reported as $1,000 change in payment. Standard errors are clustered at the physician level.

Table B- 5: Adjusted associations between untransformed same year payments and use of leadless pacemakers

VARIABLES										
Total Payments from Pacemaker Manufacturers	0.00039***					0.00018				
	(0.00013)					(0.00045)				
Payments from Medtronic Related to Micra		0.02481***			0.02399***		0.00858			0.00863
		(0.00652)			(0.00647)		(0.00988)			(0.00988)
Payments from Medtronic Unrelated to Micra			0.00061**		0.00030*			-0.00016		-0.00024
			(0.00025)		(0.00018)			(0.00098)		(0.00098)
Payments from Other Pacemaker Manufacturers				0.00031**	0.00022				0.00023	0.00023
				(0.00016)	(0.00015)				(0.00048)	(0.00048)
Observations	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862
Controls for Observable Physician Characteristics	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No
Physician Fixed Effects	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes

Robust standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Linear probability models predict whether a physician-year performed more than 10 pacemaker implants performed with a leadless pacemaker as a function of same year payments received from pacemaker manufacturers. Models control for year fixed effects and either physicians fixed effects or a physician's gender, specialty, and Census division. Coefficients are reported as $1,000 change in payment. Standard errors are clustered at the physician level.

Table B- 6: Adjusted associations between inverse hyperbolic sine-transformed same year payments and use of leadless pacemakers

VARIABLES										
Total Payments from Pacemaker Manufacturers	0.00197***					0.00107				
	(0.00047)					(0.00105)				
Payments from Medtronic Related to Micra		0.00240***			0.00200***		-0.00060			-0.00064
		(0.00055)			(0.00054)		(0.00077)			(0.00078)
Payments from Medtronic Unrelated to Micra			0.00163***		0.00101**			0.00019		0.00019
			(0.00043)		(0.00043)			(0.00084)		(0.00085)
Payments from Other Pacemaker Manufacturers				0.00094**	0.00034				0.00152	0.00153
				(0.00043)	(0.00045)				(0.00118)	(0.00118)
Observations	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862
Controls for Observable Physician Characteristics	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No
Physician Fixed Effects	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes

Robust standard errors in parentheses
*** p<0.01, ** p<0.05, * p<0.1

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Linear probability models predict whether a physician-year performed more than 10 pacemaker implants performed with a leadless pacemaker as a function of same year inverse hyperbolic sine-transformed payments received from pacemaker manufacturers. Models control for year fixed effects and either physicians fixed effects or a physician's gender, specialty, and Census division. Coefficients are reported as $1,000 change in payment. Standard errors are clustered at the physician level.

Table B- 7: Adjusted associations between untransformed rolling sums of payments and use of leadless pacemakers

VARIABLES										
Total Payments from Pacemaker Manufacturers	0.00012***					0.00019				
	(0.00004)					(0.00013)				
Payments from Medtronic Related to Micra		0.02040***			0.02023***		0.02291***			0.02284***
		(0.00414)			(0.00411)		(0.00618)			(0.00612)
Payments from Medtronic Unrelated to Micra			0.00017**		0.00003			0.00012		0.00003
			(0.00007)		(0.00004)			(0.00020)		(0.00017)
Payments from Other Pacemaker Manufacturers				0.00009*	0.00004				0.00015	0.00012
				(0.00005)	(0.00005)				(0.00015)	(0.00014)
Observations	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862
Controls for Observable Physician Characteristics	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No
Physician Fixed Effects	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes

Robust standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Linear probability models predict whether a physician-year performed more than 10 pacemaker implants performed with a leadless pacemaker as a function of a three-year rolling sum of payments (e.g., the rolling sum for 2016 includes payments for 2014, 2015, and 2016) received from pacemaker manufacturers. Models control for year fixed effects and either physicians fixed effects or a physician's gender, specialty, and Census division. Coefficients are reported as $1,000 change in payment. Standard errors are clustered at the physician level.

Table B- 8: Adjusted associations between inverse hyperbolic sine-transformed rolling sums of payments and use of leadless pacemakers

VARIABLES										
Total Payments from Pacemaker Manufacturers	0.00161***					0.00054				
	(0.00042)					(0.00099)				
Payments from Medtronic Related to Micra		0.00405***			0.00402***		0.00229**			0.00227**
		(0.00053)			(0.00052)		(0.00092)			(0.00091)
Payments from Medtronic Unrelated to Micra			0.00142***		0.00018			0.00009		-0.00054
			(0.00039)		(0.00040)			(0.00098)		(0.00104)
Payments from Other Pacemaker Manufacturers				0.00080*	-0.00014				0.00126	0.00107
				(0.00043)	(0.00047)				(0.00121)	(0.00128)
Observations	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862	9,862
Controls for Observable Physician Characteristics	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No
Physician Fixed Effects	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes

Robust standard errors in parentheses
*** p<0.01, ** p<0.05, * p<0.1

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Linear probability models predict whether a physician-year performed more than 10 pacemaker implants performed with a leadless pacemaker as a function of an inverse hyperbolic sine-transformed three-year rolling sum of payments (e.g., the rolling sum for 2016 includes payments for 2014, 2015, and 2016) received from pacemaker manufacturers. Models control for year fixed effects and either physicians fixed effects or a physician's gender, specialty, and Census division. Coefficients are reported as $1,000 change in payment. Standard errors are clustered at the physician level.

Table B- 9: Instrumental variable estimates of effect of total pacemaker manufacturer payments on use of leadless pacemakers

VARIABLES				
Total Payments from Pacemaker Manufacturers	-0.00086 [-0.002718, 0.000317]	-0.00191 [-0.004990, 0.000872]	-0.00028 [-0.000875, 0.000099]	-0.00191 [-0.004994, 0.000875]
Observations	9,862	9,862	9,862	9,862
Cragg-Donald F	37.45	174.10	39.97	150.93
Montiel Olea & Pflueger F	14.79	82.43	16.24	70.05
Critical Value, $\tau = 5\%$	37.42	37.42	37.42	37.42
Critical Value, $\tau = 10\%$	23.11	23.11	23.11	23.11
Payment Type	Same Year	Rolling Sum	Same Year	Rolling Sum
Payment Transformation	Untransformed	Untransformed	Inverse Hyperbolic Sine	Inverse Hyperbolic Sine

Anderson-Rubin confidence sets in brackets

Note: Author's analysis of physician-year observations from Medicare and Provider Other Supplier Public Use File from 2016 through 2018 with National Provider Identifier linkages to the ProPublica Dollars for Docs database who performed more than 10 leaded pacemaker implants for Medicare Fee for Service recipients. Two stage least squares instrumental variable models first predict total payments from pacemaker manufacturers as a function of physician's practice's distance from Minneapolis International Airport. Second stage predicts whether a physician-year performed more than 10 pacemaker implants performed with a leadless pacemaker as a function of predicted total payments. Total payments calculated as either same year payments or three-year rolling sum of payments and either untransformed or inverse hyperbolic sine-transformed. Three-year rolling sum refers to current year and preceding two years (e.g., the rolling sum for 2016 includes payments for 2014, 2015, and 2016). Critical values denote necessary Montiel Olea and Pflueger effective first stage F statistic in order for bias to be no worse than 5% or 10% of worst-case bias at confidence level of 5%. Models control for year fixed effects, physician's gender, and physician's specialty. Anderson-Rubin 95% confidence sets, as opposed to traditional Wald confidence intervals, are reported. Standard errors are clustered at the physician-level.