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THE LOCAL INFLUENCE OF PIONEER INVESTIGATORS ON TECHNOLOGY ADOPTION:
EVIDENCE FROM NEW CANCER DRUGS

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The Local Influence of Pioneer Investigators on Technology Adoption: Evidence from New Cancer Drugs

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ABSTRACT

Local opinion leaders may play a key role in easing information frictions associated with technology adoption. This paper analyzes the influence of physician investigators who lead pivotal clinical trials for new cancer drugs. By comparing diffusion patterns across many drugs, we separate correlated regional demand for new technology from information spillovers. Using original data on clinical trial study authors for 21 new cancer drugs along with Medicare claims data from 1998-2008, we find that patients in the lead investigator's region are initially 36% more likely to receive the new drug, but utilization converges within four years. We further demonstrate that "superstar" physicians, identified by trial role or citation history, have substantially broader influence than less prominent physicians.

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1 Introduction

Across many industries, technology adoption exhibits spatial clustering (Comin, Dmitriev, and Rossi-Hansberg, 2012). In medicine, technology diffusion shows similar patterns, with notable clustering within interpersonal networks (Coleman, Katz, and Menzel, 1957), hospitals (Escarce, 1996), and geographic regions (Baicker and Chandra, 2010). The potential for geographic proximity to facilitate the spread of knowledge and innovations across individuals or firms has been recognized at least since Marshall (1890). It has long been argued that local opinion leaders play a key role in this diffusion process (Rogers, 1962), yet direct empirical evidence has been limited. If local opinion leaders have significant sway, the value of well-informed, prominent physicians could extend beyond their contributions to the scientific literature or the treatment of their own patients; influential doctors may shape the practice of medicine across their region.

The limited evidence on the role of opinion leaders is in part due to the challenges of empirical identification. Clustered technology diffusion within a network, organization, or region could be driven by common local demand or capacity for technology adoption rather than information spillovers. Furthermore, it is difficult to isolate the role of opinion leaders as a specific pathway for knowledge spillovers. This study takes on both of these challenges, analyzing whether new cancer drugs approved by the Food and Drug Administration (FDA) are adopted more rapidly in the geographic regions containing study authors of the pivotal clinical study used in the FDA review process. First, by comparing diffusion patterns across many new drugs with different locations of study authors, we are able to separate local demand or taste for technology from the role of knowledge spillovers. Second, by comparing the influence of more and less prominent physicians as measured by academic citations and clinical trial role, we demonstrate that “superstar” authors have a substantially broader reach than their less prominent peers.

Understanding the determinants of technology adoption is of particular interest in the health care context, where new technologies are a key factor underlying both rising costs of care and improved health outcomes in the United States (Newhouse, 1992; Cutler, 1995; CBO, 2008; Smith, Newhouse, and Freeland, 2009). Against the backdrop of this aggregate growth is substantial heterogeneity across regions in the extent and speed of new technology adoption (Fisher et al., 2003a,b; Skinner and Staiger, 2005). In this setting where technology adoption decisions are made by expert physicians with high human capital and ready access to scientific information, we may expect little role for local information frictions. On the other hand, it is a setting with substantial

uncertainty about the efficacy and appropriate applications of newly introduced drugs. As a result, the clinical trial authors' detailed knowledge of drug mechanisms, patient responses, and side effects may put him and his peers at an informational advantage in the early stages of a drug's diffusion.

Existing empirical studies on the role of geographic spillovers have primarily focused on the creative process of new ideas and technologies, such as the tendency for inventors to cite patents developed in their geographic region (Jaffe, Trajtenberg, and Henderson, 1993), or for academic citation patterns to follow migrant scientists (Azoulay, Zivin, and Sampat, 2012).¹ We expand on this work to investigate the geographic connection between research activity and the subsequent adoption of resulting technologies. Further, there is relatively little evidence on how the prominence or connectedness of an opinion leader affects his influence. Banerjee et al. (2013) show that the take-up of a new microfinance product in Indian villages depends on the network centrality of the village leader who is initially informed about the product. Our study sheds light on whether opinion leaders continue to matter in a context where technology adoption decisions are made by highly specialized experts.

Our analysis is based on a novel data collection effort that identified the study authors of the pivotal clinical trials for 21 new cancer drugs and matched the locations of these authors to adoption patterns of the drugs using Medicare claims records from over 1.4 million patient cancer care episode from 1998-2008. The key finding from our baseline analysis is that patients treated in the hospital market where the first author is located are 36% more likely to receive treatment with the new drug within the first two years following a drug's FDA approval. This increased use is driven by higher rates of adoption by physicians both within and outside the author's practice group, suggesting the first author's influence extends beyond the boundaries of his organization. By contrast, other study authors boost utilization only within their own physician group; while they share the first author's enthusiasm for the drug, they have a narrower sphere of influence and have smaller effects on regional patterns of care. We show that alternative definitions of "superstar" authors based not on authorship position but on citation counts to previous publications yield similar results; across a variety of definitions of "superstar" status, proximity to high-profile authors is associated with larger increases in local drug utilization than proximity to their lower-profile coauthors.

While initial proximity effects are large, the effects fade over time so that there is no discernible effect four years after a drug's approval. Despite this eventual convergence, initial differences in new drug use have significant implications for access to care, which we explore in the penultimate

¹Audretsch and Feldman (2004) provide an extensive review.

section of this paper. This pattern of convergence also sheds light on the underlying driver of regional disparities in cancer care treatment. The Roy model of medical treatment choice by Chandra and Staiger (2007) demonstrates that in the presence of productivity spillovers, greater physician experience with a particular treatment may lead to steady-state specialization in that treatment relative to alternatives, but our findings suggest that experience-related productivity spillovers are not a key factor in explaining regional disparities in cancer treatments.

Next, we explore heterogeneity in investigator influence across regions and find that investigator proximity has the largest impact on regions with the lowest levels of adoption of other new drugs, suggesting that information frictions are particularly acute in less technology-intensive areas. From a policy perspective, this also suggests that total utilization of a new drug may be influenced by the choice of investigator locations.

Finally, we document that appropriate patients appear more likely to travel into the first author’s region to receive treatment with the new drug, suggesting that patients may benefit from access to broad provider networks. An instrumental variables estimation strategy based on whether patients reside in an author’s hospital market reveals that our main findings are not primarily driven by these differences in patient sorting.

The organization of the paper is as follows. Section 2 describes the empirical context and key data elements. Section 3 lays out the primary empirical strategies and results. Section 4 investigates the role and extent of patient travel and selective sorting, and Section 5 concludes.

2 Setting and Data

In the United States, prescription drugs are regulated by the U.S. Food and Drug Administration (FDA), which between 2004-2013 granted approval for 26 new drugs per year, on average (FDA, 2014). In order to receive approval, new drugs undergo an extensive review process, in coordination with both the drug’s sponsor (the manufacturer) and the FDA. This process begins with the submission of an Investigational New Drug application, which includes a proposal for testing the drug on human subjects through clinical trials. While each drug application may cite several studies from various stages of drug development, the applicant must pre-specify a “pivotal trial,” which is typically a randomized controlled trial that provides the most comprehensive evidence to date on the efficacy of the drug.²

²Detailed information on the development and approval process for new drugs can be found on the FDA’s website at <http://www.fda.gov/Drugs/DevelopmentApprovalProcess>.

Once clinical testing is complete, the drug sponsor submits the results as part of a New Drug Application. If approval is granted, an official prescription drug label is written describing the indications for which the drug may be legally marketed. The FDA publicly releases this label as part of a detailed approval package describing the basis for approval and the pivotal clinical trial that provided the primary support for the approval decision.

Many new cancer drugs are approved based on promising evidence for a narrowly defined indication. For example, many clinical trials are conducted on patients whose cancers have relapsed after initial treatment, in which case the efficacy of the new drug as an initial treatment is not established upon drug approval. In addition, many cancer drugs come with side effects that range from temporary but severely uncomfortable (e.g. nausea, fever, pain) to serious or life-threatening (e.g. kidney failure, lung damage, nerve damage, secondary cancers). A host of other drugs and additional monitoring may be required to mitigate these side effects, and physicians may develop expertise in this management over time.

In this study, we investigate the adoption and utilization of new cancer drugs in the years following initial approval by the FDA. There are two key data elements necessary for our analysis: the utilization of new cancer drugs across regions over time, and the location of study authors who lead the pivotal clinical trials on which each drug's initial FDA approval was based.

2.1 Measuring cancer drug use

We measure the diffusion of cancer drugs using Medicare Part B reimbursement claims over the 11-year period 1998-2008. During the study period, 21 new cancer drug agents covered by Medicare Part B were approved by the FDA. The diffusion of these drugs forms the basis of our analysis.

While Medicare Parts A and B do not pay for most outpatient prescription drugs, an exception is made for drugs that are not typically self-administered, including cancer drugs administered intravenously or intramuscularly. These expenses have comprised a rising proportion of Medicare spending in recent years. In 2004, Medicare Part B spent \$11 billion on drugs, a category dominated by cancer drug expenses; these costs rose 267% in the 7-year period since 1997, as compared to a 47% rise in total Medicare spending (Bach, 2009). Medicare Part B drug spending also comprises a significant share of total Medicare drug spending. As of 2010, spending on Part B drugs totaled \$19.5 billion, compared to the \$61.7 billion spent on Part D drugs which are typically self-administered (U. S. Government Accountability Office, 2012).

We analyze drug use at the level of Hospital Referral Regions (HRR), as defined by the Dart-

mouth Atlas of Health Care, which partition U.S. zip code areas into 306 distinct regions. Regions are defined by where the majority of the population in each zip code are referred for tertiary health care services, and are commonly used as the unit of analysis for cancer care (see e.g. Fisher et al., 2003a,b; Onega et al., 2008). The map in Figure 1 shows the boundaries of each HRR.

To track the adoption and use of new cancer drugs, we analyze a 100% sample of Medicare outpatient claims as well as a 20% sample of Medicare physician carrier claims. For each HRR, we estimate the utilization rate of each new cancer drug among “indicated” patients, i.e. patients diagnosed with the cancer (e.g. colon, lung, etc.) that the drug was approved to target. To do this, we first define a patient cancer treatment episode to include all claims with a cancer diagnosis for a patient within a given HRR and calendar year. For each patient episode, we observe any cancers for which the patient was diagnosed, as well as the cancer drugs administered to the patient. Our data comprise 1.4 million indicated cancer care episodes within the first four years following drug introduction, of which 659,000 occur within the first two years after drug introduction.

For this analysis, we identified 21 new cancer drugs that were covered by Medicare Part B and FDA approved between 1998-2007.³ Of these drugs, 17 of them had clinical trials led by researchers in the United States, and thus may be used to identify the impact of proximity to a first author on drug diffusion. The remaining four drugs are included in the sample to improve the precision of coefficients on other control variables.

The 21 drugs in our study are listed in Table 1, sorted by order of their FDA approval dates. These drugs target a variety of cancer types, including common carcinomas such as breast, lung, and colon cancer, as well as hematologic and urologic cancers. A majority of the pivotal clinical trials (13/21) were published in the Journal of Clinical Oncology; the New England Journal of Medicine was the next most frequent publication venue (4/21).

Table 1 column (8) reports the number of indicated patient cancer care episodes observed in the two calendar years following FDA approval. There is substantial heterogeneity in target population size due to variation in disease prevalence, ranging from 800 observed episodes of the relatively rare cutaneous T-cell lymphoma to 84,900 episodes of lung cancer. As described below, an observation in our regressions is a patient cancer episode, effectively weighting our regressions by the size of the target patient population; however, the results from our baseline specifications are qualitatively unchanged when each drug is given equal weight.

³We began with a list of 26 new cancer drugs that we obtained from Bach (2009). Of these drugs, five of them were billed fewer than 10 times in our sample over the first two years after approval. Given that we were not able to observe any measurable diffusion for these agents, they were excluded from the analysis.

2.2 Author locations

In addition to the Medicare claims data, we also collected a new data set linking cancer drugs to the pivotal clinical trial that provided the primary support for FDA approval. The data were collected through review of FDA approval history documentation and the relevant academic medical literature. By matching the pivotal trial information in the FDA application to the authors of the academic article reporting the trial’s findings, we are able to identify the researchers who were primarily responsible for the trial.

There were an average of 14 authors per paper in our sample, ranging from 6 to 26. We restrict our analysis to studying the influence of authors who are also practicing clinicians, excluding from analysis the drug company employed scientists who often co-author clinical trials.⁴ We categorize authors as “first” and “other” according to the order listed on the clinical trial, and we record each author’s location based on the zip code of the author’s institution at the time of the article’s publishing. Our analysis exploits the convenient fact that authorship order is a strong signal of author contribution and involvement; the first author in clinical trial articles typically represents the major contributing author (Baerlocher et al., 2007).⁵

Hospital referral regions (HRRs) can be categorized based on their geographic proximity to authors of the clinical trial. In the discussion that follows, the phrase “first author HRR” refers to the HRR where the first author for the particular drug under analysis practiced. For our main analysis, we create non-overlapping definitions of author regions, so that a region cannot simultaneously be coded as a first and other author region, with first author designation taking precedence.

The first authors on these trials practice at a wide set of academic medical centers that together span all four U.S. census regions. Author locations are pictured on a map in Figure 1, with first author locations marked by circles and other author locations by triangles. The most frequent first author locations within our sample are: Houston, Texas, (four first authors); Chicago, Illinois, (three first authors); Durham, North Carolina, (two first authors); and New York, New York (two

⁴In no cases was the first author of the study affiliated with the drug company. Often, the drug company employees’ contributions were credited with a middle or final author slot.

⁵In contrast to other types of biomedical publications where the last author is often the principal investigator, in large clinical trials, the first author is typically a senior physician who was leading the trial effort as the principal investigator. All 17 drugs in our sample with US-based clinical trials have a first author who is a practicing clinician, but only 7 drugs have a last author who is a practicing clinician. (The last author is frequently an employee of the sponsoring drug company.) Furthermore, in 8 out of 17 cases, the first author is also the single most highly cited clinical author on the trial, but this is only true for 1 of the 7 last authors. In Appendix Table 1, we break out the role of last authors separately, and find they have no significant effect on drug utilization and their influence is not statistically distinguishable from middle authors.

first authors). There are 11 unique HRRs that contain a first author for at least one drug, 54 HRRs that contain a non-lead author for at least one drug (but never contain a first author), and 252 remaining HRRs that never contain any author.

Within the HRRs that contain study authors, we further separate patients treated by doctors in the study authors' own practice groups from patients treated by other doctors in the region. To accomplish this, we group together all physicians who bill to the Medicare Carrier files using the same tax identification number as a clinical trial author. If a patient has at least one bill that year from a physician who is linked to a trial author's tax ID, then we code the patient as treated within an author's practice group. Because academic oncologists typically work as part of large group practices, this allows us to separate the author's influence within his own organization from his influence on outside physicians.

2.3 Summary statistics

The difference between a drug's utilization in the first author's region versus other regions—and how this difference changes over time since initial approval—is perhaps most easily seen in [Figure 2](#). This figure plots the fraction of indicated patients who are treated with a new drug.⁶ The solid line plots raw drug utilization rates in each drug's respective first author region (HRR), while the dashed line plots the average drug utilization in all other regions.

Two of the main results from our empirical analysis that follows are suggested by the raw data plotted in [Figure 2](#). First, the figure shows that when a new cancer drug is introduced, indicated patients in the region containing the drug's first author are more likely to be treated with the drug than are patients in other regions. Second, this gap closes over time, so that drug utilization in the first author's HRR is no more intensive than in other regions after four years. Lastly, this convergence occurs primarily because other regions increase their new drug utilization until it is similar to the first author region's use, and not due to substantial decreases in use first author's region. If physicians are learning about the drug's value over time, it appears they are learning that the drug is a valuable addition to their practice. We do observe a slight decrease in average utilization rates in first author regions between years 3 and 4, from 18.0% to 17.2%, but it should be noted that new competing drugs are entering the market and could account for these changes.

More detailed summary statistics are reported in [Table 2](#). Over the first two years following drug

⁶To make rates over time comparable, the drugs used to create this graph are restricted to the balanced sample (67%) of drugs in our sample for which four years of usage rates are available.

approval, the average utilization rate of new drugs for indicated patient episodes ranges from 15.6% in regions where the first author practices to 8.6% in regions that never contain any investigators.

Among the regions that do not contain any investigators for a given drug (columns 3-4), those regions that contain authors for other in-sample drugs (column 3) are the more intensive adopters, with 9.2% of patients receiving new drugs compared to 8.6% in regions that never contain any investigators. This suggests that authors tend to be located in regions that have a high degree of enthusiasm, expertise, or patient demand for new cancer drugs in general.

Within the set of regions that contain an author for at least one in-sample drug, the first author HRR has 70% greater utilization rates on average as compared to utilization in regions that contain no authors for that particular drug (cf. columns 1 and 3). Thus, despite the overall higher rates of new drug use in regions that contain an author, utilization is even greater when the lead researcher of the particular observed drug is in the area.

The second row of Table 2 reports the fraction of patients treated in each region type who are ever treated by a physician in an author’s practice group. 53% of patients treated in the first author’s region receive treatment from a doctor in the same practice group as a study author; only 36% of patients in a middle or last author’s region receive treatment from a doctor in an author’s practice group. Given that the authors’ practice groups do not have complete regional penetration for the targeted cancers, we can compare drug utilization within and outside the authors’ own practice groups to test whether their influence extends beyond their own organization.

3 Empirical Evidence

3.1 Empirical Strategy

Our central idea is to exploit variation in the geographic location of lead study authors across multiple new cancer drugs to identify the impact of geographic proximity to these investigators on drug utilization. If the location of study investigators were randomly assigned across the country, then we could simply compare drug utilization across locations and infer that any increased propensity to use the drug in an investigator’s geographic region was due to this proximity. However, study authors are not chosen randomly, and their locations are likely to be correlated with other regional factors (e.g. co-location with innovation-loving physicians) that influence the rate of new drug adoption. As a result, a naïve comparison of the utilization rate of a new drug in a study author’s region versus other regions does not separately identify the impact of proximity to a drug’s pivotal

study authors on the adoption rate of that drug.

The key methodological innovation in our analysis is to identify the effect of proximity to a drug’s pivotal study authors by implementing an empirical design analogous to a difference-in-differences approach. Specifically, we compare drug utilization in study author and non-author regions, controlling for baseline differences in each region’s propensity to use new cancer drugs as well as controlling for time variation in drug utilization to capture the demand for each drug. Since we observe the diffusion of 21 newly introduced drugs, our strategy allows us to exploit each region’s usage of other new drugs to establish its propensity to adopt a new drug when the region does not contain a study author. In addition, we use the time path of drug usage in non-author regions to establish how the drug usage evolved in the absence of author influence.

Our baseline regression specification takes the following form:

$$\begin{aligned}
 (drug)_{ijt} = & \beta_f \mathbf{1}(first\ author\ HRR)_{jd} + \beta_o \mathbf{1}(other\ author\ HRR)_{jd} \\
 & + \{HRR \times disease\text{-}group\ FEs\}_{ijd} + \{drug \times year\ FEs\}_{dt} + X_{it} + \varepsilon_{ijt}
 \end{aligned}
 \tag{1}$$

An observation is a patient-drug episode (patient i treated in provider region j , t years after drug d was approved), limited to episodes for which drug d is indicated based on patient diagnoses. The regression is estimated over patient-drug episodes that fall within two years following FDA approval of the drug.

The first two terms in the regression above are the key independent variables of interest: indicators for whether a study author of drug d ’s pivotal clinical trial is located in region j . To reflect the possibility that proximity effects may differ for these lead authors, we split our author proximity measures into separate indicators for whether a patient is treated in the first author HRR versus in a region containing any other author (but not the first author). The coefficients on these indicators describe how much more likely it is for a cancer patient to receive a new drug if treated in an HRR where an author of the drug’s pivotal clinical trial is located. As discussed previously in Section 2.2, the first author on large clinical trial publications is typically a senior physician leading the trial effort as the principal investigator.

The third term in this regression is a vector of fixed effects measuring each HRR’s propensity to use new cancer drugs for each of three cancer disease types. Targeted diseases are grouped based on the cancer subtype: hematologic cancers (leukemias and lymphomas), urologic cancers (kidney and bladder cancer), and other carcinomas (brain, breast, colon, and lung cancer). This allows

regions to differ in their enthusiasm and patient suitability for new cancer treatments within each disease group. The fourth term in the regression allows each drug to face an idiosyncratic yearly shock to utilization that is common across regions. Finally, we include patient characteristics X_i which include indicators for patient sex, race, age (in 5-year bins), and whether this is a new cancer treatment episode (i.e. patient had no cancer claims in the previous calendar year).

The primary threat to the validity of this approach stems from the possibility that study author regions are systematically more likely to use the new drug (for reasons not driven by author proximity) than their utilization of other new drugs for this cancer type and the national utilization of this particular new drug would predict. This could occur if, for example, clinical trials were located in areas with idiosyncratically high latent demand for that particular drug.

While latent demand is not directly observable, the raw number of patients that are treated for the cancer which a drug targets is a measurable proxy for latent demand for that drug. As we see from Table 2, among the set of regions with an author for at least one drug in our sample (columns 1-3), the average number of indicated patients in a drug’s author regions (259, from combining columns 1-2) is very similar to the number of patients in a drug’s non-author regions (253, from column 3); indeed this difference is not statistically significant ($P = 0.952$). This suggests that among the set of likely author regions, author locations for a given drug’s pivotal study do not target regions with larger numbers of indicated patients for that drug. As outlined in further detail below, we also address this potential threat to validity in a number of other ways, including limiting the analysis to regions that ever contain a study author and studying the persistence of our estimated proximity effect.

In the first set of results discussed below and presented in Section 3.2, we match patients to provider regions on the basis of where patient care is actually delivered. Thus, it is important to recognize that any effect author status has on a region’s propensity to prescribe a new cancer drug could be driven by two separate channels: (a) a *prescribing* effect in which providers in the author region have an increased propensity to treat a fixed population of patients with the new drug; and (b) a *sorting* effect in which patients suitable for particular treatments sort to providers who specialize in those treatments.⁷ For example, an increased number of suitable patients may travel into an author region for treatment, or suitable resident patients may be more likely to stay within the region for their care. (In this context, patient suitability could encompass both clinical

⁷Note that both channels would be present even under true random assignment of study authors to geographic regions.

appropriateness and the patient’s demand for a new drug.)

To exemplify this point, suppose $f_d(\theta, p)$ denotes the fraction of cancer patients treated with drug d in a given region, where p measures the drug’s suitability for patients treated in the region, and θ indexes the propensity of physicians in the region to administer the drug to a standard patient. The essential point is that both θ and p may respond to a change in a region’s author status τ , and thus the aggregate effect of author status on regional treatment intensity is given by

$$\frac{df_d}{d\tau} = \frac{\partial f_d}{\partial \theta} \frac{d\theta}{d\tau} + \frac{\partial f_d}{\partial p} \frac{dp}{d\tau}$$

The first term on the right-hand side of this equation measures the effect that first author status has on a region’s propensity to use a drug holding fixed patient suitability, while the second term measures the increased usage of the drug due to patient sorting. Our baseline specification in equation (1) measures the aggregate impact of first-author status on drug utilization, but does not disentangle the two mechanisms. Because these two channels have very different implications for policy, Section 4 applies an instrumental variables approach to isolate the change in utilization driven by prescribing, i.e. the increased propensity of first author regions to treat any particular patient.

3.2 Baseline Proximity Effects

Effects by Geographic Proximity

We begin by presenting evidence on whether geographic proximity to a new cancer drug’s pivotal study authors impacts a physician’s propensity to prescribe that drug for indicated patients. We begin by examining how the effect of geographic proximity to a study author evolves over time.

With a Roy model of productivity spillovers, we may find geographic specialization in the use of medical treatments as described by [Chandra and Staiger \(2007\)](#). High-use areas develop expertise in the technology and have higher returns to its usage, and so they continue to use it more frequently in the steady state than low-use areas that do not develop a similar expertise. Under this model of productivity spillovers, we might expect to find long-run differences in the use of new cancer drugs across author HRRs and other regions. An alternative model such as [Phelps \(2000\)](#) where information asymmetries are the reason for delayed adoption amongst non-first author regions would predict convergence in practice patterns as information about the new treatments reaches each physician.

To measure the evolution of the author proximity effect, we estimate a modified version of

specification (1) in which the author HRR indicators are interacted with a full set of event-year dummies ranging from 1-4 calendar years following drug approval (0 corresponds to FDA approval year).⁸ The coefficients on these interactions describe the corresponding proximity effect separately for each year.

The left panel of Figure 3 plots how the estimated effect of proximity to a drug’s first author on drug utilization evolves over time, while the right panel plots the effect of proximity to any of the drug’s other pivotal clinical trial authors. The time pattern of proximity effects traced out in these graphs reveals a number of insights. First, recently approved cancer drugs are used more intensively on average in regions containing a study investigator, an effect that is much stronger in the first author’s region. The second pattern highlighted by Figure 3 is that the proximity effect fades over time, so that any proximity effect on drug utilization vanishes within 4 years after drug approval.

This figure provides a novel way to benchmark the speed of technology adoption. Prior measures of the speed of technology adoption have primarily focused on absolute rates of take-up, such as the length of time since invention for an individual to adopt (e.g. Comin and Hobijn, 2010), or rate of acceptance (e.g. Griliches, 1957). However, these measures can be inappropriate in settings where the “optimal” level of adoption is difficult to ascertain (e.g. due to informational uncertainty) and may even change over time, as competing technologies are introduced and the scientific understanding evolves. In contrast, our measure of convergence describes how quickly regions conform to a benchmark adoption pattern set in regions containing the experts involved in the technology’s development.

Taken as a whole, these estimates suggest that proximity to a pivotal study trial investigator drives higher take-up of new drugs, an effect which is stronger and more persistent for first authors than for other early investigators of the drug. Yet despite the initial eagerness to use the drug, this difference in diffusion between investigator and non-investigator regions converges within a few years. This convergence provides further support for the econometric assumption that the drug’s first author is not located in a geographic area with idiosyncratically higher latent demand for that particular cancer drug; if this were the case, we may expect to see persistent differences in drug use across the first author and non-first author regions.

Table 3 shows results from our baseline specification in Equation (1). Because the main proximity effects were found in Figure 3 to be concentrated in the first two years following FDA approval,

⁸Medicare drug codes are not introduced until the calendar year following FDA approval for the large majority of drugs in our sample, limiting our ability to measure diffusion prior to the first calendar year.

we focus the remainder of our regressions on this period. As shown in column (1) of Table 3, we estimate that patients who receive cancer treatment in the first author’s HRR are 4.0 percentage points more likely to receive the new drug, significant at the 1% level. To provide a useful benchmark, this first author impact is a 36% increase over the 11.1% average utilization rate in regions that contain a first author for a different in-sample drug with US-based first authors. Patients who receive treatment in a middle or last author’s region, by contrast, are only 0.69 percentage points more likely to receive the new drug, an estimate which is positive but not statistically significant. The difference between utilization in first author and other author HRRs is statistically significant at the 5% level.

Extent of author influence: results by physician group

The average effect a study author has on prescribing behavior within the HRR may obscure important heterogeneity in regional utilization. The smaller average effect of “other” study authors relative to the first author could result from a narrower sphere of influence or from less enthusiastic adoption even within the other author’s practice group. To explore this possibility, we use physician group tax IDs from a 20% random sample of all Medicare physician claims between 1998-2008 to measure which physicians practice in the same organization as a drug’s trial authors.

Patients indicated for a given drug and treated in an author HRR are marked as treated by an author’s group if the patient was treated by a physician practicing in the same group as a trial author at any point during the year. As reported in Table 2, 53% of indicated patients treated in the first author’s region receive care from a physician who is part of a study author’s practice group; 36% of patients in other author regions are treated by a physician from a study author’s practice group.

To estimate proximity effects separately within and outside an author’s physician group, we estimate a modified version of equation (1) where the indicators for being treated in an author HRR are interacted with indicators for being treated by the author’s physician group. Column (2) of Table 3 shows the results of proximity separately by author group status. Among patients treated in the first author’s HRR, patients treated within an author’s physician group are 4.21 percentage points more likely to receive the new drug ($P < 0.01$), while patients treated outside the author group are 4.16 percentage points more likely to receive the drug ($P < 0.05$). The first author appears broadly influential, increasing new drug adoption in his region by almost equal amounts within and outside his practice group.

The results are quite different in other author regions. In those regions, patients treated within an author’s practice group are 2.8 percentage points more likely to receive the new drug ($P < 0.01$). However, there is no estimated increase in drug utilization outside the author group, and the 95% confidence interval is bounded above by 0.7 percentage points. Despite being enthusiastic adopters of new drugs within their own practice group, middle and last authors do not appear to influence practice patterns in neighboring physician groups.

An important consideration for interpreting these results is that because patients are not randomly assigned to doctors, some of the increased utilization found within author group could be driven by a compositional shift in which patients are treated by author group physicians. To the extent that patients most appropriate for the new drug sort into the author group, some of the increase in prescribing behavior within the physician group may not correspond to a net increase in overall drug prescribing. The region level results in column (1), however, indicate that overall prescribing does in fact increase at the region level.

Taken as a whole, the results from columns (1-2) provide evidence of important proximity effects within author regions. The higher rates of drug utilization in a first author region compared to other study author regions appear to be driven primarily by the first author’s broader sphere influence. While both types of study authors boost utilization within their own practice group, the evidence suggests that only first authors substantially increase drug adoption by doctors who are not part of the author’s firm.

Robustness

To probe the robustness of these findings, we run an identical analysis in a restricted sample that only includes regions that with at least one study author for a drug in our sample. Restricting the sample mitigates the concern that non-research-intensive regions provide a poor counterfactual for a new drug’s popularity in author regions. Results are reported in Table 3, Panel B, with estimates very similar to those found in the full sample reported in Panel A. We continue to find approximately 4 percentage point higher new drug use in the first author region ($P < 0.01$) and an insignificant, smaller aggregate effect on other author regions. Notably, restricting the sample in this way does not substantially attenuate the estimated effects.

As another robustness check, in Table 3, Panel C, we restrict the sample only to new cancer patients. Specifically, we exclude all patients with any cancer-related claims in the previous calendar year. In this way, we aim to exclude patients who may be receiving ongoing treatment with the

cancer drug following potential participation in the clinical trial. These “holdover” patients from the clinical trial could mechanically raise drug utilization in study author regions, which were host to the clinical trials. The results in this restricted sample are again very similar to the baseline findings; we continue to find 4 percentage point higher new drug use in the first author’s region and a small, insignificant effect in other author regions.

Mechanisms of estimated author influence

The greater impact of proximity to first authors could be driven by two potential factors: (a) first authors take on more responsibility for analyzing and writing the paper, and thus are better informed about the new drug’s value; or (b) even if all authors had the same quality of information about a new drug, first authors may be more influential due to their greater professional stature. Both channels have potential *a priori* support.

The pivotal clinical trials have an average of 14 authors per paper, and the first author often takes the lead role in trial design and preparing the manuscript (cf. Hudes et al., 2007; DeAngelo et al., 2007), suggesting he may also have the most detailed, comprehensive view of the drug’s efficacy. On the other hand, the first author is also likely to be one of the highest profile physicians involved with the research; he is the single most highly cited clinical author for 8 of the 17 drugs in our sample with US based trials. The findings reported in the previous section on authors’ scope of influence outside their practice group lends support to the idea that the first author’s status as a local opinion leader may primarily drive these differences. In the next section, we will further explore whether identifying “superstar” authors based on citation histories rather than authorship sequence leads to similar findings.

Another complementary explanation for the observed impact of first authors is that they may have stronger ties to the sponsoring drug companies and be more actively involved in drug promotion efforts. Of the 21 drugs in our sample, 9 of the published trials report disclosure statements detailing which authors have financial relationships with drug companies. For these drugs, an average of 52% of all clinical authors report financial ties to the sponsoring drug company, compared to 67% of first authors. These financial ties include consulting fees, lecture fees, research support, expert testimony, and stock ownership.

While drug companies are only 1.3 times more likely to have financial ties to a first author compared to a middle or last author, the estimated impact of being treated in the first author’s region on new drug use is over 5.5 times larger than the estimated impact of being treated in

another author's region. The observed frequency of financial ties between drug companies and clinical authors would not lead us to predict the first author's apparent outsized influence on regional drug utilization. Our assessment of these differences is limited by the fact that many drug trials did not report disclosure statements over this period, and even trials with disclosure statements do not list the amounts of money exchanged. As a result, we cannot rule out the possibility that drug companies have stronger relationships or expend more resources supporting the first author's drug promotion efforts compared to other authors. Crucially, if drug companies were investing more in the first author, this would suggest that they perceived a higher return to the first author's potential promotion efforts; in that case, the drug company's investment is complementary to the superior information or professional stature that the first author already offers.

Outside of drug company sponsored events, there are many other opportunities for oncologists to meet with their local peers and share ideas. Within a given oncology practice group, formal mechanisms may include the establishment of internal drug treatment protocols and "tumor board" meetings where treatment options for new cancer cases are often discussed with a broad team of care providers. Across separate practice groups, opportunities for sharing ideas include invited "grand rounds" seminars, local and regional professional society meetings, contact through shared patients and patient referrals, as well as casual interpersonal networks.

In personal communications with oncologists, physicians described significant barriers to the adoption of new cancer agents. Because trial participants are often selected for being in more stable health than many cancer patients, physicians cited significant concern about the risk of severe side effects and uncertainty about optimal dosing regimens. Oncologists are also aware of the potential importance of heterogeneous responses to treatment; hearing about individual successfully treated patients may be more compelling than reading about modest average response rates. The expertise of a prominent physician in the community on a new drug's applications and efficacy could substantially lessen these barriers to new drug adoption.

A final potential explanation for these regional differences in drug utilization bears further discussion: differences in drug prices. There are two relevant prices to consider in this context: the reimbursement that physicians are paid for prescribing a drug, and the cost to the physician to purchase the drug. If drug-specific reimbursements were higher or purchasing costs lower in first author regions than in other regions, prices could potentially explain our proximity findings. However, we think neither of these price effects is a likely explanation in our context. Because we are studying utilization amongst Medicare patients where reimbursement rates are set by administrative

rule, there is effectively no scope for reimbursements to be idiosyncratically higher in a given region for first author drugs. In addition, while it is conceivable that drug manufacturers could offer drug discounts to specific physicians or groups and might specifically target physician’s practicing at the first author’s hospital, our finding that the proximity effect extends to physicians who do not practice in the first author’s physician group makes it seem unlikely that drug discounts could explain our results.

3.3 Superstar Proximity Effects

Our baseline results in Section 3.2 suggest that clinical trial authors with greater expertise or prominence (as captured by first author status) have a greater impact on drug utilization in their region. To further explore the differential effect of “superstar” physicians, we develop a measure of each author’s prominence within academic medicine using data on publication and citation histories from Web of Science. We rank authors based on citation counts accruing to publications in the relevant medical field published in the 10 years leading up to FDA drug approval.⁹ Finally, we define the top 10% (or 50%) authors as the top-cited author on that drug trial plus any other author whose citation count places them in the top 10% (50%) of all authors on the same drug’s trial. This measure of “superstar” status will capture authors’ academic prominence in their field, tagging the most prominent authors on each trial on the basis of their publication history.

For any measure of superstar status, our baseline regression in Equation (1) is easily modified to estimate the differential impact of proximity to a superstar author. For these regressions, we allow author proximity effects to vary by drug, and then estimate the differential impact of proximity to a superstar author. Our superstar regression takes the form:

$$\begin{aligned} (drug)_{ijt} = & \beta_s \mathbf{1}(superstar\ author\ HRR)_{jd} + \{author\ HRR \times drug\ FEs\}_{jd} \\ & + \{HRR \times disease-group\ FEs\}_{ijd} + \{drug \times year\ FEs\}_{dt} + X_{it} + \varepsilon_{ijt}. \end{aligned} \quad (2)$$

The key coefficient of interest is β_s , which describes how much more a new drug is used in a superstar HRR relative to other author HRRs, on average. Thus, if $\beta_s = 0$, utilization in a superstar region

⁹Specifically, we find all research articles matching each author’s last name and initials over a 10 year period leading up to the year of FDA approval. We restrict to articles only within the relevant field. For all authors in our sample, this includes oncology articles. Dermatology, neurology, hematology, urology, and nephrology are added to the definition of matched articles for drugs targeting those specific cancer types. These field restrictions provide a more targeted measure of prominence within the relevant medical field, as well as help disambiguate authors with common names. Next we count all citations that have accrued to those publications to the present date.

is no more intensive than in other author HRRs, while $\beta_s > 0$ corresponds to higher utilization in superstar regions. The second term in this regression allows the effect of author proximity to vary by drug, and the last three terms are the same as in Equation (1).

The results from Regression (2) are shown in Table 4. Column (1) shows that drug utilization in first author HRRs is 3.00 percentage points higher on average than in middle or last author HRRs for the same drug, which closely matches the result obtained by differencing the first and other author HRR results in Table 3. From columns (2-3), new drug utilization is 2.27 percentage points higher in a top 50% cited author HRR (column 2), and 2.32 percentage points higher in a top 10% cited author HRR.

Columns (4-6) run horse races between these three measures of superstar status. Column (4), which includes superstar indicators for both first author and top 50% cited author shows that both indicators correspond to higher utilization; the coefficient on top 50% cited author is marginally significant, with $P = 0.056$. Column (5) includes first author and top 10% cited author indicators. In this case, both coefficients point to higher utilization, although only the first author corresponds to a statistically significant increase. Similarly, in column (6) which includes all three measures of superstar status, all coefficients are positive, but only significant for the first author.

Each of the author regions contains a physician investigator who is well informed about the new drug, but among those regions, those with the most prominent authors are the ones that experience the most substantial increases in new drug use. These findings suggest the important role of local opinion leaders even in the context of drug adoption by highly expert decisionmakers with access to clinical trial findings. Regional information frictions may dissipate within 3-4 years, but during the initial two years after drug introduction, local opinion leaders have substantial influence on adoption rates in their region. A subtle but important note is that these results do not estimate the causal impact of increasing an individual author's citation history or authorship order *ceteris paribus*; principal investigators and authors with high citation counts are likely to be exceptional along other unmeasured dimensions as well.

3.4 Geographic Extent of Investigator Influence

In this section, we probe the extent of drug authors' influence. In particular, we test which types of regions are most heavily influenced by investigator proximity; whether study authors affect utilization in neighboring regions; and lastly, whether study authors affect off-label drug use.

First, we test whether regions that are typically slow to adopt new cancer drugs experience a

greater boost in utilization when a study author is located in the region. There may be greater scope for the study author to affect practice patterns in slower-adopting regions that are not already very high users of new cancer drugs.

We develop a measure of each region’s speed of new cancer drug adoption by looking at the average rates of new drug use when no author is present in the region. In particular, we regress an indicator for new drug use on a series of region dummy variables, controlling for drug by year fixed effects, patient demographic characteristics and whether this is a new cancer spell. To avoid including the direct impact of author proximity in this measure of regional adoption speed, we exclude from the sample any observations where an author for the relevant drug was located in that region. This regression includes only observations in the first two years following initial FDA approval. The region fixed effects from this regression form the basis of our measure of regional technology adoption speed.

For ease of interpretation, we standardize this measure of technology adoption speed by demeaning the variable and dividing each fixed effect by the standard deviation. As a result, the average regional technology adoption speed index is 0, and a value of 1 corresponds to a region with average new drug use 1 standard deviation above the national mean.

We augment our baseline estimating Equation (1) to include interaction terms between whether the first (or other) author is located in the region and the region’s technology adoption speed index. Results are reported in Table 5, columns (1-2). We find that the first author’s influence is greatest in regions that are typically slower to adopt new drugs; the interaction term is negative and statistically significant at the 5% level. For regions near the mean of the adoption speed index, patients are 4.1 percentage points more likely to receive treatment with the new drug when the first author is located in that region. The impact of being treated in a first author HRR increases to 6.2 percentage points for regions that are typically 1 standard deviation slower to adopt than the average region; the effect falls to 1.9 percentage points for regions that are typically 1 standard deviation faster to adopt.

We continue to find no significant effect of being treated in a middle or last author’s region. The coefficient on the interaction between other author HRR and regional adoption speed index similarly suggests that slower-adopting regions experience a greater effect of proximity to other study authors; however, the result is not statistically significant.

The first author’s influence boosts regional use more for regions that tend to be technology adoption laggards. From a policy perspective, this suggests that investment in clinical research

may yield the greatest spillovers to medical practice in regions that are not already among the fastest adopters of new technologies. It should be noted that this effect is estimated only using variation in adoption speed within the set of regions that contain a first author for at least one in-sample drug.

Next, we test the geographic extent of investigator influence. This analysis not only addresses the geographic extent of the authors’ reach, but also impacts the interpretation of our baseline estimates from specification (1). There, we estimated the wedge between investigator HRRs relative to non-investigator HRRs. If proximity effects extend more broadly than an investigator’s own HRR, some of the comparison non-investigator regions are themselves influenced by the treatment, resulting in estimated proximity effects that are too small.

In principle, if oncologists were sufficiently dispersed geographically, it would be feasible to non-parametrically identify precisely how the influence of proximity to an investigator changes as distance from the investigator grows. However, cancer care in the U.S. is highly specialized and major cancer care sites are often geographically dispersed (Onega et al. 2008). To the extent that cancer care is primarily delivered in distinct geographic clusters, testing the extent of investigator influence amounts to testing how usage varies across cancer care sites based on distance to the investigator’s site. If influence is confined to the investigator’s site, then even adjacent regions will show no increased use of the new drug.

To measure whether investigator influence extends beyond his own HRR, for each drug we identify the “neighbor” HRRs that share a border with the HRR in which the drug’s first author is located. We then measure the degree to which investigator regions and their neighbors increase drug utilization relative to non-neighbor regions, by estimating:

$$\begin{aligned}
 (drug)_{ijt} = & +\beta_f \mathbf{1}(first\ author\ HRR)_{jd} + \beta_{nf} \mathbf{1}(neighbor\ of\ first\ author\ HRR)_{jd} \\
 & + \beta_o \mathbf{1}(other\ author\ HRR)_{jd} + \beta_{no} \mathbf{1}(neighbor\ of\ other\ author\ HRR)_{jd} \\
 & + \{HRR \times disease\text{-}group\ FEs\}_{ijt} + \{drug \times year\ FEs\}_{dt} + X_{it} + \varepsilon_{ijt}.
 \end{aligned} \tag{3}$$

Table 5 shows in columns (3-4) that while first author HRRs have a 4.0 percentage point increase in their propensity to use the new drug, there is no observed increase in drug use of neighboring HRRs. The point estimate suggests a 0.2 percentage point increase in new drug utilization in neighboring HRRs, which is small in magnitude and statistically not distinguishable from zero. The 95% confidence interval bounds the effect by at most 1.4 percentage point higher drug utilization in

first author neighbors HRRs. There is a similarly small, insignificant effect estimated for neighbors of other author HRRs. Although the first author’s influence extends beyond physicians in his own practice group to other physicians practicing in the same region, there is no evidence that his influence raises utilization in neighboring regions; these results are precise enough to rule out effect sizes that are one third as large as the impact of being treated in the first author’s HRR.

Finally, we investigate whether study authors influence the use of new drugs for applications not covered by the initial FDA approval label. While drug labels typically provide relatively narrow indications for application, physicians have wide latitude in determining how they will prescribe the drug. For example, capecitabine was initially approved in 1998 for the treatment of metastatic breast cancer that had already proved resistant to both paclitaxel and an anthracycline-containing chemotherapy regimen. In the preceding analysis, we analyzed the use of capecitabine across all breast cancer patients, since our data do not allow us to capture the more specific clinical conditions defining the label indications. However, in the first two years after capecitabine’s introduction, a full 39% of its use was on colon cancer patients; colon cancer and breast cancer may be biologically similar, but robust clinical trial evidence was not yet available for the application to colon cancer. (The FDA eventually added colon cancer to the label in 2001—after the two-year period covered by our main analysis.)

In this section, we study the application of new drugs to cancers types that were not covered by the initial label. Across our 21 drugs, 22% of utilization within the first two years was for patients with diseases not indicated on the FDA label, which we will call “far” off-label drug use. In columns (5-6) of Table 5, we estimate whether the study authors’ influence increases the use of new drug for other applications. The sample is restricted to patients who do *not* have the broad cancer type covered by the initial FDA label, and mirrors the specification in Equation (1).

We find no evidence of higher use of the drug for off-label patients in the authors’ regions, suggesting the authors’ influence is largely local to the cancer type on the initial label. A limitation of this analysis is that it is relatively unusual for any given off-label cancer patient to receive treatment with a particular new drug; mean utilization is 0.37 percentage points in regions that ever contain a study author. The point estimate from column (5) suggests that off-label utilization increases by 0.06 percentage points when the first author is in the region; the 95% confidence interval bounds the effect as no larger than 0.16 percentage points.

If increased use in the first author’s region was driven by a pure “advertising” or “salience” effect boosting awareness or enthusiasm of the new drug, we might have expected greater spillovers

to off-label applications. On the other hand, the authors' expertise may be local to the indications studied in the clinical trial they led; they may not have a strong informational advantage when it comes to applications of the drug beyond that population. Taken as a whole, the evidence in this section suggests that first authors boost on-label drug use within their own region, especially when they are located in a region of relative technology laggards, but that authors have little measurable influence on the use of neighboring regions or on applications of the drug to other populations.

4 Patient Travel and Selective Sorting

As discussed in Section 3.1, there are two possible channels through which the observed increased propensity to prescribe new drugs in first author regions may occur: first, an increased propensity to use the drug on a fixed set of patients; and second, a change in patient sorting such that the first author regions see patients with higher latent demand. In this section, we test directly for changes in patient sorting as indicated by patient travel patterns, and then use an instrumental variables strategy to identify the differences in drug utilization that occur over a fixed set of patients.

In Table 6, we begin by testing whether patients with the targeted diagnosis who seek treatment in the first author's HRR are more likely to have traveled from a different HRR of residence. This would occur if, for example, savvy patients travel into author regions for treatment in order to gain access to the new cancer drugs. In columns (1-2), the regression specification mirrors that in the main specification described in equation (1) above, but the outcome variable has been replaced with an indicator variable for travel, defined by whether the patient's HRR of residence is not the same as the HRR where he receives care.

In the baseline specification reported in column (1), we find a 3.3 percentage point increase in the fraction patients treated in the first author's HRR who do not live in the region, significant at the 10% level; on average 22.2% of patients treated in an author region reside outside the region. There is a similar 3.0 percentage point increase in the fraction of traveling patients treated in other author's HRRs, significant at the 1% level. Restricting to the set of regions that ever contain a study author in column (2) yields similar results.

This evidence suggests that some patients are aware of new centers of expertise for the new cancer drug (perhaps due to physician referral) and are willing to travel further to improve their access to the drug. If these patients who are newly traveling into an author's HRR are either more clinically appropriate for the new drug or have higher demand for trying the new technology, then

part of the increased levels of drug utilization may be driven by the changing patient composition.

In Table 6, columns (3-4), we test whether the patients who travel from outside HRRs differ in their propensity to receive the new drug relative to non-movers. In these columns, we report results from a regression that augments our baseline Equation (1) by interacting the author proximity indicators with a binary indicator *traveler* for whether the observed patient is seeking care outside his HRR of residence. Based on this regression, we estimate that patients traveling to the first author’s HRR are 2.2 percentage points more likely to receive treatment with the new drug than patients treated in the first author HRR who also reside within that HRR, although the result is not statistically significant at conventional levels. Travelers to other author regions are only 0.1 percentage points more likely to get the drug, which is also not significant. The confidence intervals on these travel estimates allow the possibility that the overall 4.0 percentage point higher new drug use in first author regions may be driven in part by changing patient composition, and not solely by a higher propensity to use the drug on a fixed set of patients.

Although these estimates do not precisely measure the degree of patient travel response, the direction in which they point is particularly relevant considering the new attention to provider networks available on the Affordable Care Act’s health insurance exchanges. A common feature of these new insurance plans is restricted provider networks (Hancock, 2013), with consumers facing much higher prices for out-of-network care. Our findings on travel suggest that severely ill patients, such as the cancer patients in our study, may travel strategically to improve access to new treatments. The instrumental variable results presented below further suggest that these traveling patients are more likely to receive treatment with the new cancer drug than if they had remained under the care of their local provider. As a result, restricting provider networks could lead to changes in how these patients are treated and reduce their access to new treatments.

Instrumental variable analysis

To isolate whether first author regions are indeed more likely than other regions to use the drug on any given patient, we pursue an instrumental variables (IV) strategy. In particular, we use indicators for whether the patient resides in the first or other author’s HRR as an instrumental variable to predict whether they will seek treatment in an HRR that contains the first or other author for the relevant drug. This instrumentation strategy mitigates the concern that patient sorting renders the patients treated in the first author region more suitable to treatment with the new cancer drug.

The reduced form equation of the IV model takes the following form:

$$(drug)_{ijt} = \gamma_1 \mathbf{1}(\text{reside in first author HRR})_{ij} + \gamma_2 \mathbf{1}(\text{reside in other author HRR})_{ij} \quad (4) \\ + \{HRR \times \text{disease-group FEs}\}_{ij} + \{drug \times \text{year FEs}\}_{dt} + X_{it} + \varepsilon_{ijt}$$

Note that paralleling the baseline regression specification, we include fixed effects for HRR by disease group and for drug by year. We also report results from an enriched IV specification where in addition to using the two indicators for residence in an author HRR as instrumental variables, we also include two additional instruments: (1) residence in a first author’s neighboring HRR (i.e. a region that shares a border with the first author HRR); and (2) residence in an other author’s neighboring HRR (i.e. a region that shares a border with an other author HRR).

The exclusion restriction requires that, after conditioning on the included fixed effects, where a patient lives is uncorrelated with his suitability or demand for treatment with the new cancer drug. For example, because we include region by drug class fixed effects, this allows regions to vary in their latent demand for drug classes, but does not allow author regions to have higher latent demand for the author’s drug compared to other drugs in the same class.

The exclusion restriction could be violated under a few conditions. One possibility is that patients with the targeted cancer who reside in the first author region could have idiosyncratically high demand for the drug; this could occur if, for example, the drug targets a particular sub-type of colon cancer that has a higher-than-typical prevalence in the first author’s region, so that a larger fraction of colon cancer patients in the region are appropriate for treatment. Second, the instrument would be invalid if patients change their HRR of residence in response to the availability of new cancer drugs.

Under the IV framework, the exclusion restriction is not directly testable, but it seems plausible that the fraction of targeted cancer patients suitable for treatment with the new drug would not vary systematically across regions and that elderly Medicare patients would be very unlikely to move across regions within a three-year period in response to the location of a new cancer drug trial. This assumption is further bolstered by the observed convergence in drug usage across first author and non-first author regions, as reported in Figure 3, suggesting no permanent differences in patient eligibility for treatment in the first author’s region.

Results from the IV regressions are reported in Table 7. The reduced form results find that patients residing in the first author’s HRR are 2.3 percentage points more likely to receive treatment

with the new drug, significant at the 5% level; there is no significant increase in use for patients residing in other author regions. The IV estimate reported in the final rows of the table rescale the reduced form estimate and reports that providers in the first author’s region are 2.9 percentage points more likely to prescribe the new drug compared to other providers, significant at the 5% level. The finding is robust to restricting the sample only to patients residing in HRRs that contain a first author for any drug, as reported in column (2). Adding the instrumental variables for residence in neighbor HRRs to the model also does not substantially change the estimated IV coefficient (cf. column 3).

The IV results suggest that physicians in the first author’s region of residence are approximately 2.9 percentage points more likely to use the new drug on a given set of patients (namely, the subpopulation of patients for whom location of residence determines location of care), which is a somewhat smaller effect than the baseline regression results reporting a 4.0 percentage point increase in drug utilization across all patients treated in the first author region. Patients suitable for treatment with the new drug sorting into the region may have contributed to the high observed point estimate in the baseline regression, but the result remains large and statistically significant in the IV specification.

Taken together, the patient traveling results and the IV regressions find support for both hypothesized channels by which the presence of a first author may affect care in his region. Patients with high latent demand for the drug seem to seek out care in areas with high expertise in the new technology. In addition, doctors in the first author’s region are more likely to use the new drug, holding fixed the population of patients seeking treatment.

Extrapolating from the IV regression result, if all providers behaved like those in the first author’s region, approximately 2500 additional Medicare Fee for Service (FFS) patients would be treated with each new cancer drug in the first two years after initial drug approval. This amounts to an estimated 53,000 Medicare FFS patients in total over the 11 years of our sample who did not receive treatment with one of the 21 drugs under study due to the lower patterns of initial usage in areas that didn’t contain the study’s first author. If doctors converge to appropriate, productivity-maximizing technology choice over time, then the observed increases in new drug utilization over time in the non-first author regions (cf. Figure 2) suggest this slower diffusion in the non-first author regions may reduce welfare.

5 Conclusion

The results above suggest that information frictions significantly affect the adoption of new cancer drugs in the first few years after drug introduction. Prominent physicians who are well-informed about a new drug in the early stages of diffusion may play a key role in easing these frictions. Our results show that new drug utilization is 36% higher in the hospital market where the lead physician investigator on the drug’s pivotal clinical trial practices, over the two years following FDA approval.

While both first authors and other authors increase new drug utilization within their physician practice group, the influence of first authors also extends outside their organization to increase drug adoption for other physicians in the same region. Further, we show that relying on publication and citation history rather than authorship order to identify “superstar” study authors yields similar results, suggesting that investigators with greater professional status are more influential in increasing drug adoption in their region. We also find that investigator proximity has the largest impact on regions with the lowest levels of adoption of other new drugs, pointing to greater adoption frictions in less technology-intensive areas. An instrumental variables strategy based on patient residence shows that the higher utilization in investigator regions is not driven primarily by patient sorting across regions to obtain access to a new drug.

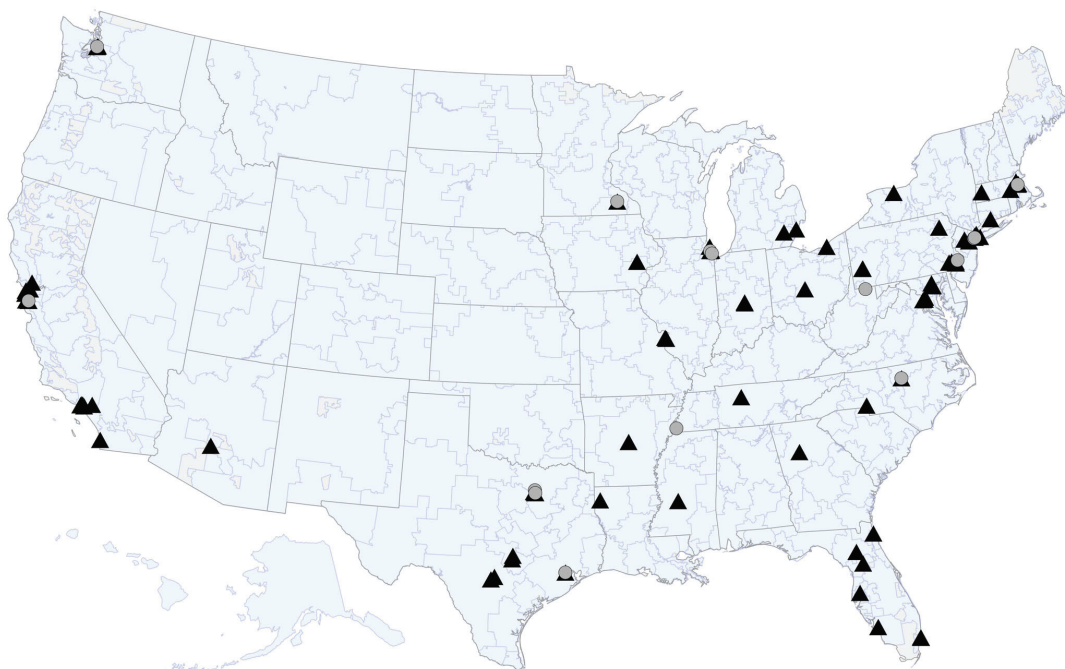
Despite the marked regional differences in early adoption of new cancer drugs, there is no evidence that early expertise with a drug drives higher rates of long-term utilization. Author HRRs are no more likely to specialize in treatment with the new drug than other regions by the fourth year following drug introduction. Thus, the information frictions that may hamper early adoption seem to ease over time and the utilization of first author and other HRRs converges within a four-year period. Although long-run prescription patterns for any particular drug may converge across regions, overall treatment patterns for cancer patients may persistently differ as the research-intense regions continue to house investigators for each wave of new treatment innovations.

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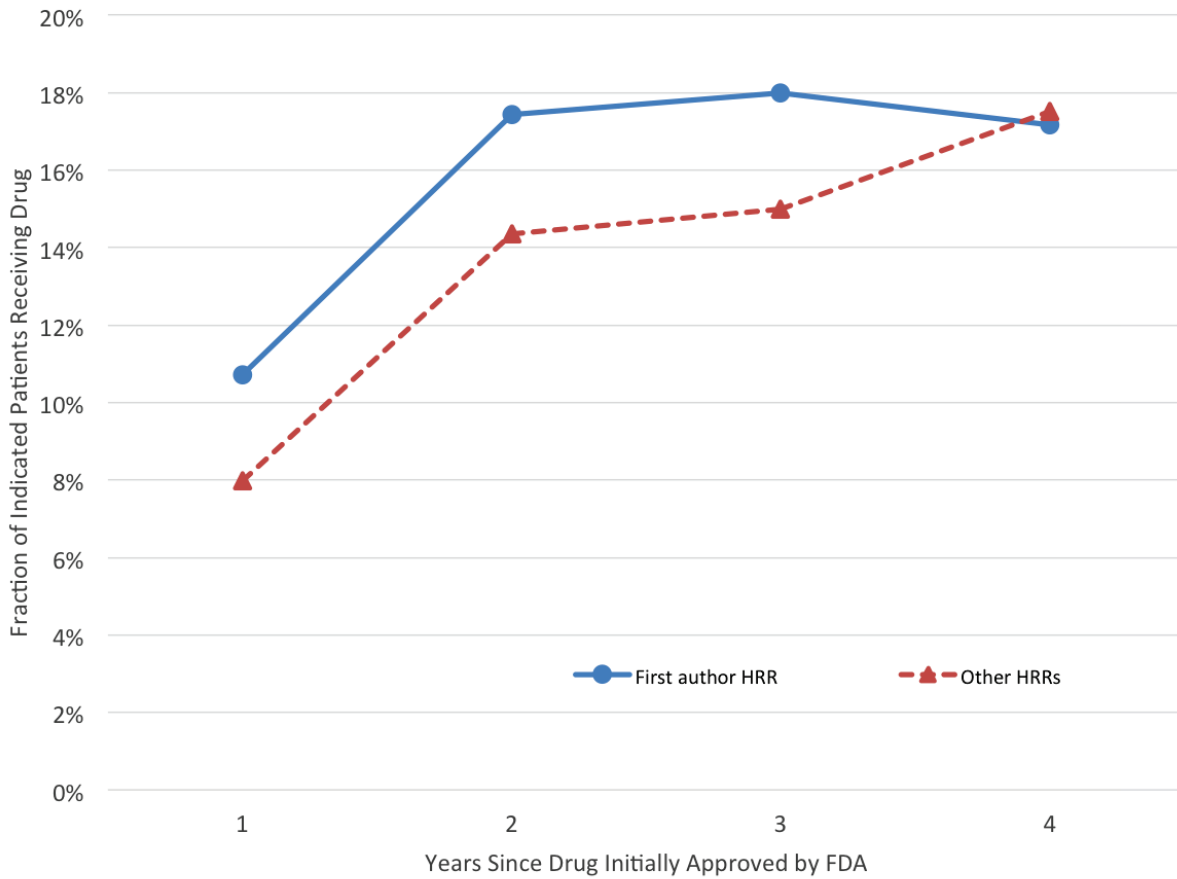
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Figure 1: Locations of Drug Pivotal Study Authors



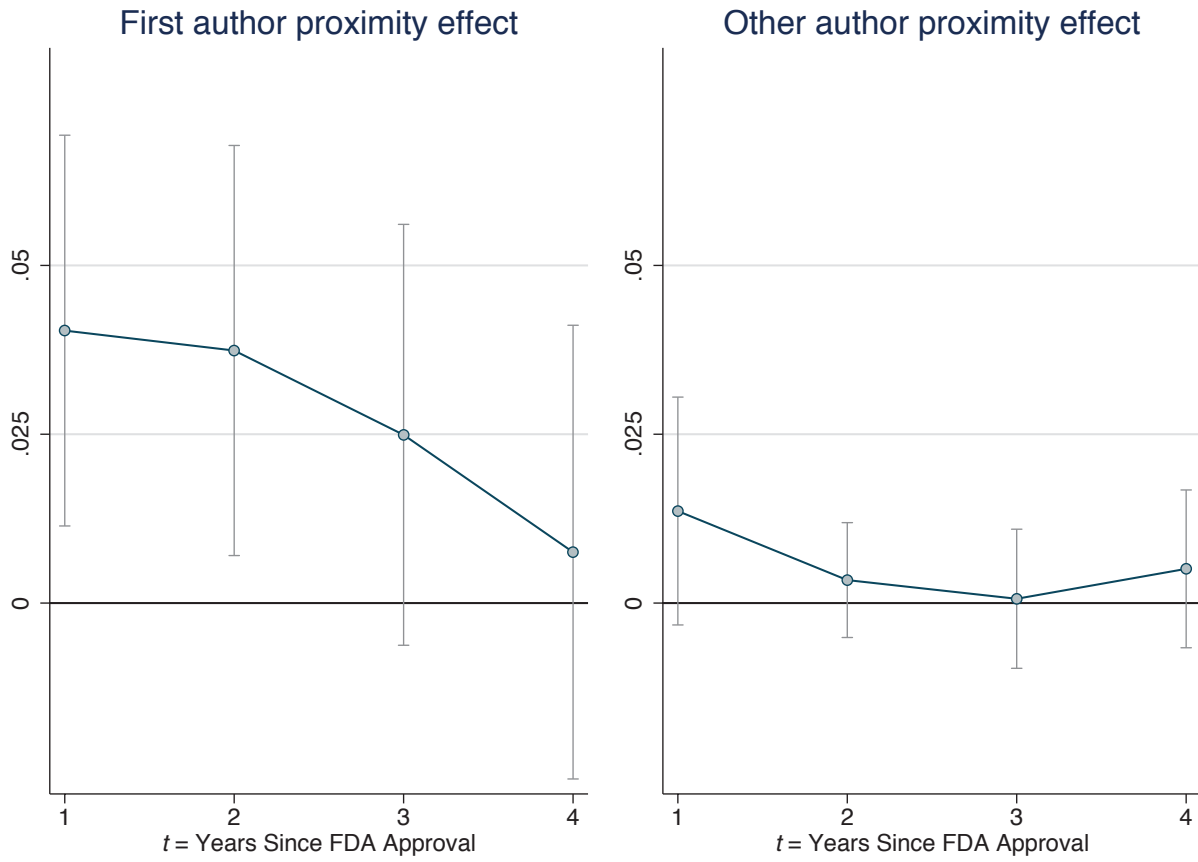
Notes: Circles mark the Hospital Referral Regions (HRR) that contain a first author for the pivotal clinical trial of a cancer drug in our sample. Some regions are the site of multiple first authors: Houston, Texas, (four first authors); Chicago, Illinois, (three first authors); Durham, North Carolina, (two first authors); and New York, New York (two first authors). Triangles mark HRRs that contain other authors.

Figure 2: New Cancer Drug Utilization Rates, by Years Since FDA Approval



Notes: The figure plots raw usage for new drugs in the first author’s HRR versus all other HRRs. The “First author HRR” and “Other HRRs” rates are generated by averaging over the drug-specific first author HRR and non-first author HRR rates calculated separately for each drug in each year. To make rates over time comparable, we restrict to the 67% of drugs in our sample for which four years of usage rates are available.

Figure 3: Influence of Author Proximity on Drug Use



Notes: Graphs plot estimates of the effect pioneer investigator proximity has on drug utilization, t years since the corresponding cancer drug became FDA approved. Bands indicate 95% confidence intervals constructed from standard errors clustered at the provider HRR-drug level.

Table 1: List of Studied Cancer Drugs

Generic drug name (1)	Trade name (2)	FDA approval date (3)	Target disease (4)	1st author city (5)	Year of pivotal trial publication (6)	Journal of pivotal trial (7)	Size of target population (8)	No. of authors on pivotal trial (9)
Capecitabine	Xeloda	4/30/1998	breast cancer	Dallas, TX	1999	Journal of Clinical Oncology	26,410	10
Trastuzumab	Herceptin	9/25/1998	breast cancer	Chicago, IL	1999	Journal of Clinical Oncology	26,410	11
Valrubicin	Valstar	9/25/1998	bladder cancer	Chicago, IL	2000	Journal of Urology	13,557	6
Denileukin diftitox	Ontak	2/5/1999	cutaneous T-cell lymphoma	Durham, NC	2001	Journal of Clinical Oncology	819	26
Temozolomide	Temodar	8/11/1999	brain cancer	Houston, TX	2000	British Journal of Cancer	1,797	22
Epirubicin hydrochloride	Ellence	9/15/1999	breast cancer	Canada	1998	Journal of Clinical Oncology	53,762	18
Gemtuzumab ozogamicin	Mylotarg	5/17/2000	acute myeloid leukemia	Seattle, WA	2001	Journal of Clinical Oncology	2,192	17
Arsenic trioxide	Trisenox	9/25/2000	acute myeloid leukemia	New York, NY	2001	Journal of Clinical Oncology	1,079	15
Alemtuzumab	Campath	5/7/2001	chronic lymphocytic leukemia	Houston, TX	2002	Blood	12,027	11
Zoledronic acid	Zometa	8/20/2001	hypercalcemia of malignancy	Canada	2001	Journal of Clinical Oncology	2,694	11
Ibritumomab tiuxetan ¹	Zevalin	2/19/2002	non-Hodgkin's lymphoma	Rochester, MN	2002	Journal of Clinical Oncology	51,042	13
Fulvestrant	Faslodex	4/25/2002	breast cancer	Houston, TX	2002	Journal of Clinical Oncology	64,045	14
Oxaliplatin	Eloxatin	8/9/2002	colon cancer	Nashville, TN	2003	Journal of Clinical Oncology	52,778	8
Bortezomib ²	Velcade	5/13/2003	multiple myeloma	Boston, MA	2003	New England Journal of Medicine	23,819	21
Tositumomab-I 131	Bexxar	6/27/2003	non-Hodgkin's lymphoma	Stanford, CA	2005	Journal of Clinical Oncology	54,275	7
Pemetrexed	Alimta	2/4/2004	lung cancer	Chicago, IL	2003	Journal of Clinical Oncology	84,918	13
Cetuximab	Erbix	2/12/2004	colon cancer	United Kingdom	2004	New England Journal of Medicine	55,528	12
Bevacizumab	Avastin	2/26/2004	colon cancer	Durham, NC	2004	New England Journal of Medicine	55,528	15
Decitabine	Dacogen	5/2/2006	myelodysplastic syndromes	Houston, TX	2006	Cancer	15,460	16
Panitumumab	Arranon	9/27/2006	colon cancer	Belgium	2007	Journal of Clinical Oncology	59,028	12
Temsirolimus	Torisel	5/30/2007	kidney cancer	Philadelphia, PA	2007	New England Journal of Medicine	3,794	19

¹There were two pivotal trials for Ibritumomab tiuxetan; the second trial had 1 total authors, with the same first author also in Rochester, MN, and was also published in the Journal of Clinical Oncology.

²There were two pivotal trials for Bortezomib; the second trial had 15 total authors, with the first author in New York, NY, and was published in the British Medical Journal 2004.

Table 2: Drug Use Summary Statistics

<i>Variables:</i>	First author HRR (1)	Other author HRR (2)	Author HRR for different drug (3)	HRR with no authors (4)
Drug utilization rate	0.156	0.097	0.092	0.086
Fraction treated in author's group	0.534	0.357	0.000	0.000
Number of observations	6,985	29,322	250,330	372,831
Avg. no. of patients per HRR per drug	388	236	254	75
No. of HRR-drug pairs	18	124	986	4958
No. of unique HRRs	11	54	54	252

Notes: Regions are defined by the 306 Dartmouth Atlas Hospital Referral Regions (HRRs). For each drug, regions are partitioned into four groups, corresponding to the four columns in the table. Statistics are then reported for each column by aggregating over the set of drugs in our sample. Reported statistics reflect drug utilization over the first two years following initial introduction. Data on drug utilization comes from Medicare claims 1998-2008.

Table 3: Author Proximity Effect on Drug Utilization

Dependent variable: (drug)_id in {0,1}, indicates receipt of new cancer drug d by patient i

Proximity Measures	Panel A: All HRRs		Panel B: Author HRRs only		Panel C: New Cancer Patients	
	(1)	(2)	(3)	(4)	(5)	(6)
First author HRR	0.0404*** (0.0131)		0.0383*** (0.0122)		0.0399*** (0.0154)	
Other author HRR	0.0069 (0.0048)		0.0068 (0.0051)		0.0059 (0.0053)	
First author HRR & in author group		0.0421*** (0.0125)		0.0417** (0.0124)		0.0421*** (0.0162)
First author HRR & non-author group		0.0416** (0.0211)		0.0392** (0.0195)		0.0409** (0.0203)
Other author HRR & in author group		0.0276*** (0.0074)		0.0286*** (0.0073)		0.0271*** (0.0082)
Other author HRR & non-author group		-0.0031 (0.0054)		-0.0033 (0.0058)		-0.0036 (0.0057)
Number of observations	659,468	659,468	286,637	286,637	393,618	393,618

Notes: This table reports results from 6 separate regressions, where the dependent variable is an indicator that equals 1 if the patient is treated with the new drug over the observed episode of care. Each observation is a patient-episode, i.e. a 1 year episode of care during which the patient receives treatment for the indicated cancer type and so may be eligible for the new drug. "First author HRR" (hospital referral region) is an indicator variable that equals 1 if the patient is treated in the same HRR as the trial's first author. "Other author HRR" indicates treatment in the same HRR as another trial author (but not the first author). Author physician group indicators equal 1 if the patient was at any point during the year treated by a physician practicing in the same group as a trial author. Author HRR, non-author group indicators equal 1 if the patient is treated in the author's HRR but never by a doctor practicing in the same group as a trial author. All regressions include drug-year fixed effects; HRR-cancer type fixed effects defined using three categories of cancer drugs: urologic, hematologic, and other (including breast, colon, lung, and brain); and indicators for patient age, race, sex, and new cancer treatment episode. Standard errors clustered at the HRR-drug level shown in parentheses. *: p<0.10; **: p<0.05; ***: p<0.01.

(1-2) All HRRs and patient episodes within two calendar years after drug's FDA approval

(3-4) Sample limited to HRRs which ever contain any pivotal trial author

(5-6) All HRRs, but limited to new cancer patients, defined as patients with no cancer treatment in previous calendar year

Table 4: Superstar Author Proximity Effect on Drug Utilization

<i>Dependent variable: (drug)_id in {0,1}, indicates receipt of new cancer drug d by patient i</i>						
<i>Independent variables:</i>	(1)	(2)	(3)	(4)	(5)	(6)
First author HRR	0.0300** (0.0124)			0.0246** (0.0119)	0.0242** (0.0111)	0.0230** (0.0110)
Top 50% cited author HRR		0.0227** (0.0090)		0.0154* (0.0081)		0.0144 (0.0090)
Top 10% cited author HRR			0.0232** (0.0122)		0.0100 (0.0108)	0.0034 (0.0117)
Number of observations	659,468	659,468	659,468	659,468	659,468	659,468

Notes: These regressions test whether "superstar" authors are more influential than other study authors for the same drug; to that end, the baseline regression specification is augmented to include a vector of (drug)*(any author HRR) fixed effects. Reported coefficients describe whether regions with authors of the noted type have higher new drug use compared to the rest of the author regions for the same drug. Top 50% and top 10% authors are defined as the most prominent academic authors for each drug, as measured by citation counts accruing to publications produced over the 10 years leading up to FDA drug approval in the relevant field. All regressions include drug-year fixed effects; HRR-cancer type fixed effects defined using three categories of cancer drugs: urologic, hematologic, and other (including breast, colon, lung, and brain); and indicators for patient age, race, sex, and new cancer treatment episode. See notes to Table 3 for further details. *: p<0.10; **: p<0.05; ***: p<0.01.

Table 5: Scope of Author Influence

Dependent variable: (drug)_id in {0,1}, indicates receipt of new cancer drug d by patient i

<i>Independent variables:</i>	Regional technology intensity		Neighbor region drug adoption		Off-label drug use	
	(1)	(2)	(3)	(4)	(5)	(6)
First author HRR	0.0409*** (0.0112)	0.0385*** (0.0105)	0.0402*** (0.0131)	0.0402*** (0.0130)	0.0006 (0.0005)	0.0007 (0.0005)
First author HRR * Fast adoption index	-0.0215** (0.0084)	-0.0197*** (0.0077)				
Neighbor of first author HRR			0.0017 (0.0066)	0.0014 (0.0066)		
Other author HRR	0.0064 (0.0047)	0.0063 (0.0050)	0.0066 (0.0048)	0.0067 (0.0049)	0.0002 (0.0004)	0.0003 (0.0004)
Other author HRR * Fast adoption index	-0.0042 (0.0052)	-0.0035 (0.0053)				
Neighbor of other author HRR			-0.0031 (0.0030)	-0.0030 (0.0031)		
Sample						
Restricted sample?	No	Yes	No	Yes	No	Yes
Number of observations	659,468	286,637	659,468	547,256	7,712,248	3,063,237

Notes: This table reports coefficients and standard errors from 6 separate regressions. See notes to Table 3 for further details. Columns 2 and 6 restrict the sample to only include regions that contain at least one study author. Column 4 restricts the sample to include only regions that contain a study author or border an author region. p<0.10; **: p<0.05; ***: p<0.01. (1-2) Fast adoption index summarizes regional utilization rates of new drugs when there is no author present in the region; the variable is normed to be mean zero and have a standard deviation of 1. Higher values correspond to regions that are quicker to adopt new cancer drugs. (3-4) Neighbor regions are defined as those that share a border with author regions. (5-6) Sample is changed to include all cancer care episodes treating patients who do not have the indicated disease type for the observed drug (e.g. testing use of a colon cancer drug in patients with other cancer types, such as breast cancer or lung cancer).

Table 6: Patient Travel and Proximity Effects

<i>Independent variables:</i>	<i>Dependent variables:</i>			
	Travel		New drug use	
	(1)	(2)	(3)	(4)
First author HRR	0.0329* (0.0192)	0.0309* (0.0197)	0.0327*** (0.0124)	0.0311*** (0.0116)
Traveler to first author HRR			0.0224 (0.0140)	0.0226 (0.0138)
Other author HRR	0.0295*** (0.0094)	0.0285*** (0.0089)	0.0066 (0.0052)	0.0064 (0.0056)
Traveler to other author HRR			0.0012 (0.0061)	0.0011 (0.0064)
<i>Sample</i>				
Author HRRs only?	No	Yes	No	Yes
Number of observations	659,468	286,637	659,468	286,637

Notes: Columns 1 and 2 report results from regressions where the dependent variable indicates whether patient received care outside the patient's HRR of residence. Columns 3 and 4 report results from regressions where the dependent variable indicates whether the patient received treatment with the new drug. Columns 2 and 4 restrict the sample to regions that contain a study author for at least one drug in our sample. See notes to Table 3. *: p<0.10; **: p<0.05; ***: p<0.01.

Table 7: IV Estimates of Proximity Effect on Drug Utilization

	Outcome: new drug use		
	(1)	(2)	(3)
<i>A. Reduced form: drug receipt effect</i>			
Residence in first author HRR	0.0228** (0.0099)	0.0217** (0.0099)	0.0228** (0.0099)
Residence in other author HRR	0.0038 (0.0044)	0.0044 (0.0050)	0.0046 (0.0061)
Residence in first author's neighbor HRR			0.0035 (0.0045)
Residence in other author's neighbor HRR			-0.0028 (0.0028)
<i>B. Two Stage Least Squares</i>			
Provider in first author HRR	0.0293** (0.0127)	0.0259** (0.0114)	0.0263** (0.0115)
Provider in other author HRR	0.0056 (0.0058)	0.0060 (0.0061)	0.0065 (0.0061)
Sample			
Author HRR only?	No	Yes	No
Number of observations	659,468	286,637	659,468

Notes: Reduced form results report coefficients from 3 regressions where the outcome variable is new drug use and the key explanatory variables are indicators for whether a given patient resides in the same region as the study author (or in column 3, in a neighboring region). In Panel B, the Two Stage Least Squares results use patient residence variables as instrumental variables for whether the patient is treated in author region. All regressions include drug-year fixed effects, and HRR-cancer type fixed effects defined using three categories of cancer drugs: urologic, hematologic, and other (including breast, colon, lung, and brain). Standard errors clustered at the HRR-drug level shown in parentheses. *: $p < 0.10$; **: $p < 0.05$; ***: $p < 0.01$.

Appendices

Table A1: Author Proximity Effect on Drug Utilization: Finer divisions of author role

	Panel A: All HRRs		Panel B: Author HRRs only		Panel C: New Cancer Patients	
	(1)	(2)	(3)	(4)	(5)	(6)
First author HRR	0.0406*** (0.0131)		0.0385*** (0.0122)		0.0403*** (0.0154)	
Middle author HRR	0.0077 (0.0050)		0.0074 (0.0054)		0.0076 (0.0055)	
Last author HRR	0.0006 (0.0140)		0.0028 (0.0127)		-0.0064 (0.0175)	
First author physician group		0.0422*** (0.0125)		0.0407*** (0.0126)		0.0422*** (0.0162)
First author HRR, non-author group		0.0417** (0.0211)		0.0395** (0.0196)		0.0411** (0.0203)
Middle author physician group		0.0273*** (0.0074)		0.0273*** (0.0074)		0.0259** (0.0082)
Middle author HRR, non-author group		-0.0018 (0.0059)		-0.0023 (0.0064)		-0.0007 (0.0060)
Last author physician group		0.0324 (0.0324)		0.0314 (0.0319)		0.0438 (0.0329)
Last author HRR, non-author group		-0.0137 (0.0016)		-0.0101 (0.0097)		-0.0275*** (0.0087)
Number of observations	659,468	659,468	281,253	281,253	393,618	393,618

Notes: Each observation is a patient-episode, i.e. a 1 year episode of care during which the patient has the indicated cancer type and so may be eligible for treatment with the new drug. First author HRR (hospital referral region) is an indicator variable that equals 1 if the patient is treated in the same region as the trial's first author. Other author HRR indicates treatment in the same region as another trial author (besides the first author). Author physician group indicators equal 1 if the patient was at any point treated by a physician practicing in the same group as the trial author. HRR, non-author group indicators equal 1 if the patient is treated in the author's HRR but never by a doctor practicing in the same group as a trial author. All regressions include drug-year fixed effects, and HRR-cancer fixed effects defined using three categories of cancer drugs: urologic, hematologic, and other (including breast, colon, lung, and brain). Standard errors clustered at the HRR-drug level shown in parentheses. ***: $p < 0.10$; **: $p < 0.05$; *: $p < 0.01$.

(1-2) All HRRs and patient episodes within 1-2 calendar years after drug's FDA approval

(3-4) Sample limited to HRRs which ever contain any pivotal trial author

(5-6) All HRRs, but limited to new cancer patients, defined as patients with no cancer treatment in previous calendar year

Notes on Appendix Table 1

This table reports results from 6 separate regressions that mirror our baseline specification (1), but further subdivide other authors into middle authors and last authors on the basis of authorship order on the academic publication. For new drug clinical trials, the first author is typically the principal investigator and the last author is often a scientist employed by the sponsoring drug company. In fact, only seven drugs in our sample have a last author who is a practicing clinician, whereas all 18 drugs with US-based trials have a practicing clinician as the first author. Note that we only investigate the role of practicing physicians; for the many drugs with a non-clinical final author, there is no last author region coded.

Results reported here find that patients treated in last author regions are not significantly more likely to receive the new drugs compared to other regions; however, the estimates are relatively imprecise due to the small number of drugs with clinicians in the last author position. In particular, the 95% confidence interval includes an up to 2.8 percentage point higher utilization in last author regions, reported from the column (1) baseline specification. Point estimates are suggestive of 3.2 percentage point higher use within the last author's physician group, as reported in column (2), but the findings are not statistically significant.