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Information Integration, Coordination Failures, and Quality of Prescribing*

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Abstract

Poor information flows hamper coordination, potentially leading to suboptimal decisions in health care. We examine the effects of a nationwide policy of information integration on the quality of prescribing. We use the rollout of an electronic prescribing system in Finland and prescription-level administrative data. We find no effect on the probability of co-prescribing harmful drug combinations in urban regions. In rural regions, this probability reduces substantially, by 35 percent. The effect is driven by prescriptions from unspecialized physicians and from multiple physicians. Improving the local information environment thus enhances coordination and narrows differences in the quality of prescribing.

Keywords: Health information technology, digitalization, e-prescribing, integration, quality of prescribing, public policy
JEL Codes: H51, H75

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1 Introduction

The essential purpose of organizations is to improve the coordination of interdependent decisions to achieve more desirable outcomes (Gibbons and Roberts 2012). The challenge for improving coordination is that information is incomplete and dispersed among decision makers (Hayek 1945). Health care is a prominent example: a patient's care delivery is spread across multiple organizations and physicians, and each physician has different knowledge of the patient's health and medical history. The relevant medical information is costly for the physicians to search and imperfectly shared between them, for example because of incompatible health information systems. (Arrow 1963; Cebul et al. 2008.) Critically, information integration systems offer policy tools to improve coordination by sharing the relevant information more easily within and across organizational boundaries. However, because large-scale implementation of such systems has been difficult and costly, there is only little empirical evidence of their effectiveness in achieving the goal of improved coordination.

We analyze a public policy of health information integration between regional care providers. Our empirical setting is based on the rollout of a nationwide electronic prescribing (e-prescribing) system across all the municipalities in Finland over a period of four years. In comparison to providers' pre-existing incompatible health information systems, e-prescribing systems provide more comprehensive information on prescriptions across multiple physicians involved in a patient's care.

We estimate the effects of the policy of information integration on the quality of prescribing, which we measure by using comprehensive administrative data on (interacting) prescriptions for one of the most common and harmful combinations of drugs: blood thinners and anti-inflammatory drugs (NSAIDs) such as ibuprofen and aspirin (Malone et al. 2005b; Roughead et al. 2010; Rikala et al. 2015). The data allow us to analyze the effects across different types of regions and physicians, highlighting the underlying mechanisms through which the policy acts. The data also identify interacting prescriptions obtained from multiple physicians over time, allowing us to provide direct evidence of the effects in terms of coordination.

The economic burden of coordination failures is high in health care. For example, in the U.S., the total annual cost of waste due to failures in care coordination has been estimated at between $27.2 and $78.2 billion (Shrank et al. 2019). Prescriptions for harmful drug combinations are a clear consequence of coordination failure. The prevalence of harmful drug combinations has increased in recent decades and is particularly high among individuals with multiple chronic diseases and older

patients (Mallet et al. 2007; Qato et al. 2016).

Besides providing a large-scale quasi-experiment, our empirical setting has other major advantages for analyzing the effects of information integration policies. Blood thinners, warfarin in particular, are widely prescribed to prevent serious conditions such as strokes and heart attacks (Kirley et al. 2012; Fimea and Kela 2019). The medical guidelines, however, clearly caution against combining warfarin with NSAIDs because of the increased risk of major bleeding complications (Lindh et al. 2014; Malone et al. 2005a). We expect medical information and better coordination to be crucial in avoiding prescriptions for such drug combinations.

Our administrative data contain 1.7 million prescriptions for over 250,000 warfarin patients in the period 2007–2014. Despite there being well-established guidelines, the co-prescribing of warfarin and NSAIDs was fairly common before the adoption of e-prescribing in our data.[1] The regional share of these interacting prescriptions was 6 percent on average in the pre-adoption period, with substantial variation across municipalities (between 2 and 19 percent). The worst-performing municipalities, as measured by the fourth quartile of the regional interaction share, were typically rural (80 percent of all cases).

Using our prescription-level data, we find that information integration through e-prescribing differentially impacts the quality of prescribing across municipalities. There is no statistically significant effect on the probability of co-prescribing warfarin with NSAIDs in urban municipalities; the confidence intervals of our baseline difference-in-differences (DiD) models rule out effects larger than 9 percent compared to the mean. However, in rural municipalities, the measure of low-quality prescribing reduces substantially, by approximately 35 percent. Thus, the estimated benefits of information integration are much larger in rural than in urban municipalities, possibly because of pre-existing regional differences in the local information environment or physician expertise.

We find that the improvements in rural prescribing patterns are driven by unspecialized physicians (general practitioners). They supply a disproportionate amount of prescriptions in rural municipalities and have fewer years of education than specialized physicians.[2] E-prescribing may reduce information frictions for these unspecialized physicians and narrow differences in physicians' expertise or knowledge by integrating medical information between them.

[1] For comparison, in a large U.S. prescription claims study 24 percent of warfarin patients received an NSAID during a two-year follow-up (Malone et al. 2005b).

[2] In our data the share of prescriptions from unspecialized physicians is 46 percent in urban regions and 55 percent in rural municipalities. From an international perspective, there is a greater proportion of generalists (and fewer specialists) in rural than in urban areas (Rabinowitz and Paynter 2002), suggesting regional differences in medical expertise.

Consistent with improved coordination between physicians, we find that the improvements in rural prescribing are also driven by interacting prescriptions from different physicians, rather than from the same physician. However, the resulting direct health benefits seem to be marginal: using additional administrative data, we find no evidence of a reduction in severe and relatively rare bleeding complications among warfarin patients as a result of e-prescribing. Based on our findings, we conclude that the improvements in the physicians' information environment facilitate coordination and reduce some (but not all) gaps in the quality of prescribing.

Our paper contributes to the empirical literature on coordination by studying the effects of a nationwide policy of information integration. Previous literature has analyzed monetary incentives and various organizational or management structures (e.g. hospital-physician integration, accountable care organizations (ACOs), hospitalists) as potential means for improving coordination (Gaynor et al. 2004; Cebul et al. 2008; Meltzer and Chung 2010). However, empirical work examining other fundamental components such as those affecting information is very limited (Bloom et al. 2014). Our results support the view that information integration improves coordination and mitigates the harms of fragmentation in health care (Cebul et al. 2008; Elhauge 2010).

Our results complement prior work on fragmented care delivery and related patient outcomes (Skinner et al. 2006; Agha et al. 2019). The findings are also broadly consistent with prior work on the determinants of physician practice style (e.g. education or information) within and across geographic regions (Epstein et al. 2016; Molitor 2018; Schnell and Currie 2018; Cutler et al. 2019).

We also contribute to the literature analyzing how information technology affects patient health (e.g. McCullough et al. 2010; Miller and Tucker 2011; Agha 2014; McCullough et al. 2016; Böckerman et al. 2019). The paper closest to ours is McCullough et al. (2016), who examine the effects of health information technology on mortality for the most complex patients whose diagnoses require cross-specialty care coordination. In contrast to their work, we explicitly analyze potential improvements in physicians' coordination or treatment choices, which are the determinants of patient health and one of the key objectives of health information technology.

Much of the evidence is from the U.S., where providers' incompatible, non-standardized health information systems integrate information locally, *within* a hospital. However, in a fragmented health care delivery system, high-quality care requires smooth information flows between different providers and organizations (Cebul et al. 2008). By analyzing a nationwide information integration, we provide evidence on the effectiveness of a broader policy intervention to improve the quality of health care than local policy designs. Our study also complements prior research on local

interventions (randomized controlled trials) aiming to reduce medication errors (Khalil et al. 2017).

2 Setting

2.1 Organizational Fragmentation and Coordination Failures in the Finnish Health Care System

Finland has a decentralized single-payer health care system, in which decisions related to the organization and provision of health care are moved closer to the users of health services than in a centralized system. By law, primary heath care is organized by municipalities ($N = 304$ in 2014) and specialized health care is organized by hospital districts ($N = 20$). Furthermore, physicians are usually employed by the public sector (FMA 2016), where they have weaker financial incentives to influence prescribing than in the private sector. The sectors providing complementary private and employer-sponsored occupational health care services are fairly small due to the provision of universal public health care services (Vuorenkoski et al. 2008; THL 2019).[3] Because service delivery and decisions related to organization is distributed across distinct care providers and regions, the system are highly fragmented. Fragmentation makes transmission of relevant medical information between providers crucial.

Before e-prescribing, health information systems were incompatible and operated within a region or even single health care unit. The platforms (electronic medical records, EMRs) were produced by private companies for different health care providers (Keskimäki et al. 2019). Also, the development of health information systems was uncoordinated at the national level (Teperi et al. 2009). The local and separate EMR systems generally contained information on a patient's prescription history as it was collected by the individual health care provider or unit, and this information was not available in a uniform and transferable electronic format at the national level. The transfer of prescription information was not possible even between providers that had the same EMR platform. Similarly, prescription information did not transfer between pharmacies because of their incompatible information systems.[4] Moreover, a lack of information integration made it more difficult to establish care coordination and to avoid prescriptions for harmful combinations of drugs.[5]

[3] In 2014, private health care covered by the National Health Insurance Scheme accounted for 6 percent and occupational health care for 4 percent of total health care costs (THL 2019).

[4] The pharmacy market is also fragmented because regulation prohibits pharmacy chains and all pharmacies are operated by private providers.

[5] This occurred despite the fact that physicians and pharmacies had access to a drug interaction database (INXBASE). INXBASE was/is integrated with many EMR and pharmacy platforms and automatically warns about drug interactions using information on a patient's prescriptions in that *local* platform. However, INXBASE is not

2.2 E-prescribing: Information Integration and Quality of Prescribing

E-prescribing is a widely used, but understudied health information technology for digitizing prescriptions and transfer of information on these across providers. In addition to Finland, e-prescribing systems have been adopted in many other European countries, the U.S., Australia, and Canada, among others, in the recent decade. Next, we describe the key mechanisms through which e-prescribing affects the quality of prescribing, as measured by prescriptions for harmful drug combinations.

The central goal of implementing an integrated e-prescribing system is to enhance the quality of prescribing by improving coordination and information flows across multiple physicians involved in a patient's care (Bell and Friedman 2005). In contrast to providers' pre-existing incompatible health information systems, e-prescribing systems provide physicians (and pharmacies) access to a patient's complete e-prescription history; this information is illustrated in online Appendix Figure A1 from the Finnish health care provider setting. Better availability of prescription information reduces the chance that one physician will not know about prescriptions from another physician. Therefore, the system can reduce prescriptions for harmful drug combinations, especially when they are written by different physicians.[6] Similarly, by integrating prescription information across pharmacies, the system can reduce the purchasing of harmful combinations of drugs from multiple pharmacies.

Our earlier work (Böckerman et al. 2019) focuses on another central goal of e-prescribing: improvements in the efficiency of the prescribing process through digital generation and transfer of a patient's prescriptions between physicians and pharmacies. Compared to traditional paper prescriptions, e-prescribing reduces the hassle and time costs of renewing and filling prescriptions, also eliminating lost prescriptions. E-prescribing can thus increase prescription drug use. This in turn can increase the use of harmful drug combinations. Taken together, the net effect of e-prescribing (through information integration and digitization of prescriptions) on the quality of prescribing is ambiguous.

integrated with the e-prescribing system and does not create flags about possible interacting prescriptions.

[6] E-prescribing may also reduce or eliminate the risks of misinterpretation and illegal falsification of handwritten paper prescriptions.

2.3 Adoption of the Nationwide E-prescribing System

We evaluate a large-scale public policy change: the adoption of the nationwide e-prescribing system, including all e-prescriptions and their dispensing records, and covering both public and private health care providers. The common standards and interoperability of the fully integrated nationwide system enable access to prescriptions for all physicians and pharmacies involved in a patient's care. This access, however, requires a patient's permission.

We focus on the staggered adoption of e-prescribing by municipalities in (public) primary care for three reasons. First, primary care physicians write most prescriptions, especially for warfarin and NSAIDs (Lindh et al. 2014). Second, in Section 4, we document a sharp increase in the take-up rate of e-prescriptions by physicians and their warfarin patients after the patients' municipality adopted e-prescribing. Third, there is substantial and plausibly exogenous regional heterogeneity in the adoption time of the e-prescribing system. As explained in Böckerman et al. (2019), the adoption time was determined by technical difficulties in the integration of the e-prescribing system with the pre-existing information technology systems in health care units and pharmacies, rather than by trends in prescribing and health outcomes.

Figure 1 documents the staggered rollout of the e-prescribing system across municipalities over the period 2010-2014.[7] The figure shows the adoption time at the quarter-level and we also use this level of precision in our estimations. By the first quarter of 2013, all municipalities had adopted the new system. The figure also indicates some geographical clustering of the reform. Municipalities are affiliated with one of the hospital districts, which coordinate some of their activities. However, the clustering is not a threat for identification of the effects, and there is also relevant variation for identification within hospital districts.

[7] Adoption of the system became mandatory in public health care units by 2014 and in private health care units by 2015. Very small private units issuing less than 5,000 prescriptions annually were excepted, and had the system by 2017.

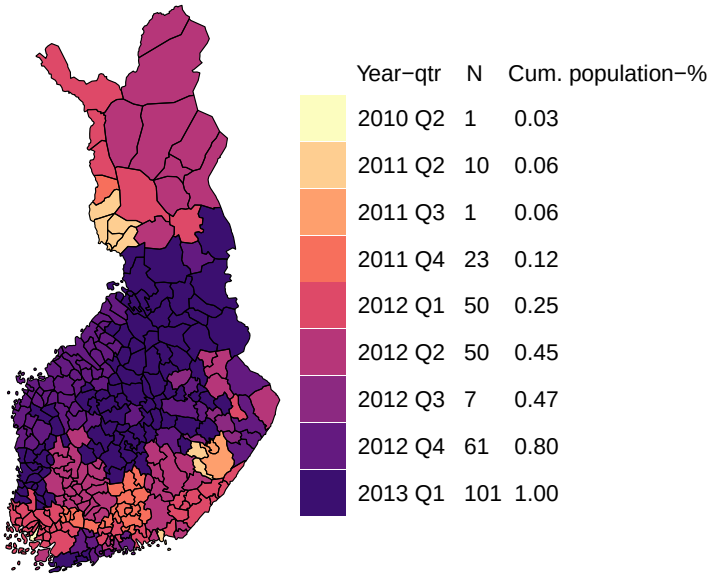

FIGURE 1: Staggered Adoption of E-prescribing in Municipalities

Note: This figure plots the year-quarter when e-prescribing was adopted by a municipality in (public) primary care. The figure also shows the number of municipalities and the cumulative population share by the period of adoption.

Source: National Institute for Health and Welfare, and Statistics Finland: Population Statistics

2.4 MARKET DESCRIPTION

We study the nationwide e-prescribing system as a policy tool for information integration to improve provider coordination and the quality of prescribing. Our measure of the quality of prescribing is one of the most common and harmful combinations of drugs in primary care settings (Andersson et al. 2018): warfarin (international brand names Coumadin, Marevan, among others) and anti-inflammatory drugs (NSAIDs) such as aspirin and ibuprofen.

Warfarin is one of the most commonly prescribed anticoagulants or blood thinners. It is an effective treatment for blood clots, which can cause serious health problems such as heart attacks and strokes (Beckman et al. 2010). In Finland, warfarin expenditures totaled approximately 3 million euros and 13 defined daily doses per 1,000 inhabitants per day in 2018 (Fimea and Kela 2019). For comparison, in the U.S., approximately 8–9 million prescriptions for warfarin are written per quarter and the total quarterly expenditures were approximately 144 million dollars in 2011/Q4 (Kirley et al. 2012).

Despite the proved effectiveness of warfarin, making safe, clinically appropriate prescribing decisions for warfarin patients is challenging. It has clinically significant, potentially dangerous,

but preventable interactions with other medications, especially with NSAIDs. Although NSAIDs are available over the counter (OTC) in lower dosages in most countries, these drugs are also widely prescribed to treat conditions such as acute or chronic pain and inflammation.[8] As warfarin and NSAIDs have blood-thinning effects and can cause bleeding (hemorrhage), combinations of them increase the risk of bleeding even more. As a result, a patient may experience, for example, continuous bleeding, especially in the gastrointestinal tract (Battistella et al. 2005), which can result in hospitalization and even death.

Against this institutional background, we turn next to documenting significant shortcomings and variations in provider coordination and the quality of prescribing using comprehensive administrative datasets on warfarin (and NSAID) patients in Finland.

3 Administrative Datasets

We analyze prescriptions for harmful drug combinations, which is our measure of the quality of prescribing and an outcome of coordination and information failures. We focus on combinations of warfarin and NSAIDs because they are relatively common and their direct health harms (bleeding complications) are well-documented and clinically significant (Section 2.4).

We primarily use administrative data on warfarin patients and their NSAID prescriptions over the period 2007–2014. We measure their bleeding complications using additional administrative data on discharges in specialized health care. Obviously, these complications are only one subset of health outcomes. Also, the main results for warfarin patients do not necessarily generalize to users of other prescription drugs or to the Finnish population.

Our sample construction covering warfarin patients improves statistical power, since we focus on prescriptions for those who may have harmful drug combinations and are thus targeted by the e-prescribing policy.[9] We examine separately the extensive margin of prescription drug use and return to the issues more closely in Section 5.3. Next we provide an overview of the datasets, sample construction and key variables.

Prescription Data—The Prescription Data are from the Social Insurance Institution of Finland. The data record the universe of warfarin and NSAID prescriptions that are filled at Finnish

[8] In Finland, expenditures for NSAIDs totaled approximately 44 million euros and there were 1.4 million recipients of reimbursement for prescription drugs under the NHI in 2018 (Fimea and Kela 2019).

[9] The sample construction is also fairly similar to those used in related work on drug interactions (Holbrook et al. 2005; Rikala et al. 2015).

pharmacies and are covered by the National Health Insurance (NHI) scheme over the period 2007–2014.[10] The key advantage of our comprehensive register-based data is that we can follow patients over time, even if they switch physicians, providers or employers. Using these data, we construct our main sample of patients, who filled at least one warfarin prescription during the observation period. This sample construction leads to a relatively homogeneous group of patients, who are mostly elderly (Section 3.1). For warfarin patients, we include the complete records of all their NSAID prescriptions throughout the years. We also confirm that our main results are robust to using an alternative sample, including all NSAID patients in the Prescription Data. The unit of observation is a prescription.

The data record the coded patient identifier, the patient's date of birth and death, and the municipality of residence. We use the 2013 municipality classification because Finland experienced a substantial number of municipal mergers in the years in the data (but not in 2014). Using the municipality of residence, we link the Prescription Data to additional data on the municipality's official statistical group from Statistics Finland; we thus identify patients in urban, semi-urban and rural municipalities.[11] We use two aggregated municipality groups in our analysis: urban (or semi-urban) and rural. See online Appendix Figure A2 for the map of municipalities by group. We group together urban and semi-urban municipalities (and call them urban municipalities for brevity) because there is no apparent heterogeneity in the main effects of e-prescribing between these two groups (Section 5).

The Prescription Data also record the physician identifier, the date of prescribing, the e-prescribing status, the Anatomical Therapeutic Chemical (ATC) code of the prescription, and the number of defined daily doses (DDD) of the prescription.[12] The WHO's defined daily dose is a widely used international metric, defined as the assumed average maintenance dose per day for a drug used for its main indication in adults. In our data, a very small fraction of prescriptions, less than one percent, is missing this information, and we drop these observations. Additionally, our data record unique identifiers for prescribing physicians, as well as their specialties and the date of

[10]The original data record all purchases related to a prescription (the items of the prescription may be purchased on multiple occasions). Here we rather use prescription-level data and identify prescriptions based on the patient and physician identifier, active ingredient, and the date of prescribing.

[11]Statistics Finland defines rural municipalities as including those in which less than 60 percent of the population live in urban settlements and in which the population of the largest urban settlement is less than 15,000 individuals; and those in which at least 60 percent but less than 90 percent of the population live in urban settlements and in which the population of the largest settlement is less than 4,000 individuals. All other municipalities are classified as urban or semi-urban.

[12]Our data may include a limited number of prescriptions issued by nurses, who have been able to administer drugs in Finland since 2012. However, the total number of prescriptions written by nurses is very small during our observation period, only 3,310 prescriptions in 2013 (Virta 2014).

specialization.

Our measure of the quality of prescribing is an indicator for co-prescribing potentially harmful combinations of warfarin and NSAID medications. See online Appendix A.1 for the ATC codes. To construct the measure, we take advantage of the amount of defined daily doses a patient filled from each prescription and the date of prescribing. We define and assume that one (theoretically) defined daily dose corresponds to one (actual) day of drug consumption. If the previous prescription is not fully consumed before the current prescription is issued, we flag the current prescription as an interacting prescription. Also, a necessary condition for a harmful interaction is that the previous prescription is for warfarin and the current prescription is for NSAID, or *vice versa*.[13] In addition to the quality of prescribing, we measure the intensive and extensive margins of warfarin and NSAID use, as described in Section 5.3.

Discharge Data—The Discharge Data are from the the National Institute for Health and Welfare. The data contain comprehensive information on Finnish public inpatient and outpatient specialized health care discharges in 2007–2014. The deidentified data record coded patient identifiers, the patient's diagnoses (ICD-10 coding), the date of discharge, and the patient's municipality of residence. Using the unique coded patient identifiers, we link the Discharge Data to the Prescription Data for the population of interest (warfarin patients).

From the data, we construct a dummy variable that equals one if the patient has a gastrointestinal hemorrhage (bleeding) diagnosis in specialized health care during a 3-month period. To calculate this outcome, we aggregate the data into a balanced panel form in which observations are at the patient-quarter-level. See online Appendix A.1 for the ICD-10 codes.

E-prescribing Adoption Data—Our analysis uses data on the dates of the adoption of e-prescribing by municipalities from the National Institute for Health and Welfare. We link the data on regional adoption dates to our other two datasets (Prescription Data and aggregated Discharge Data) by the patient's municipality of residence.[14] Because the aggregated disharge data are at the patient-quarter level, we consider the adoption of e-prescribing within the period of 3 months.

[13] We compare the current prescription to all the patient's previous prescriptions rather than only to the previous one. This is important, because elderly patients have typically several overlapping and potentially interacting prescriptions. In constructing the interaction indicator, we take into account (unsual) cases where warfarin and NSAIDs are prescribed at the same time.

[14] A patient typically chooses a public health care unit in his/her municipality of residence. For this reason, the municipality of residence also serves as a good proxy for the location of the prescribing physician.

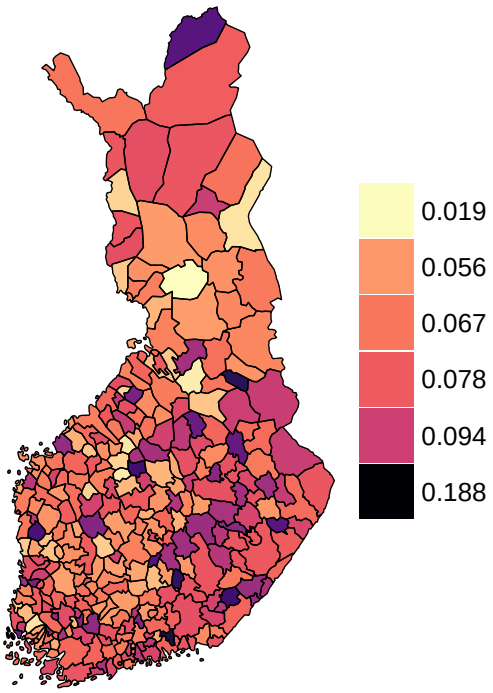

FIGURE 2: Average Interaction Probability in Municipalities

Notes: This figure plots the regional variation in the average probability of co-prescribing interacting drugs (NSAIDs) for warfarin patients by their municipality of residence in the pre-adoption period 2007-2009 ($N = 191,614$ patients).

3.1 DESCRIPTIVE EVIDENCE

Consistent with prior research in other settings (Zhang et al. 2011), we find substantial geographical variation in the quality of prescribing for warfarin patients in the pre-adoption period 2007–2009: the share of their interacting warfarin and NSAID prescriptions varies between 2 and 19 percent across municipalities. The average municipality has an interaction share of 8 percent for warfarin patients, with a standard deviation of 3 percent.

Table 1 shows that if we divide municipalities into quartiles by the regional interaction share, 80 percent of the worst performing regions (quartile 4) are rural. This stylized fact is further highlighted in Figure 3, which plots the histograms of the regional interaction share for rural and urban municipalities. Overall, these findings show evidence that coordination and information failures in prescribing were prominent in rural regions before e-prescribing.

Table 2 reports the summary statistics separately for patients in urban and rural regions in

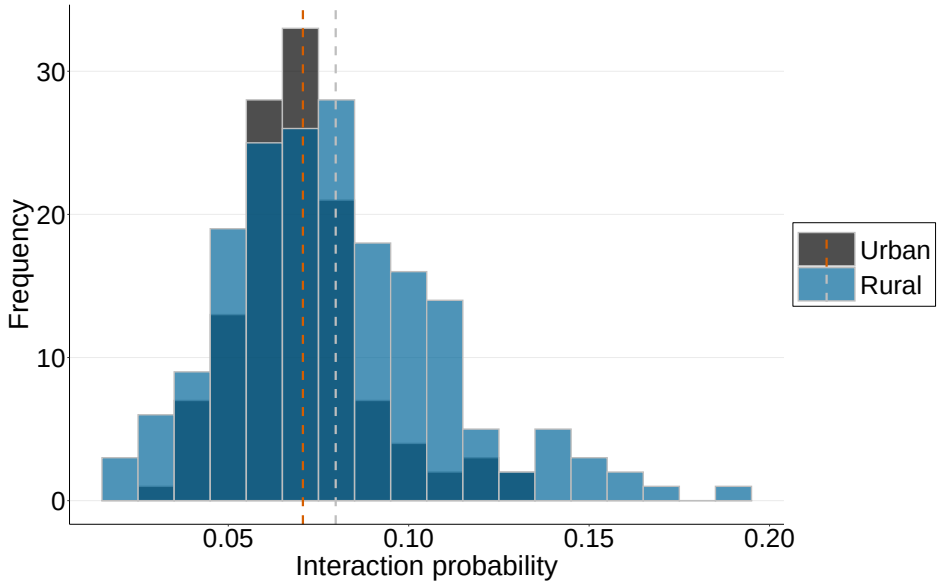

FIGURE 3: Average Interaction Probability in Urban and Rural Municipalities

Notes: The histograms in this figure plot the regional variation in the average probability of co-prescribing interacting drugs (NSAIDs) for warfarin patients by their municipality of residence and municipality group (rural or urban) in the pre-adoption period 2007-2009.

TABLE 1: Regional Variation in Interaction Probability, by Quantile

Quantile	Mean	Min	Max	SD	N	Share of rural areas
1	0.048	0.019	0.059	0.010	76	0.632
2	0.066	0.059	0.072	0.004	75	0.413
3	0.079	0.072	0.088	0.005	77	0.558
4	0.112	0.089	0.188	0.022	76	0.803
Total	0.076	0.019	0.188	0.027	304	0.602

Notes: This table reports summary statistics for the average probability of co-prescribing interacting drugs (NSAIDs) for warfarin patients by their municipality of residence in the pre-adoption period 2007-2009. The table also reports the share of rural regions by the quantile of this regional interaction probability.

the pre-adoption period, using the prescription-level data. Panel A shows that approximately 17 percent of warfarin patients were using interacting drugs (NSAIDs) in rural regions, and this share is 1 percentage point (8 percent) higher than for patients in urban regions. At the prescription level, the mean values of the probability of co-prescribing these interacting drugs were, however, fairly similar between these two regions (8 and 7 percent, respectively), but the corresponding standard deviations are very large (27 and 26 percent). Our findings on the fairly high rates of interacting prescriptions are consistent with prior research using Finnish data covering warfarin patients (Rikala et al. 2015).

Panel B shows only little difference in warfarin use, but there was some difference in NSAID use between patients in urban and rural regions. The average number of defined daily doses of NSAIDs per patient was 59 in rural regions, which was 16 percent higher than in urban regions. Moreover, as the data are constructed using warfarin users, warfarin use per patient was much higher than that of NSAIDs.

Panel C shows a striking regional variation in the supply of warfarin and NSAID prescriptions by physician specialty. In rural regions, unspecialized physicians supplied a much larger share of prescriptions compared to rural regions (55 versus 46 percent, respectively).[15] Lack of access to specialists in rural regions limits the provision of services, but potentially also the opportunities for unspecialized physicians to consult specialists.

Panel C also reveals that disrupted treatment relationships are common in Finland: the probability of getting a prescription from a different physician than last time was 53 percent in rural regions and 52 percent in urban regions. The ratio of unique physicians to patients was, however, much larger in rural regions (0.25) compared to urban regions (0.16).

Warfarin use, and especially its combination with NSAIDs, increases the risk of bleeding (Section 2.4). Panel D shows that the share of patients with a hemorrhage (bleeding) diagnosis was 7 percent in rural regions, which was only 6 percent higher than in urban regions. Bleeding can be particularly harmful, even lethal, for older patients; in fact, the panel also shows that warfarin users were typically elderly, approximately 70-years-old on average[16] and their mortality was high, approximately 10 percent.

Finally, the number of physicians per municipality was much smaller in rural than in urban

[15]Generally in Finland, physicians without a specialization (also called unspecialized physicians) are licensed physicians with a Licentiate's degree, which is a degree below a Doctoral degree and above a Master's degree. Physicians with a specialization are usually medical doctors also with a Doctoral degree.

[16]This fact is further highlighted in online Appendix Figure A3, which plots the histogram of the age of warfarin users.

municipalities (35 versus 135). The local networks of physicians may have affected information sharing and prescribing patterns, especially before nationwide information integration through e-prescribing.

TABLE 2: Summary Statistics for Pre-Adoption Period 2007–2009

	Urban				Rural			
	Mean	Q10	Q90	SD	Mean	Q10	Q90	SD
Panel A. Quality of prescribing								
Share of patients with an interaction	0.154				0.167			
Interaction probability								
Any warfarin-NSAID interaction	0.070			0.255	0.080			0.272
NSAID on top of warfarin	0.042			0.200	0.050			0.218
Warfarin on top of NSAID	0.028			0.166	0.031			0.172
Overlapping days, conditional on interaction	38.821	8.000	80.000	36.467	39.086	8.000	80.000	36.478
Panel B. Utilization								
Warfarin DDDs per patient	390.705	66.660	799.920	292.427	382.999	66.660	799.920	283.287
Warfarin Rx per patient	2.858	1.000	5.000	1.579	2.853	1.000	5.000	1.623
NSAID DDDs per patient	51.092	0.000	134.000	145.929	59.056	0.000	164.000	163.520
NSAID Rx per patient	0.994	0.000	3.000	1.966	1.105	0.000	3.000	2.229
Panel C. Physician variables								
Share of prescriptions by specialty								
Unspecialized	0.458				0.548			
General medicine	0.205				0.214			
Internal medicine	0.059				0.037			
Different prescriber	0.515			0.500	0.531			0.499
Panel D. Other patient variables								
Age (on the date of prescribing)	70.666	53.000	85.000	13.421	72.327	56.000	86.000	12.177
Share of patients who die	0.101				0.114			
Share of patients with a Hemorrhage diagnosis	0.067				0.071			
	N				N			
Observations (prescriptions)	382,823				101,424			
Patients	99,380				25,623			
Physicians	16,390				6,357			
Municipalities	121				183			

Notes: This table reports summary statistics for warfarin patients in the pre-adoption period 2007-2009. The variables are calculated from the prescription-level data, including both warfarin and NSAID prescriptions for these patients. The only exception is "Share of patients with a hemorrhage diagnosis" in Panel D, which is from the Discharge Data. In Panel A, "Probability of any warfarin-NSAID interaction" depicts the probability of this interaction (drug combination), resulting from NSAIDs (warfarin) prescribed on top of the existing warfarin (NSAID) prescriptions. "Share of patients with an interaction" shows the share of patients with a warfarin-NSAID interaction.

4 Econometric Approach

We use the staggered adoption of the nationwide e-prescribing system across municipalities and over four years to estimate the effects on our measure of the quality of prescribing for patient i in municipality m in period t, y_{imt} (Section 3). We estimate the effects on average and separately for each municipality group (urban or rural). Specifically, we estimate the following parametric event study specification, using the prescription-level data:

$$y_{imt} = \sum_{\tau=-8}^{8} \delta_\tau D_{\tau,mt} + X_{imt}^{'}\beta + \alpha_m + \gamma_t + \epsilon_{imt}, \tag{1}$$

where $D_{\tau,mt}$ indicates the period relative to the adoption period of e-prescribing in municipality m. Thus, the parameter vector of interest, δ, measures the changes in the outcome around the e-prescribing adoption in municipality m. We omit the first leading period to the adoption ($\tau = -1$). Thus, the other δ_τ parameters are normalized relative to this period. Also, $D_{-8,mt}$ ($D_{8,mt}$) equals one when the relative period is eight or more periods before (after) adoption. We include in the model the full set of the municipality fixed effects, α_m, which absorb any differences between municipalities that do not change over time; time fixed effects γ_t, which capture time-varying national-level shocks that may affect the outcome; and controls for patient-specific covariates, X_{imt}, which include age and the square of age. We also report the results for a specification in which we replace municipality fixed effects, α_m, with patient fixed effects, η_i. This specification uses within-patient variation in identification and controls for unobserved, time-invariant heterogeneity across patients such as their gender. To allow for within-municipality correlation in patients' unobservables, we cluster standard errors at the municipality level.[17]

To summarize the event study estimates δ_τ as short- and long-run point estimates, we also estimate the following DiD model:

$$y_{imt} = \rho_1 SR + \rho_2 LR + X_{imt}^{'}\beta + \alpha_m + \gamma_t + \epsilon_{imt}. \tag{2}$$

Here ρ_1 and ρ_2 denote the short-run and long-run point estimates, respectively. We define the short run as the first three quarters after the e-prescribing adoption and the long run as the subsequent remaining quarters.

Because of the staggered adoption of e-prescribing, the later-treated units use already-treated

[17] The number of clusters (municipalities) is 304.

units as controls in estimation. Goodman-Bacon (2018) shows that the treatment effect estimated by the two-way fixed effects DiD estimator (the so-called pooled DiD estimator) is the weighted average of all possible two-group, two-period treatment effects. He shows that if the treatment effect varies over time, negative weights could arise for later-treated units, potentially biasing the treatment effect estimate. We present robustness checks to address these concerns in online Appendix Section B and conclude that negative weighting is not an issue in our setting.

The take-up of e-prescriptions by physicians and their patients was voluntary during the observation period. This implies that the parameters of interest (δ_τ for $\tau \geq 0$, ρ_1, ρ_2) are the intention-to-treat (ITT) effects of e-prescribing. Figure 4 shows the take-up rate of e-prescriptions for warfarin patients around the adoption of e-prescribing by their municipality of residence (in primary care). The take-up rate of e-prescriptions increases sharply in the adoption period (quarter) and continues to increase gradually over time on average. One year after adoption approximately 60 percent of prescriptions are issued electronically on average. The take-up rate is only slightly higher for rural than urban patients after the adoption. A marginally higher take-up rate for rural patients may result from the fact that their prescriptions are more frequently obtained from primary care, as opposed to specialized health care (Section 3.1). This observation is further highlighted in Online Appendix Figure A5, which shows a higher take-up rate after adoption for patients who get their prescriptions from nonspecialists or specialists in general medicine than from internists. Overall, these findings show that our results for the adoption of e-prescribing are not driven by low take-up rates and also provide additional support for our empirical approach, which is based on the adoption of the technology by municipalities in primary care.

5 Results

5.1 Quality of Prescribing: Harmful Drug Combinations

Average Effects and Regional Heterogeneity.—Information integration can improve coordination, especially in settings in which for some reason information flows between physicians are being hampered. Geographical dispersion (and lack) of information is one example of this. We begin our analysis by presenting the main results from estimating the effects of e-prescribing on the probability of a warfarin-NSAID interaction on average and by municipality group (urban/semiurban or rural), using the prescription-level data.[18] Our regional heterogeneity analysis is motivated by the

[18]Our classification of urban includes both urban and semiurban municipalities because the main effects of e-prescribing are very similar in these two municipality groups, as shown in online Appendix Figure A6.

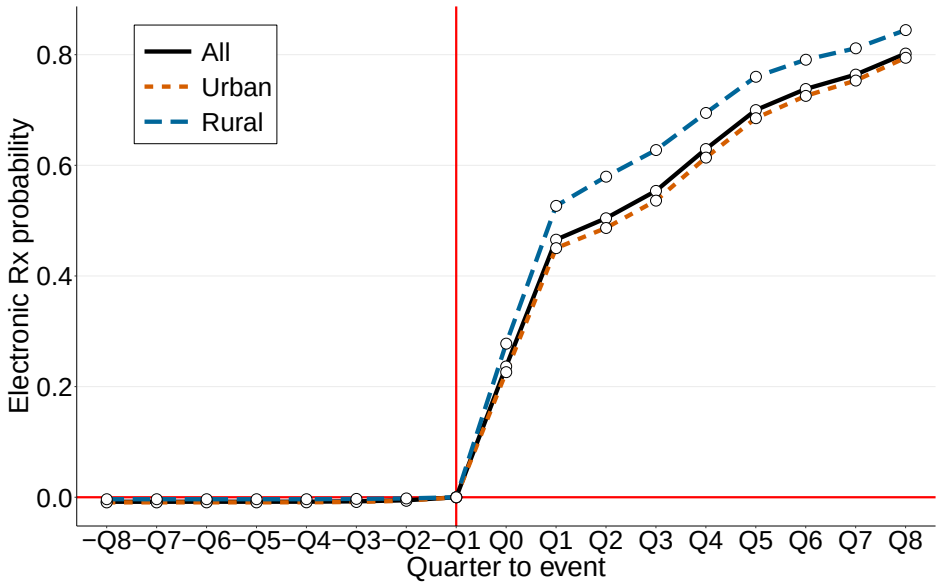

FIGURE 4: Take-up Rate of E-prescriptions, by Municipality Group

Notes: This figure plots the coefficient estimates from an event study framework using the prescription-level data from warfarin patients. The outcome is a dummy variable that equals to one if the prescription (warfarin or NSAID) is an e-prescription. Each line is plotted from a separate regression.

descriptive evidence, which suggests that coordination and information failures are more prominent in rural than urban regions (Section 3.1).[19]

Figure 5 plots the δ_τ coefficients and their confidence intervals from estimating the event study specification in Equation (1). Panel A shows that e-prescribing has a statistically insignificant effect on the interaction probability on average. The average effects are driven by prescriptions in urban/semiurban municipalities, as shown in Panel B. The corresponding DiD estimates from Equation (2) are very close to zero and precisely estimated (column 1 of Table 3). In contrast, Panel C of the figure shows a statistically significant and large decrease in the interaction probability in rural regions after e-prescribing. The magnitude of the corresponding long-run point estimate is -36 percent compared to the mean (Table 3). The decrease is gradual, coinciding with the increasing take-up rate of e-prescribing technology over time. Overall, the figure does not reveal clear pre-trends, supporting the key identification assumption of our empirical specification.

In our setting, information integration can affect the drug combination risk for all-aged patients. On the one hand, the medical literature has documented that the concurrent use of multiple medications is most common among elderly patients (Mallet et al. 2007). Thus, elderly patients are at

[19]Online Appendix Table A2 confirms that the largest effects occur in the worst-performing municipalities, as measured by the fourth quartile of the municipalities' pre-adoption interaction rate. The vast majority (80 percent) of the worst-performing municipalities are rural (Section 5).

TABLE 3: Effects of E-Prescribing on Warfarin-NSAID Interaction Probability

	Baseline (1)	Patient FE (2)	Hosp. distr. trend (3)	ATC trend (4)	No private visits (5)	All NSAID patients (6)	No dying patients (7)
Panel A. All municipalities							
Short-run	−0.002	−0.002**	−0.003*	−0.002	−0.002	−0.000	−0.002
	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.000)	(0.001)
Long-run	−0.003	−0.004*	−0.001	−0.002	−0.003	−0.000	−0.003
	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)	(0.000)	(0.002)
Mean outcome	0.045	0.045	0.045	0.045	0.044	0.010	0.046
Observations	1,689,506	1,689,506	1,689,506	1,689,506	1,624,852	7,752,317	1,243,189
Panel B. Urban municipalities							
Short-run	0.000	−0.001	−0.001	0.000	0.000	0.000	−0.000
	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.000)	(0.002)
Long-run	0.000	−0.001	0.000	0.000	0.000	0.000	−0.000
	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)	(0.000)	(0.002)
Mean outcome	0.044	0.044	0.044	0.044	0.043	0.009	0.045
Observations	1,347,198	1,347,198	1,347,198	1,347,198	1,289,846	6,548,763	1,000,947
Panel C. Rural municipalities							
Short-run	−0.011***	−0.009***	−0.013**	−0.010***	−0.011***	−0.003***	−0.010***
	(0.003)	(0.003)	(0.005)	(0.002)	(0.003)	(0.001)	(0.003)
Long-run	−0.018***	−0.014***	−0.023***	−0.016***	−0.017***	−0.004***	−0.015***
	(0.004)	(0.004)	(0.009)	(0.003)	(0.004)	(0.001)	(0.004)
Mean outcome	0.050	0.050	0.050	0.050	0.049	0.014	0.049
Observations	342,308	342,308	342,308	342,308	335,006	1,203,554	242,242

Notes: This table reports the coefficients from the Difference-in-Differences regressions using the prescription-level data. The outcome is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. "Short-run" refers to the first year after adoption, and "Long-run" refers to all subsequent periods. Each panel-column combination is estimated from a separate regression. All specifications include municipality fixed effects, time fixed effects, and age and age squared, except that column 2 replaces municipality fixed effects with patient fixed effects, column 3 adds hospital district specific time trends, and column 4 adds ATC-code specific time trends. Column 5 eliminates all prescriptions with a private physician visit from the regressions. Column 6 uses data on prescriptions for all patients who have at least one NSAID prescription, but not necessarily a warfarin prescription, as opposed to using the baseline sample that limits the data to prescriptions for patients who have at least one warfarin prescription over the period 2007–2014 (other columns). Column 7 excludes all prescriptions for patients who die during the observation period of the data. The standard errors are clustered at the municipality level.

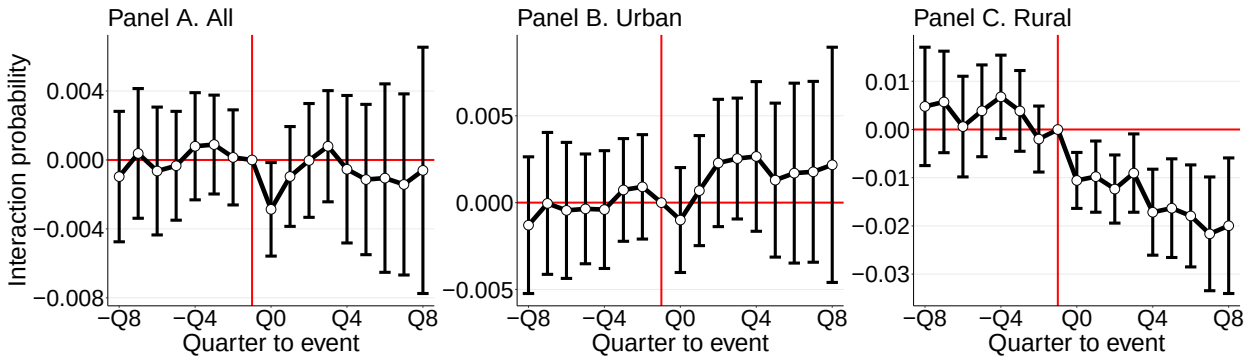

FIGURE 5: Probability of Warfarin-NSAID Interaction, By Municipality Group

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data on warfarin patients. The outcome is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. The omitted period is $-Q1$ and thus the coefficient estimates are relative to this period. The controls include municipality fixed effects, time fixed effects, age and age squared. Panel A plots the results for the whole sample of municipalities, Panel B plots for urban and semi-urban municipalities, and Panel C plots for rural municipalities, according to the classification by Statistics Finland. The standard errors are clustered at the municipality level.

a much higher risk of getting prescriptions for harmful drug combinations. On the other hand, our Appendix Figure A3 shows that there are more NSAID prescriptions among non-elderly warfarin patients (age under 65).

To study the potential age differences in more detail, we plot the long-run coefficients from the baseline specification, which is estimated separately for each municipality group and three different age groups: below 65, between 65 and 75, and above 75 (Figure 6). For urban regions, the point estimates are again close to zero and precisely estimated across the three age groups. For rural regions, the largest long-run reduction occurs among patients aged under 65. For the other two age groups, the reduction is approximately three times smaller than for the non-elderly patients.

Sensitivity Analyses.—To establish the robustness of our main findings, the remaining columns in Table 3 report the results from making various changes to the baseline specification. These changes include using patient fixed effects instead of municipality fixed effects (column 2); adding hospital district specific linear time trends (column 3); adding an extra linear time trend for individual ATC-codes or active ingredients (column 4); excluding all prescriptions with a visit to a private physician from the estimation sample, as we are investigating the adoption of e-prescribing in public primary care (column 5); including prescriptions for all patients who have at least one NSAID prescription, but not necessarily a warfarin prescription (column 6), as opposed to using the baseline sample that limits the data to prescriptions for warfarin patients; and including pre-

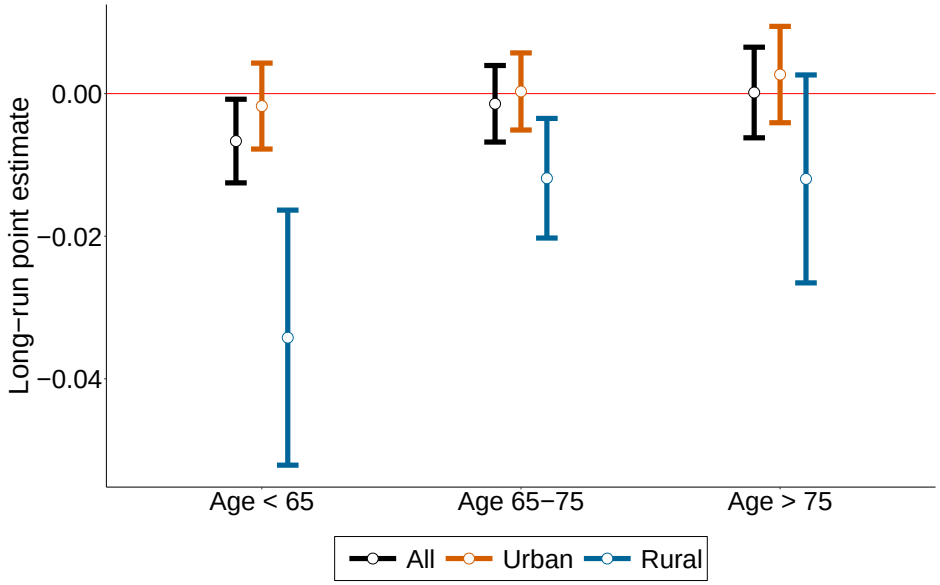

FIGURE 6: Long-Run Point Estimates, by Age and Municipality Group

Notes: These figures plot the long-run coefficients from Difference-in-Differences regressions using the prescription-level data on warfarin patients. Each coefficient is plotted from a separate regression. "Long-run" refers to all quarters after the first year of e-prescribing adoption. All regressions control for municipality fixed effects, time fixed effects, patient's age, and square of age. The urban/semi-urban and rural classification is from Statistics Finland. The standard errors are clustered at the municipality level.

scriptions only for patients who do not die during the observation period, in order to confirm that nonrandom attrition caused by mortality does not bias the baseline estimates (column 7).[20] The point estimates and their standard errors remain remarkably similar across all these specifications. Figures A8 and A9 plot the results of these robustness checks in the event study framework.

When a harmful drug combination occurs, it may be easier for the patient to stop using NSAIDs than warfarin as the latter is an essential, even life-saving medication. Failing to find similar results when considering only one-way interactions where NSAID is prescribed on top of warfarin would cast doubt on the validity of our results. Online Appendix Figure A13 shows that the results for these one-way interactions are very similar to our main results for two-way interactions (warfarin on top of NSAIDs or the other way round).

We additionally conduct several sensitivity tests regarding the measurement of the main outcome variable. First, we artificially decrease (increase) the length of prescriptions in Panels A–C (D–F) of Figure A10. Second, we exclude all interactions that interact for less than 10 days (and

[20] Mortality among warfarin patients is approximately 10 percent in both urban and rural regions (Section 3.1). If patients who have a higher probability of suffering from harmful drug interactions during the pre-adoption period are also more likely to die, attrition due to mortality would bias downwards the estimated impact of e-prescribing on the interaction probability. The specification in column 2 (with patient fixed effects) is an alternative approach to address this concern.

over 100 days) in Panels A–C (D–F) of Figure A11.[21] Our baseline results are not sensitive to these changes in the model specification. In Figure A12 and Table A3 we confirm that our estimates are not sensitive to using patient-specific average prescribing intervals as an alternative proxy for prescription length.

Placebo Regressions.—As a supplementary analysis, we estimate placebo regressions for the interaction probability. For this purpose, we use an interaction between warfarin and benzodiazepines as an outcome. Benzodiazepines are widely used medications for treating anxiety and sleep disorders (Olfson et al. 2015), and they do not have known harmful interactions with warfarin, according to the medical literature (Orme et al. 1972). Therefore, e-prescribing should not reduce warfarin-benzodiazepine interactions. As expected, Figure A14 shows no statistically significant reduction in these interactions, supporting the validity of our earlier findings.

5.2 Mechanisms Behind the Improvement in Quality of Prescribing

Improvement in the Information Environment.—Next we turn to investigate the potential mechanisms driving the improvement in the quality of prescribing in rural regions. We begin by assessing the role of physician expertise and medical education as well as changes in the treating physician. For the expertise, we consider the three most common types of medical specialties in our data: unspecialized, general medicine, and internal medicine. Compared to specialized physicians, unspecialized physicians have less medical education.[22] Similar to specialists of general medicine, unspecialized physicians are likely to work in primary care, in which patients are usually healthier than in specialized (hospital) care.

Figure 7 presents the event studies for the three specialties in rural regions. Column 3 of online Appendix Table A4 shows the corresponding short- and long-run point estimates. Column 2 of the table shows that there are no statistically significant effects in urban regions. In rural regions, the interaction probability decreases substantially for unspecialized physicians, who write a disproportionate amount of prescriptions in those regions (Panel A). For specialists in general medicine the decrease is much smaller and statistically insignificant (Panel B). For internists, the event study estimates are also negative but more imprecisely estimated than for the other specialties (Panel C). Interestingly, internists have the highest probability of writing an interacting prescription, most

[21] See online Appendix Figure A4 for the density of interaction days.

[22] In Finland, unspecialized physicians have the basic medical education that lasts for a minimum of six years and leads to the degree of Licentiate of Medicine. Additional specialist education typically takes 5-6 years.

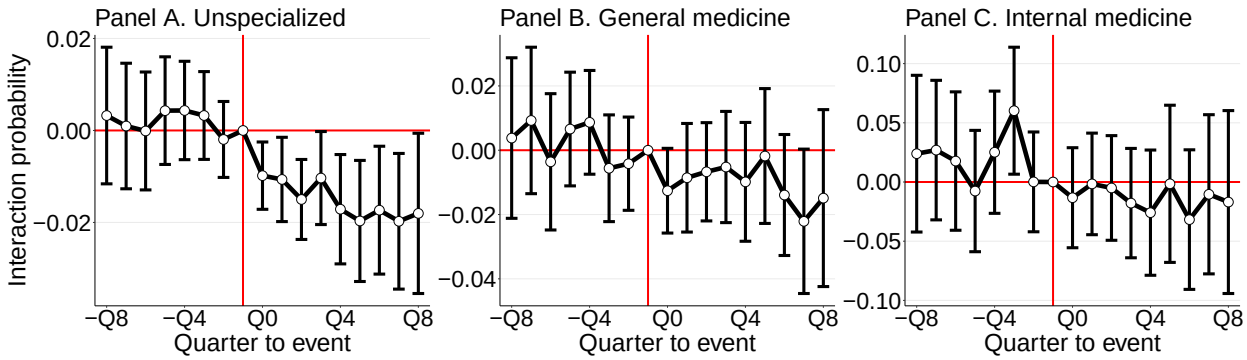

FIGURE 7: Probability of Warfarin-NSAID Interaction in Rural Municipalities, by Physician Speciality

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data on warfarin patients in rural municipalities. Panels A, B, and C plot the results for prescriptions written by unspecialized physicians, and physicians specialized in general medicine and internal medicine, respectively. See Figure 5 for more information on the specification of the model.

likely because of the complexity of their patient population. Based on these analyses, we conclude that the improvements in the quality of prescribing in rural areas are driven by unspecialized physicians. Lack of specialization and relevant information may have limited their ability to detect harmful drug combinations before e-prescribing.[23]

Coordination and Information Integration Between Physicians.—We proceed to look further into the mechanisms of information integration and coordination. E-prescribing should especially improve the quality of prescribing by improving a physician's information on the medication choices of the patient's previous physicians. To test this, we construct a binary outcome variable that equals one if the prescription interacts (overlaps) with the previous underlying prescription *and* the two prescriptions are from different physicians. Figure 8 plots the event study results in rural regions.[24] For comparison, we present the results for the outcome that the same physician writes the interacting prescriptions. We also present the results on the baseline (overall) effect that equals the sum of the two decomposed effects.

Figure 8 shows that the overall reduction in the interaction probability is predominantly driven by interacting prescriptions from different physicians, rather than from the same physician. The decrease for different physicians is statistically significantly larger in the short and long run than

[23] Also, more highly educated patients may be better aware of potential dangers of interactions. As we do not observe the patient's education or other socioeconomic background characteristics in the data, we do not investigate this issue further.

[24] Figure A7 shows that the results do not differ from the baseline estimates in urban regions.

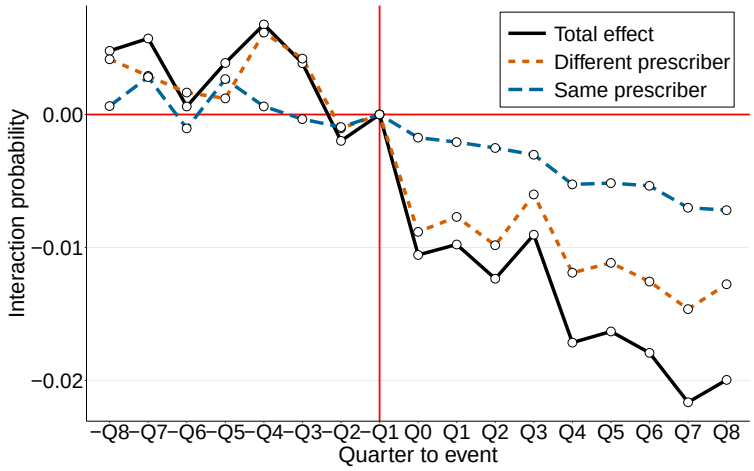

FIGURE 8: Probability of Warfarin-NSAID Interaction in Rural Municipalities, Different Versus Same Prescribing Physician

Notes: This figure plots the coefficient estimates from an event study framework using the prescription-level data on warfarin patients in rural municipalities. The outcome labeled as "Total effect" is the baseline outcome and is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. The outcome labeled as "Different physician" adds an additional condition to the baseline outcome that the interacting prescriptions are written by different physicians. The outcome labeled as "Same physician" adds an extra condition to the baseline outcome that the interacting prescriptions are written by the same physician. See Figure 5 for more information on the specification of the model.

for the same physician (online Appendix Table A5). Note that in the table the coefficient estimates for a different physician are estimated relative to the same physician. This finding suggests that e-prescribing provides critical information to physicians in settings with changing health care providers and mitigates coordination failures in the system.

Information Integration Between Pharmacies.—Pharmacies also adopted the e-prescribing system and, as a result, information flows between different pharmacies may have improved. We proceed similarly as above and decompose the main outcome to interactions where the patient fills the interacting prescriptions in different pharmacies versus the same pharmacy. Figure 9 shows the results from this decomposition in rural municipalities. The decrease in interactions comes almost entirely from prescriptions filled in the same pharmacy. Thus, information integration between pharmacies does not drive our main results.

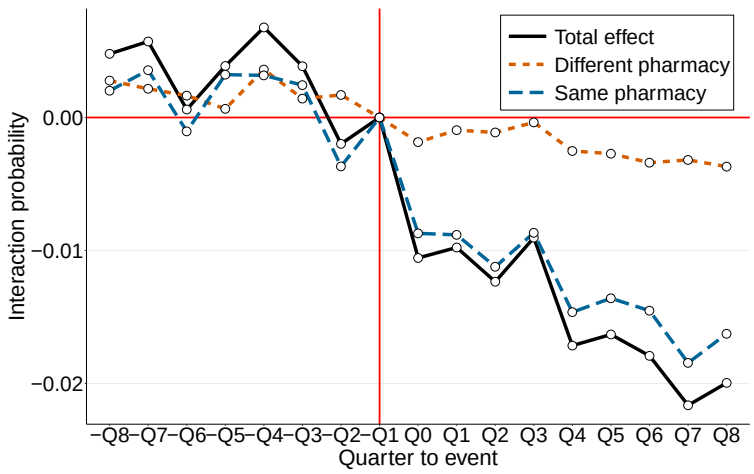

FIGURE 9: Probability of Warfarin-NSAID Interaction in Rural Municipalities, Different Versus Same Pharmacy

Notes: This figure plots the coefficient estimates from an event study framework using the prescription-level data on warfarin patients in rural municipalities. The outcome labeled as "Total effect" is the baseline outcome and is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. The outcome labeled as "Different pharmacy" adds an additional condition to the baseline outcome that the interacting prescriptions are fully filled at different pharmacies. The outcome labeled as "Same pharmacy" adds an extra condition to the baseline outcome that the interacting prescriptions are (at least partly) filled at the same pharmacy. See Figure 5 for more information on the specification of the model.

5.3 Quantity of Prescribing: Adjustment at Intensive And Extensive Margins

We then analyze the effects on prescription drug use to get a broader picture of the effects of e-prescribing and of the underlying mechanisms such as changes in the patient population. E-prescribing can either decrease (better monitoring) or increase prescription drug use (easier renewal and decreased hassle costs), see Section 2.2. If more drugs are being prescribed, there is a greater chance that there will be an interaction among the drugs. The effect is obviously the opposite if e-prescribing leads to less drugs being prescribed.

We analyze the effects on the intensive and extensive margins of prescription drug use. The intensive margin (prescription size) is measured by the number of defined daily doses per prescription. The extensive margin is measured by the total number of new and repeat prescriptions that a patient has in a given quarter. In the extensive margin analysis we aggregate the data to the patient-quarter-level balanced panel.

We find that the size of warfarin prescriptions increases by 4 percent in urban regions and by 6 percent in rural regions in the long run after e-prescribing, as shown in Figure 10 and Online Appendix Table A6. However, the effects are overestimated in the two municipality groups because the prescription size is smaller one quarter before the adoption of e-prescribing ($-Q1$) than in the

previous periods.[25] We interpret this decrease to be consistent with anticipation effects, in which physicians wrote shorter warfarin prescriptions in $-Q1$ as they expected that patients would benefit from the new technology. However, because prescriptions were shorter, physicians had to renew more prescriptions in the next periods right after the adoption of e-prescribing. Consistent with this, we find that the number of a patient's warfarin prescriptions increases by approximately 1 percent in the short run after e-prescribing, but remains close to zero in the long run in the two municipality groups.[26]

Figure 11 and Online Appendix Table A8 show no statistically significant effect on the intensive and extensive margins of NSAID use in urban regions. In rural regions physicians write smaller NSAID prescriptions after e-prescribing, but they do not increase the quarterly number of NSAID prescriptions for warfarin patients.

E-prescribing could affect initial warfarin prescriptions, and thereby change the warfarin patient population. To evaluate this possibility, Online Appendix Table A10 shows the effects separately on the number of all and new warfarin prescriptions per municipality and quarter, using aggregated data and population weights in the estimation. We find the point estimates to be small and imprecisely estimated, especially for the outcome of new warfarin use. However, for the quarterly number of warfarin prescriptions, the point estimates suggest a 3–4 percent increase in rural municipalities. Overall, the extensive margin adjustments are much smaller compared to the main effects on harmful drug combinations.

Theoretically, e-prescribing could change the composition of the patient population through the extensive margin adjustments. This poses a potential threat for the identification of the main effects using prescription-level data. For example, if warfarin users were less likely to need NSAIDs after e-prescribing, the coefficients of interest would reflect the change in the patient composition rather than the true effects of information on the interaction probability. Therefore, as an additional check, we also estimate regressions for the total number of warfarin-NSAID interactions per municipality and quarter, as shown in Table A10. Using municipality aggregates, we estimate the effects without any concern about the potential effects of compositional changes. Consistent with our main results, e-prescribing decreases the number of interactions by 19 percent in the long run in rural municipalities and the effect is statistically significant. Online Appendix Table A9

[25] If we omit the period $-Q1$ from the sample, the long-run increase is 2 percent in urban regions and 3 percent in rural regions, and the latter effect is statistically insignificant (Online Appendix Table A7). Moreover, we have checked that the decrease in prescription size is not mechanically caused by the event study design and its normalization. The decrease occurs in $-Q1$ even if we normalize a different period than $-Q1$ to zero.

[26] Our extensive margin results are robust to using the inverse hyperbolic sine transformation.

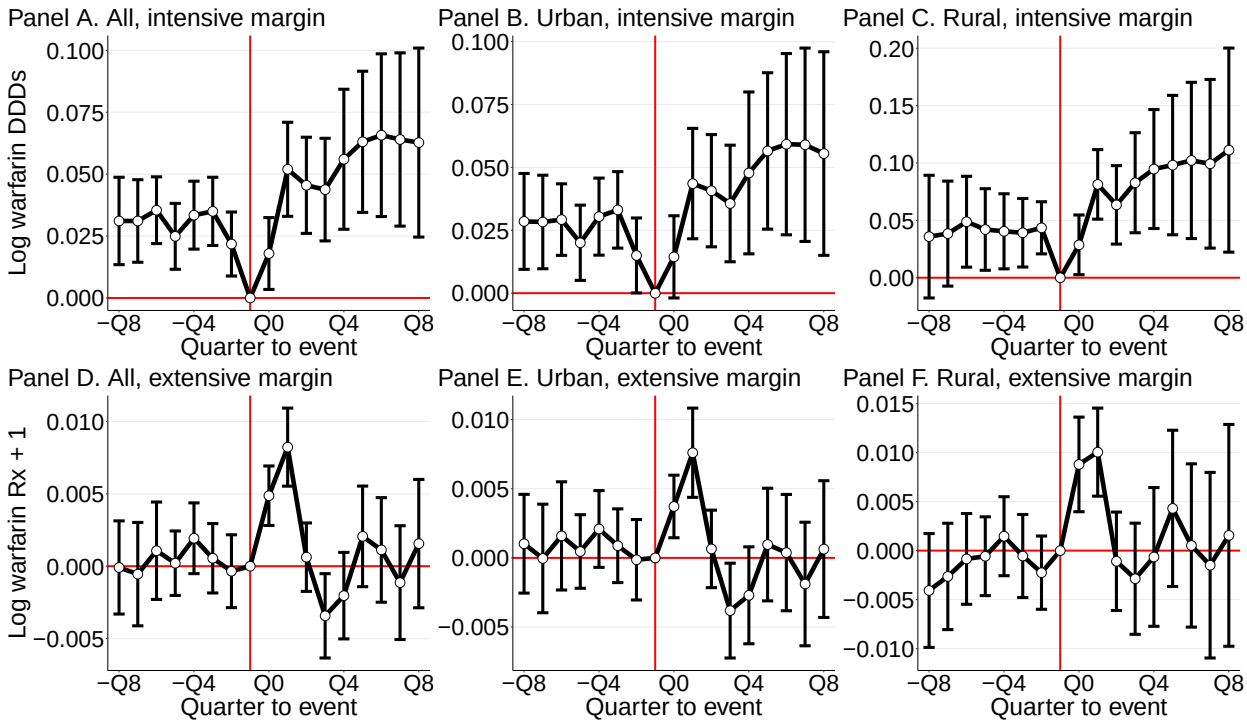

FIGURE 10: Intensive and Extensive Margins of Warfarin Prescriptions, by Municipality Group

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data (Panels A–C) and patient-quarter-level balanced data (Panels D–F) on warfarin patients. In Panels A–C, the intensive margin outcome is the log number of defined daily doses of warfarin prescriptions, and the data include only warfarin prescriptions. In Panels D–F, the extensive margin outcome is the log number of warfarin prescriptions+1 to adjust for zeros in the balanced panel. The controls include municipality fixed effects, time fixed effects, age and age squared. The urban/semi-urban and rural classification is from Statistics Finland. The standard errors are clustered at the municipality level.

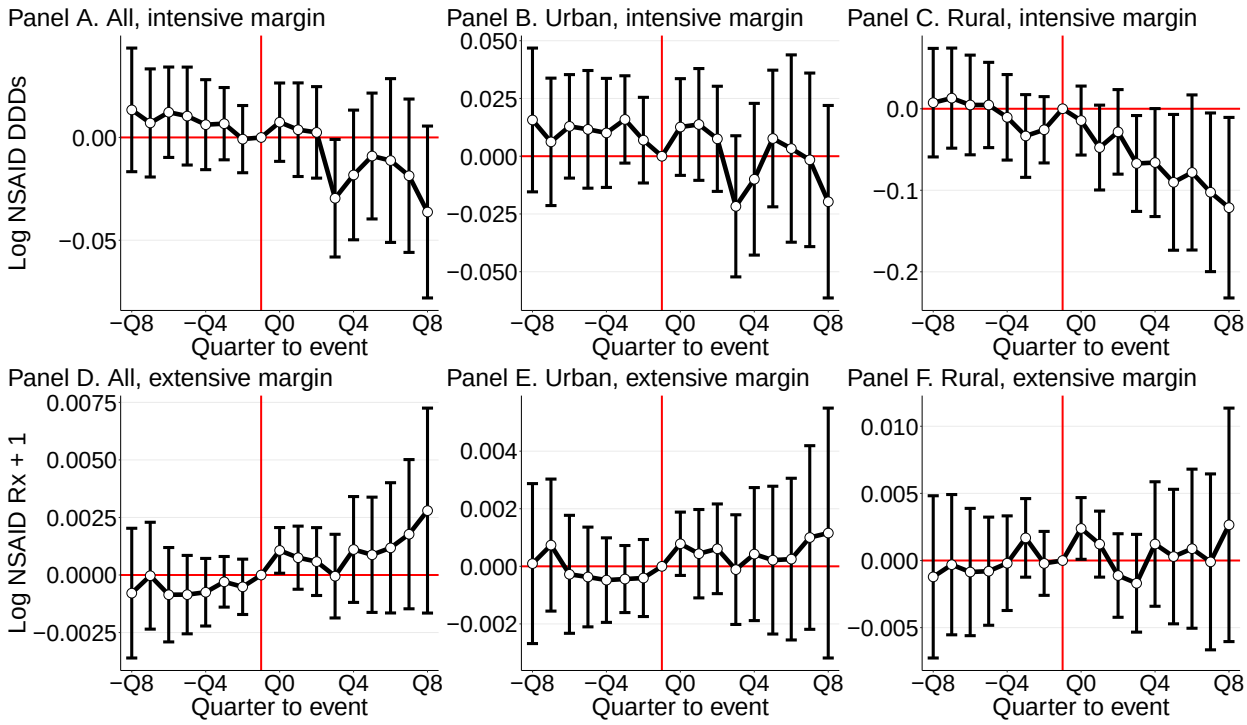

FIGURE 11: Intensive and Extensive Margins of NSAID Prescriptions, by Municipality Group

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data (panels A–C) and patient-quarter-level balanced data (panels D–F) on warfarin patients. In Panels A–C, the intensive margin outcome is the log number of defined daily doses of NSAID prescriptions, and the data include only NSAID prescriptions. In Panels D–F, the extensive margin outcome is the log number of NSAID prescriptions+1 to adjust for zeros in the balanced panel. The controls include municipality fixed effects, time fixed effects, age and age squared. The urban/semi-urban and rural classification is from Statistics Finland. The standard errors are clustered at the municipality level.

additionally confirms that the characteristics of new warfarin patients and their prescriptions look fairly similar one year before versus after the adoption of e-prescribing.

The earlier results indicate that in rural regions the size of warfarin prescription increases while the size of NSAID prescription decreases as a result of e-prescribing. Next, we proceed to analyze whether the decreasing probability of a harmful interaction originates solely from the decrease in the length of NSAID prescription. Any major decreases in the length should not only show up as a reduction at the extensive margin of the interacting prescription (our baseline results), but also as a reduction at the intensive margin (interaction time). Note that the length of NSAID prescriptions does not affect one-way interactions of prescribing NSAIDs on top of warfarin, which decreased after e-prescribing (Section 5).

Online Appendix Figure A15 plots the event study estimates for the number of interacting days of each interacting prescription. As the number of observations is quite small, the estimates are more imprecisely estimated, but show no clear evidence of a decrease in the outcome. Online Appendix Figure A16 shows the density of interaction time separately for the pre-reform period and the long-run post-reform period. Again, no discernible differences can be detected between the densities. In sum, the decrease in the probability of a harmful interaction is not solely explained by the decrease in the length of NSAID prescription. In rural regions, e-prescribing seems to help physicians to better target prescription NSAIDs to warfarin users.

5.4 Effects on Health: Gastrointestinal Bleeding

The main focus of this paper is to study the effects of information integration on the coordination and quality of prescribing. However, it might be of interest to investigate whether improvements in coordination translated into improvements in patient health. As a comprehensive analysis of various direct and indirect health effects is out of the scope of our paper, we focus on the most direct health outcome of interaction of warfarin and NSAID: gastrointestinal bleeding.

The medical literature has documented that the simultaneous use of NSAIDs and warfarin significantly increases the risk of major bleeding complications, especially in the gastrointestinal tract (Battistella et al. 2005). We examine whether the e-prescribing-induced decrease in drug interactions affected the probability of a gastrointestinal hemorrhage diagnosis in specialized health care among warfarin patients, using aggregated patient-quarter-level data.

We find no evidence of a decrease in this diagnosis after e-prescribing, not even in rural regions (Figure 12 and online Appendix Table A11). This finding can be rationalized by two main

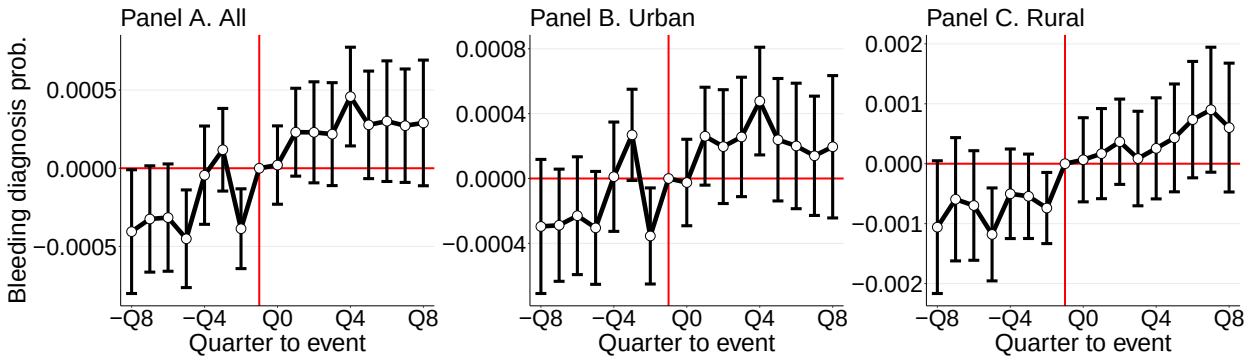

FIGURE 12: Probability of Hemorrhage (Bleeding) Diagnosis, by Municipality Group

Notes: These figures plot the coefficient estimates from an event study framework using patient-quarter-level balanced data on warfarin patients. The outcome is a dummy variable that equals one if the patient has a gastrointestinal hemorrhage diagnosis in specialized health care in a given period. The controls include municipality fixed effects, time fixed effects, age and age squared. The urban/semi-urban and rural classification is from Statistics Finland. The standard errors are clustered at the municipality level.

factors. First, warfarin use by itself can cause excessive bleeding, especially when used in higher doses. Moreover, we found that e-prescribing (digitization or easier renewal of prescriptions) increased the number of defined daily doses of warfarin prescriptions in rural regions. The increase in bleeding complications stemming from this increased size of warfarin prescriptions may counteract the complications stemming from fewer interacting prescriptions.[27] Second, our health outcome is rare in the patient population (mean quarterly probability of 0.2 percent). Also, not all warfarin patients have an interacting prescription in a given quarter. Thus, the bleeding outcome may not be sensitive enough to capture the full (long-term) positive effects of the decreased warfarin-NSAID interaction risk on latent health.

6 CONCLUSIONS

This paper studies a large-scale policy of health information integration between different care providers, using the rollout of a nationwide e-prescribing system in Finland. The fully digitalized system provided a unique opportunity to improve coordination and the quality of prescribing by sharing information on prescriptions among all physicians involved in a patient's care. Comprehensive administrative data on prescriptions for one of the most common and harmful combinations of drugs (warfarin and NSAIDs) allow a rare opportunity to analyze the consequences of information

[27]Table A11 shows positive and statistically significant effects. Diagnosing bleeding complications is complex (Kim et al. 2014), and e-prescribing (improved information on a patient's prescriptions) may also improve diagnoses, thereby increasing their prevalence.

and coordination frictions across all regions of the country.

We observe substantial variation in the quality of prescribing before the adoption of e-prescribing; the prevalence of harmful drug combinations varied between 1–19 percent across municipalities. The worst performing regions were typically rural, where unspecialized physicians write most of the prescriptions.

We find no evidence that e-prescribing improves the quality of prescribing in urban regions. In rural regions, the probability of co-prescribing warfarin with NSAIDs reduces substantially, by approximately 35 percent. This improvement in the quality of prescribing is driven by unspecialized physicians. Our interpretation of this result is that information frictions were higher for unspecialized physicians, which hampered their decision making before e-prescribing. We also find evidence of improved care coordination: e-prescribing predominantly reduces interacting prescriptions when they are obtained from different physicians, rather than from the same physician. However, the resulting direct health benefits seem to be marginal.

Coordinating care is a major policy challenge for health systems around the world (Doty et al. 2020). In complex systems such as health care, information is dispersed and the organizational structures are decentralized, with decision making allocated to separate agents or providers (e.g. by region or speciality). Although decentralization often improves efficiency, it can also lead to fragmentation and a breakdown of coordination. As decentralization has been the focus of many health systems, much less attention has been paid to optimizing and integrating a patient's care across different providers. Our findings show that a nationwide policy of information integration can mitigate coordination failures across different providers, thereby enabling patient medication to be tracked efficiently and improving the quality of care.

References

Agha, L. (2014). The effects of health information technology on costs and quality of medical care. *Journal of Health Economics 34*, 19–30.

Agha, L., B. Frandsen, and J. B. Rebitzer (2019). Fragmented division of labor and healthcare costs: Evidence from moves across regions. *Journal of Public Economics 169*, 144–159.

Andersson, M. L., Y. Böttiger, H. Kockum, and E. Birgit. (2018). High prevalence of drug–drug interactions in primary health care is caused by prescriptions from other healthcare units. *Basic & Clinical Pharmacology & Toxicology 122*(5), 512–516.

Arrow, K. J. (1963). Uncertainty and the welfare economics of medical care. *The American Economic Review 53*(5), 941–973.

Battistella, M., M. M. Mamdami, D. N. Juurlink, L. Rabeneck, and A. Laupacis (2005). Risk of upper gastrointestinal hemorrhage in warfarin users treated with nonselective NSAIDs or COX-2 inhibitors. *Archives of Internal Medicine 165*(2), 189–192.

Beckman, M. G., W. C. Hooper, S. E. Critchley, and T. L. Ortel (2010). Venous thromboembolism: A public health concern. *American Journal of Preventive Medicine 38*(4, Supplement), S495 – S501.

Bell, D. S. and M. A. Friedman (2005). E-prescribing and the Medicare modernization act of 2003. *Health Affairs 24*(5), 1159–1169.

Bloom, N., R. Lemos, R. Sadun, D. Scur, and J. Van Reenen (2014). JEEA-FBBVA Lecture 2013: The new empirical economics of management. *Journal of the European Economic Association 12*(4), 835–876.

Böckerman, P., M. Kortelainen, L. T. Laine, M. Nurminen, and T. Saxell (2019). Digital waste? Unintended consequences of health information technology. Working Paper No. 12275, IZA Discussion Paper.

Cebul, R. D., J. B. Rebitzer, L. J. Taylor, and M. E. Votruba (2008). Organizational fragmentation and care quality in the US healthcare system. *Journal of Economic Perspectives 22*(4), 93–113.

Cutler, D., J. S. Skinner, A. D. Stern, and D. Wennberg (2019). Physician beliefs and patient preferences: A new look at regional variation in health care spending. *American Economic Journal: Economic Policy 11*(1), 192–221.

Doty, M. M., R. Tikkanen, A. Shah, and E. C. Schneider (2020). Primary care physicians' role in coordinating medical and health-related social needs in eleven countries. *Health Affairs 39*(1), 115–123.

Elhauge, E. (2010). *The Fragmentation of U.S. Health Care: Causes and Solutions*. OUP Catalogue. Oxford University Press.

Epstein, A. J., S. Nicholson, and D. A. Asch (2016). The production of and market for new physicians' skill. *American Journal of Health Economics 2*(1), 41–65.

Finnish Institute for Health and Welfare (THL) (2019). Health expenditure and financing in 2017 (in Finnish). Technical Report 15.

Finnish Medical Association (FMA) (2016). *Physicians in Finland: Statistics on physicians and the health care system 2016*. Helsinki: The Finnish Medical Association. `https://www.laakariliitto.fi/site/assets/files/5223/ll16_tilasto2016_net1_170114.pdf`.

Finnish Medicines Agency (Fimea) and Social Insurance Institution (Kela) (2019). Finnish statistics on medicines 2018.

Gaynor, M., J. Rebitzer, and L. Taylor (2004). Physician incentives in health maintenance organizations. *Journal of Political Economy 112*, 915–931.

Gibbons, R. and J. Roberts (2012). *The Handbook of Organizational Economics*. Princeton University Press.

Goodman-Bacon, A. (2018). Difference-in-differences with variation in treatment timing. NBER Working Paper No. 25018.

Hayek, F. (1945). The use of knowledge in society. *American Economic Review 35*(4), 519–530.

Holbrook, A. M., J. A. Pereira, R. Labiris, H. McDonald, J. D. Douketis, M. Crowther, and P. S. Wells (2005). Systematic overview of warfarin and its drug and food interactions. *Archives of Internal Medicine 165*(10), 1095–1106.

Keskimäki, I., L.-K. Tynkkynen, E. Reissell, M. Koivusalo, V. Syrjä, L. Vuorenkoski, B. Rechel, M. Karanikolos, W. H. Organization, et al. (2019). Finland: Health system review. *Health System Review 21*(2), 1–166.

Khalil, H., B. Bell, H. Chambers, A. Sheikh, and J. Avery, Anthony (2017). Professional, structural and organisational interventions in primary care for reducing medication errors. *Cochrane Database of Systematic Reviews* (10).

Kim, B. S. M., B. T. Li, A. Engel, J. S. Samra, S. Clarke, I. D. Norton, and A. E. Li (2014). Diagnosis of gastrointestinal bleeding: A practical guide for clinicians. *World Journal of Gastrointestinal Pathophysiology 5*(4), 467.

Kirley, K., D. M. Qato, R. Kornfield, R. S. Stafford, and G. C. Alexander (2012). National trends in oral anticoagulant use in the United States, 2007 to 2011. *Circulation: Cardiovascular Quality and Outcomes 5*(5), 615–621.

Lindh, J. D., M. L. Andersson, and B. Mannheimer (2014). Adherence to guidelines for avoiding drug interactions associated with warfarin-a nationwide Swedish register study. *PloS One 9*(5), e97388.

Mallet, L., A. Spinewine, and R. Town (2007). The challenge of managing drug interactions in elderly people. *Lancet 370*, 185–191.

Malone, D. C., D. S. Hutchins, H. Haupert, P. Hansten, B. Duncan, R. C. Van Bergen, S. L. Solomon, and R. B. Lipton (2005a). Assessment of potential drug–drug interactions with a prescription claims database. *American Journal of Health-System Pharmacy 62*(19), 1983–1991.

Malone, D. C., D. S. Hutchins, H. Haupert, P. Hansten, B. Duncan, R. C. Van Bergen, S. L. Solomon, and R. B. Lipton (2005b). Assessment of potential drug–drug interactions with a prescription claims database. *American Journal of Health-System Pharmacy 62*(19), 1983–1991.

McCullough, J. S., M. Casey, I. Moscovice, and S. Prasad (2010). The effect of health information technology on quality in U.S. hospitals. *Health Affairs 29*(4), 647–654.

McCullough, J. S., S. T. Parente, and R. Town (2016). Health information technology and patient outcomes: The role of information and labor coordination. *The RAND Journal of Economics 47*, 207–236.

Meltzer, D. O. and J. W. Chung (2010). Coordination, switching costs and the division of labor in general medicine: An economic explanation for the emergence of hospitalists in the United States. NBER Working Paper No. 16040.

Miller, A. R. and C. Tucker (2011). Can health care information technology save babies? *Journal of Political Economy 119*(2), 289–324.

Molitor, D. (2018). The evolution of physician practice styles: Evidence from cardiologist migration. *American Economic Journal: Economic Policy 10*(1), 326–56.

Olfson, M., M. King, and M. Schoenbaum (2015). Benzodiazepine use in the United States. *JAMA Psychiatry 72*(2), 136–142.

Orme, M., A. Breckenridge, and R. Brooks (1972). Interactions of benzodiazepines with warfarin. *British Medical Journal 3*(5827), 611–614.

Qato, D. M., J. Wilder, P. Schumm, V. Gillet, and G. C. Alexander (2016). Changes in prescription and over-the-counter medication and dietary supplement use among older adults in the united states, 2005 vs 2011. *JAMA Internal Medicine 176*(4), 473–482.

Rabinowitz, H. K. and N. P. Paynter (2002). The rural vs urban practice decision. *JAMA 287*(1), 113–113.

Rikala, M., M. Hauta-Aho, A. Helin-Salmivaara, R. Lassila, M. J. Korhonen, and R. Huupponen (2015). Co-prescribing of potentially interacting drugs during warfarin therapy – a population-based register study. *Basic & Clinical Pharmacology & Toxicology 117*(2), 126–132.

Roughead, E. E., L. M. Kalisch, J. D. Barratt, and A. L. Gilber (2010). Prevalence of potentially hazardous drug interactions amongst Australian veterans. *British Journal of Clinical Pharmacology 70*(2), 252–257.

Schnell, M. and J. Currie (2018). Addressing the opioid epidemic: Is there a role for physician education? *American Journal of Health Economics 4*(3), 383–410.

Shrank, W. H., T. L. Rogstad, and N. Parekh (2019, 10). Waste in the us health care system: Estimated costs and potential for savings. *JAMA 322*(15), 1501–1509.

Skinner, J. S., D. O. Staiger, and E. S. Fisher (2006). Is technological change in medicine always worth it? the case of acute myocardial infarction. *Health Affairs 25*(Supplement 1), W34–W47.

Teperi, J., M. E. Porter, L. Vuorenkoski, and J. E. Baron (2009). The Finnish health care system: A value-based perspective. SITRA Report No. 82.

Virta, L. (2014). Hoitajareseptin merkitys vielä vähäinen. *Lääkärilehti 4*.

Vuorenkoski, L., P. Mladovsky, and E. Mossialos (2008). Finland: Health system review. *Health Systems in Transition 10*(4), 1–168.

Zhang, Y., J. P. Newhouse, and K. Baicker (2011). Are drugs substitutes or complements for intensive (and expensive) medical treatment. *American Economic Review 101*(3), 393–97.

A Online Appendix

A.1 ATC and ICD-10 codes

Warfarin and NSAID ATC codes used in the data.

- Warfarin: B01AA03
- NSAID: M01AB01, M01AB02, M01AB05, M01AB08, M01AB51, M01AB55, M01AC01, M01AC02, M01AC06, M01AE01, M01AE02, M01AE03, M01AE11, M01AE52, M01AG01, M01AG02, M01AH01, M01AH05, M01AX01

ICD-10 codes used for hemorrhage diagnosis in the data.

- All hemorrhages: I60*, I61*, I62*, K920, K921, K922, I850, K221, K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K290, K625, N02*, K661, N938, N939, N950, R041, R042, R048, R049, R31, R58, D683, H356, H431, H450, M250
- Gastrointestinal: K920, K921, K922, I850, K221, K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K290, K625

A.2 Figures

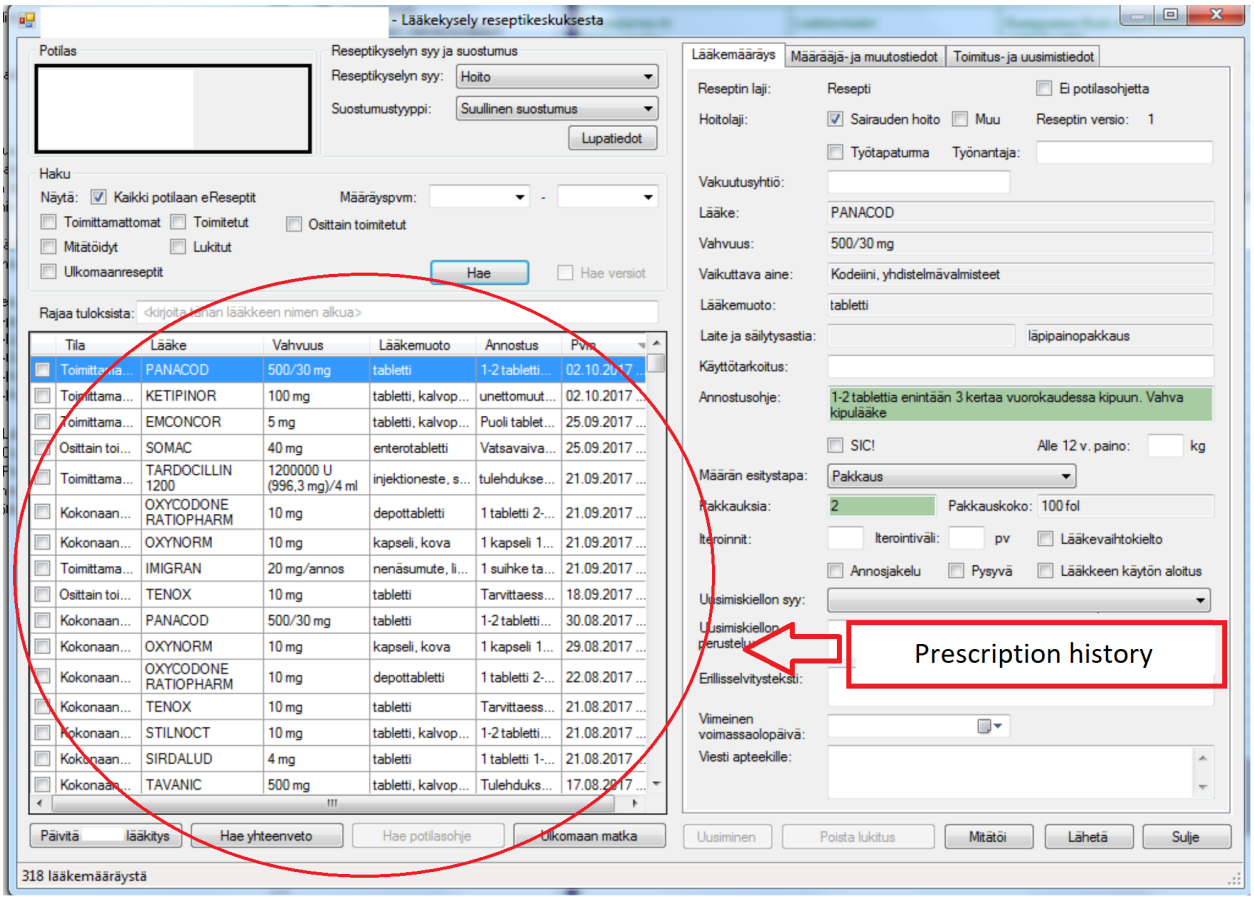

Figure A1: E-Prescribing Technology and Information Integration: Physician's View

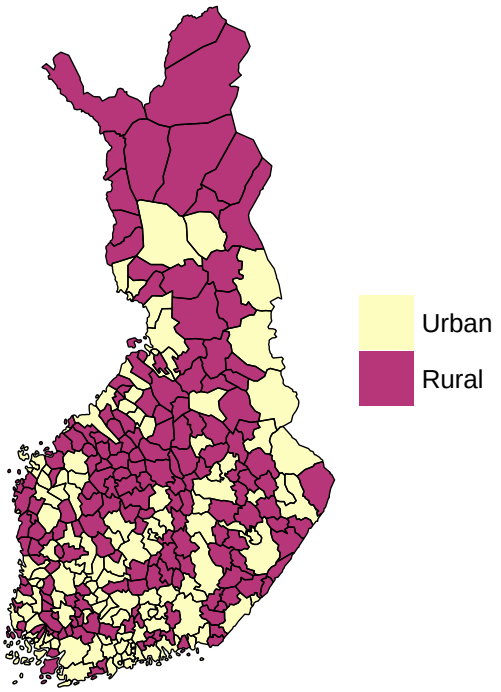

FIGURE A2: Regional Classification

Notes: This figure plots municipality groups (urban/semiurban or rural), according to the classification of Statistics Finland.

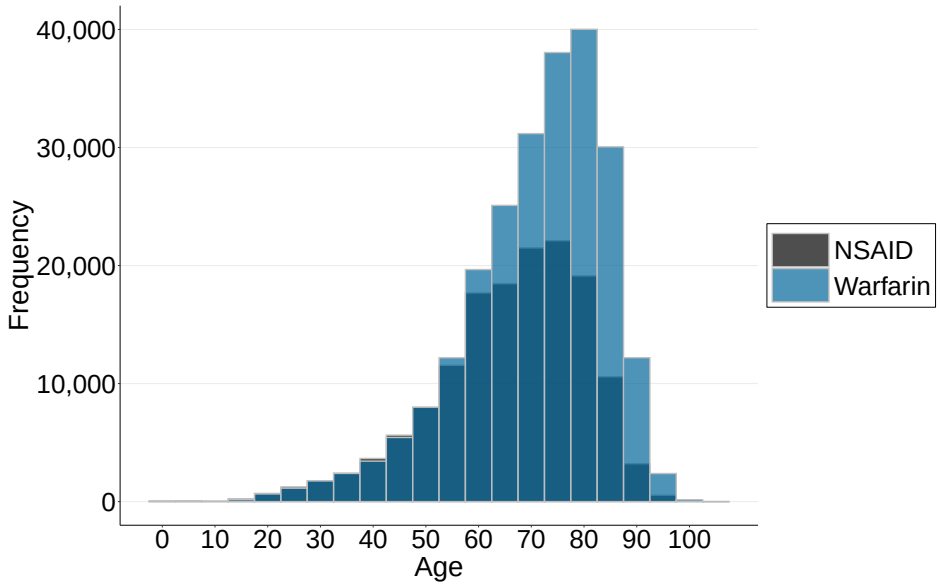

FIGURE A3: Age Profile of Warfarin Patients

Notes: The patient's age is calculated separately for NSAID and warfarin prescriptions from the period of the patient's first prescription for the respective drug in the data.

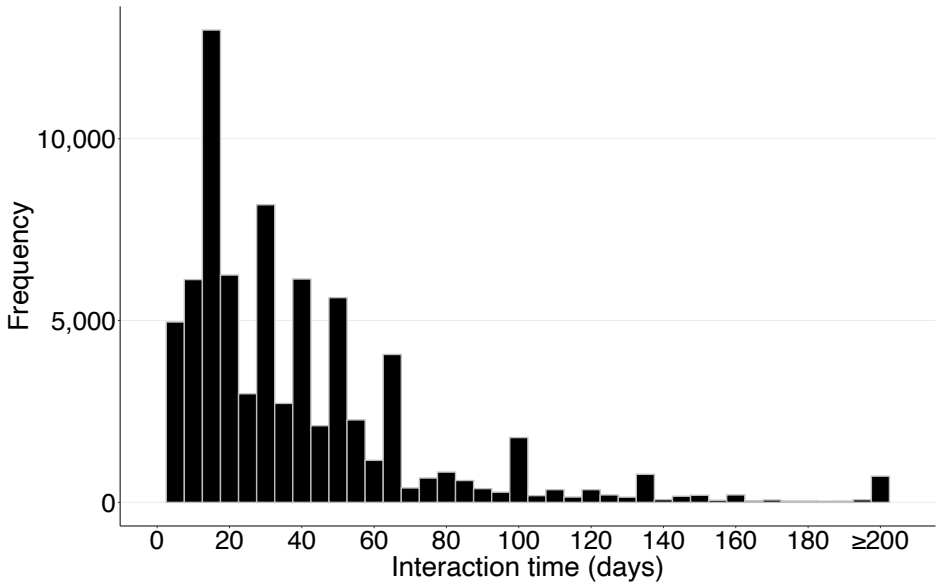

FIGURE A4: Duration of Warfarin-NSAID Interactions

Notes: The plot shows the conditional distribution of the duration of each overlapping warfarin and NSAID prescription, calculated in days. The length of warfarin and NSAID prescriptions is calculated using the number of defined daily doses of each prescription, where one day is assumed to equal one unit of daily dose. Bin width equals 5.

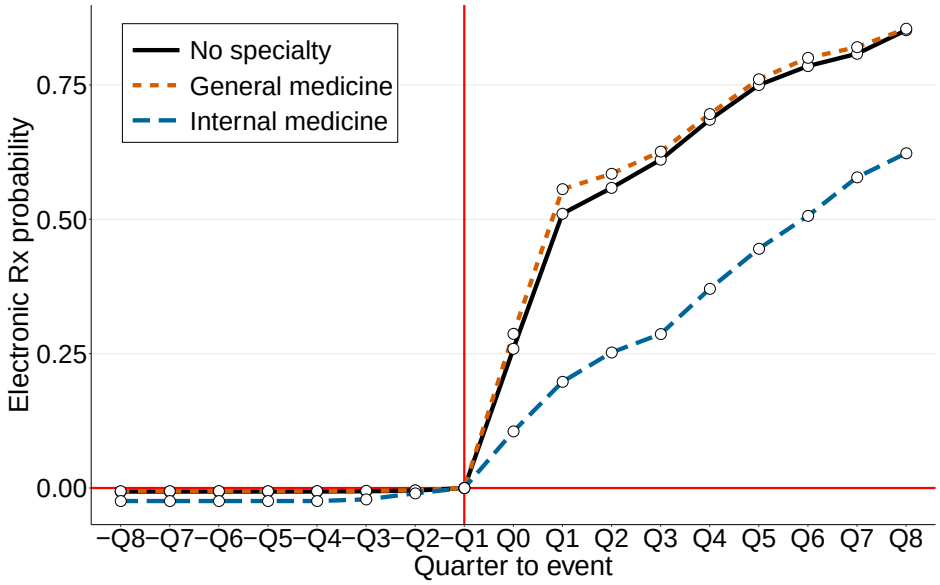

FIGURE A5: Take-up Rate of E-prescriptions, by Physician Speciality

Notes: This figure plots the coefficient estimates from an event study framework using the prescription-level data on warfarin patients. Each line is plotted from a separate regression using data on the corresponding physician specializations. The outcome is a dummy variable that equals one if the prescription is an e-prescription.

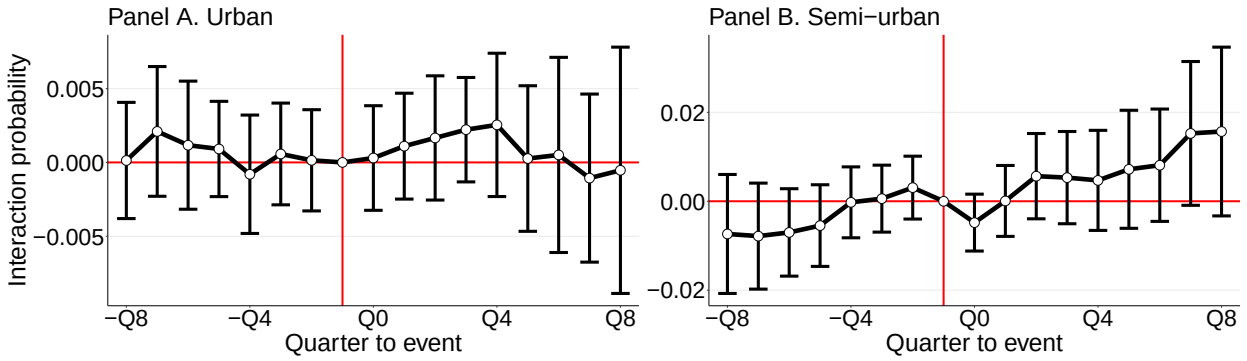

FIGURE A6: Probability of Warfarin-NSAID Interaction in Urban and Semi-Urban Municipalities

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data on warfarin patients. The outcome is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. The omitted period is $-Q1$ and thus the coefficient estimates are relative to this period. The controls include municipality fixed effects, time fixed effects, age and age squared. Panel A plots the results for the urban municipalities, and Panel B plots for semi-urban municipalities, according to the classification by Statistics Finland. The standard errors are clustered at the municipality level.

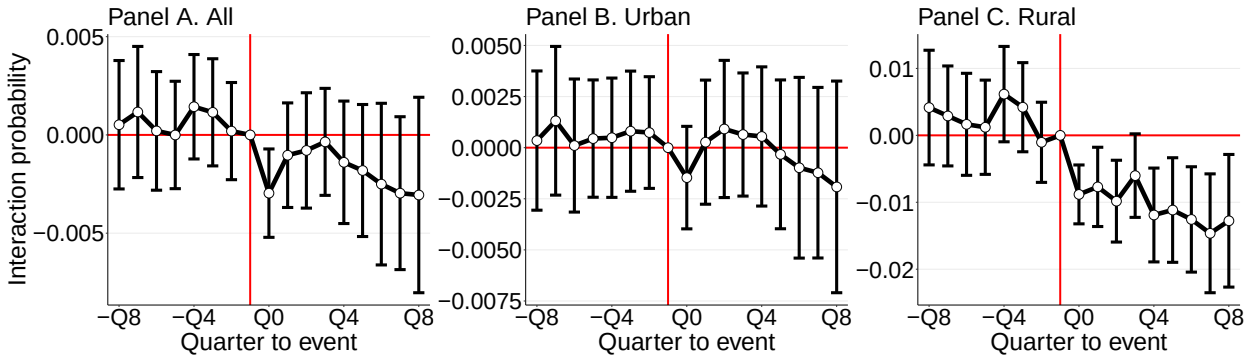

FIGURE A7: Probability of Warfarin-NSAID Interaction With Different Prescribing Physicians, by Municipality Group

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data on warfarin patients. The outcome is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription and the interacting prescriptions are written by different physicians. Panel A plots the results for the whole sample of municipalities, Panel B plots for urban and semi-urban municipalities, and Panel C plots for rural municipalities, according to the classification by Statistics Finland. See Figure 5 for more information on the specification of the model.

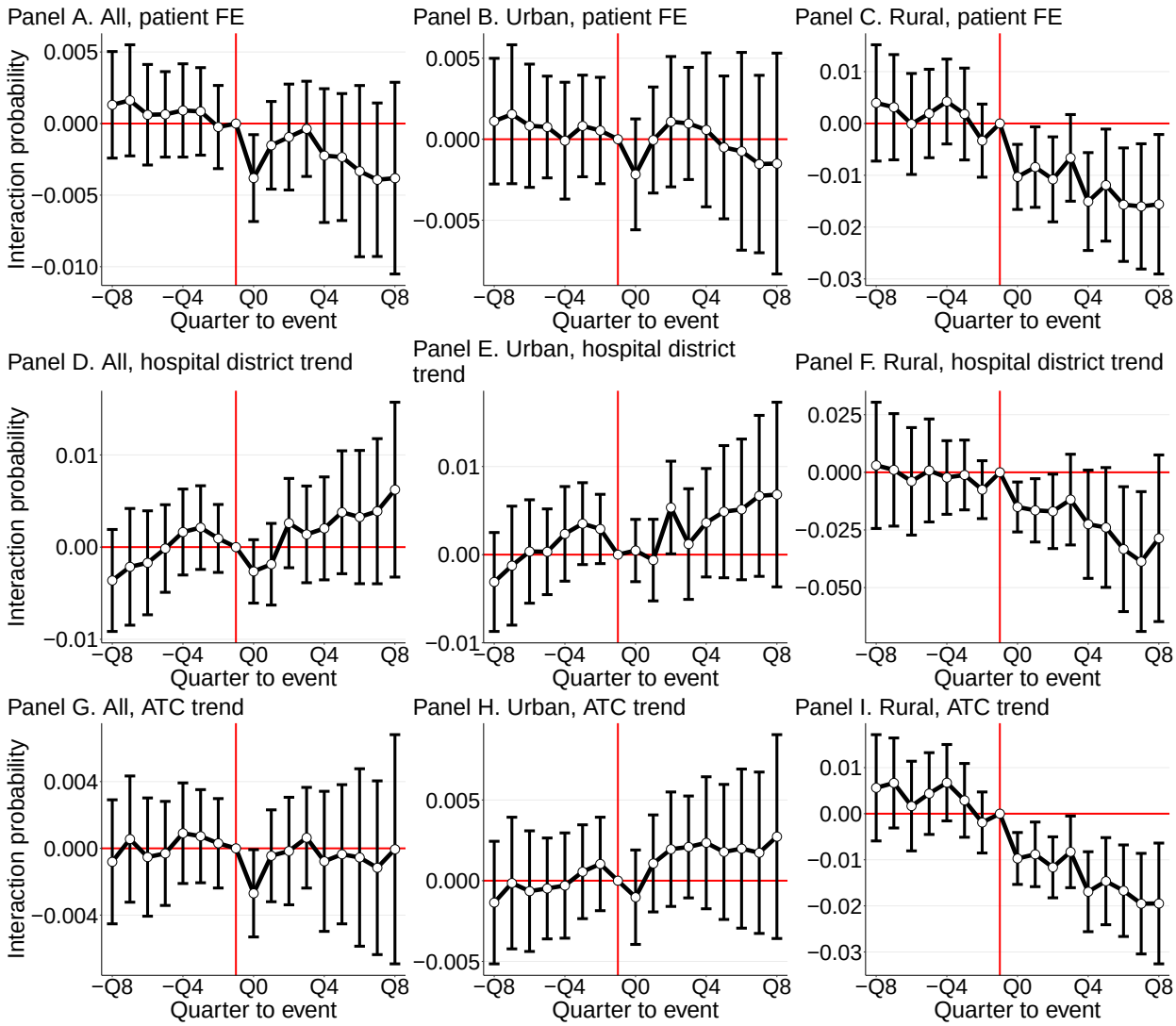

FIGURE A8: Probability of Interaction, Additional Robustness Checks to Baseline Results Part 1

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data on warfarin patients. The outcome is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. The omitted period is $-Q1$ and thus the coefficient estimates are relative to this period. The controls include municipality fixed effects, time fixed effects, age and age squared. Panels A, B, and C replace municipality fixed effects with patient fixed effects. Panels E, F, and G add interactions of hospital district and time fixed effects to the regressions. Panels G, H, and I plot the interaction probability with additional ATC-code specific linear time-trends added to the regressions. The first, second and third column of the panels plot the results using data on all municipalities, urban and semi-urban municipalities, and rural municipalities, respectively, according to the classification by Statistics Finland. The standard errors are clustered at the municipality level.

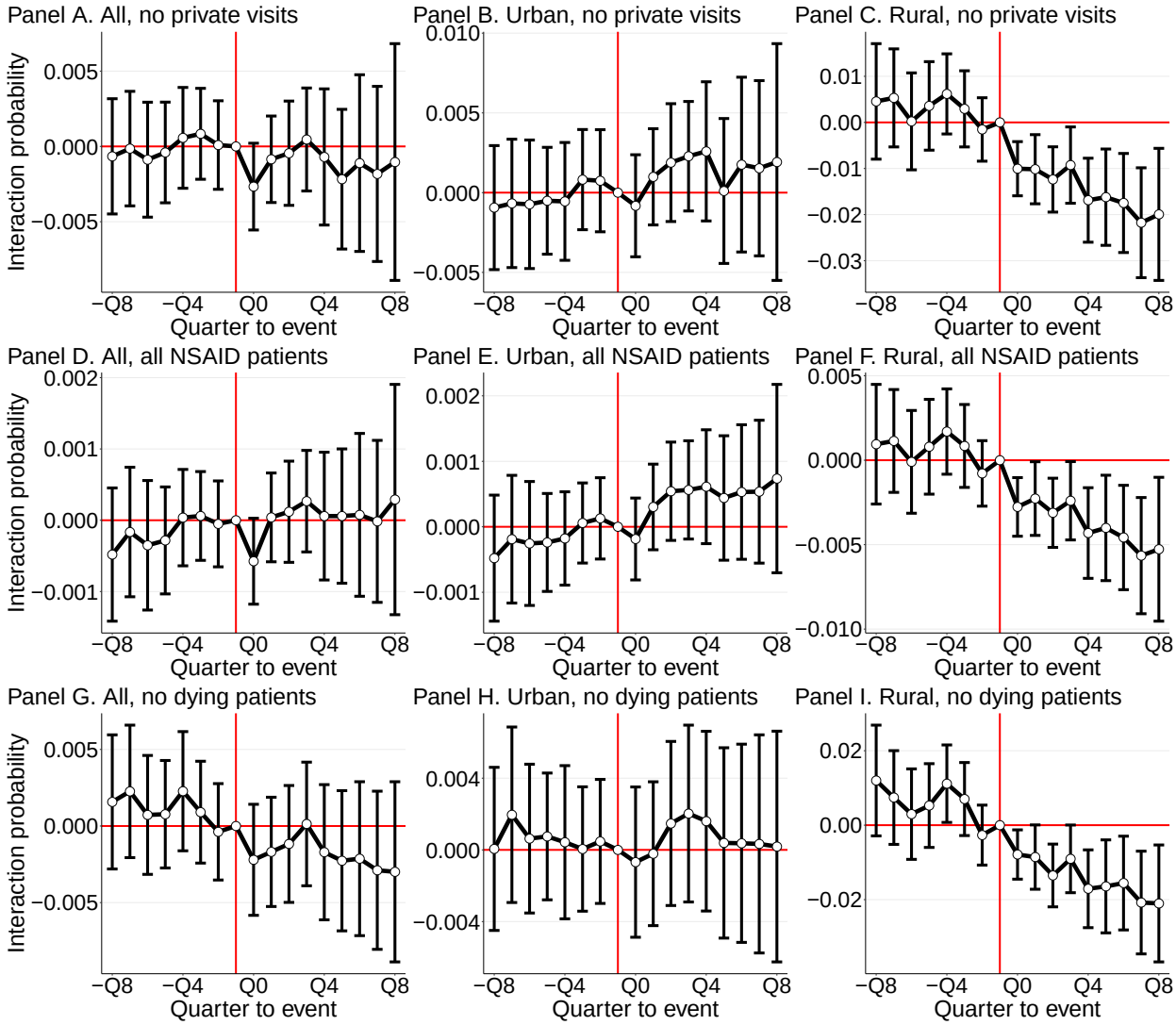

FIGURE A9: Probability of Interaction, Additional Robustness Checks to Baseline Results Part 2

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data on warfarin patients. The outcome is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. The omitted period is $-Q1$ and thus the coefficient estimates are relative to this period. The controls include municipality fixed effects, time trend fixed effects, age and age squared. Panels A, B, and C exclude all observations where the visit was to a private physician. Panels D, E, and F include all patients that have an NSAID prescription and that may not have a warfarin prescription during the periods in the data. Panels G, H, and I, exclude all patients that died during the periods in the data. The first, second and third column of the panels plot the results using data on all municipalities, urban and semi-urban municipalities, and rural municipalities, respectively, according to the classification by Statistics Finland. The standard errors are clustered at the municipality level.

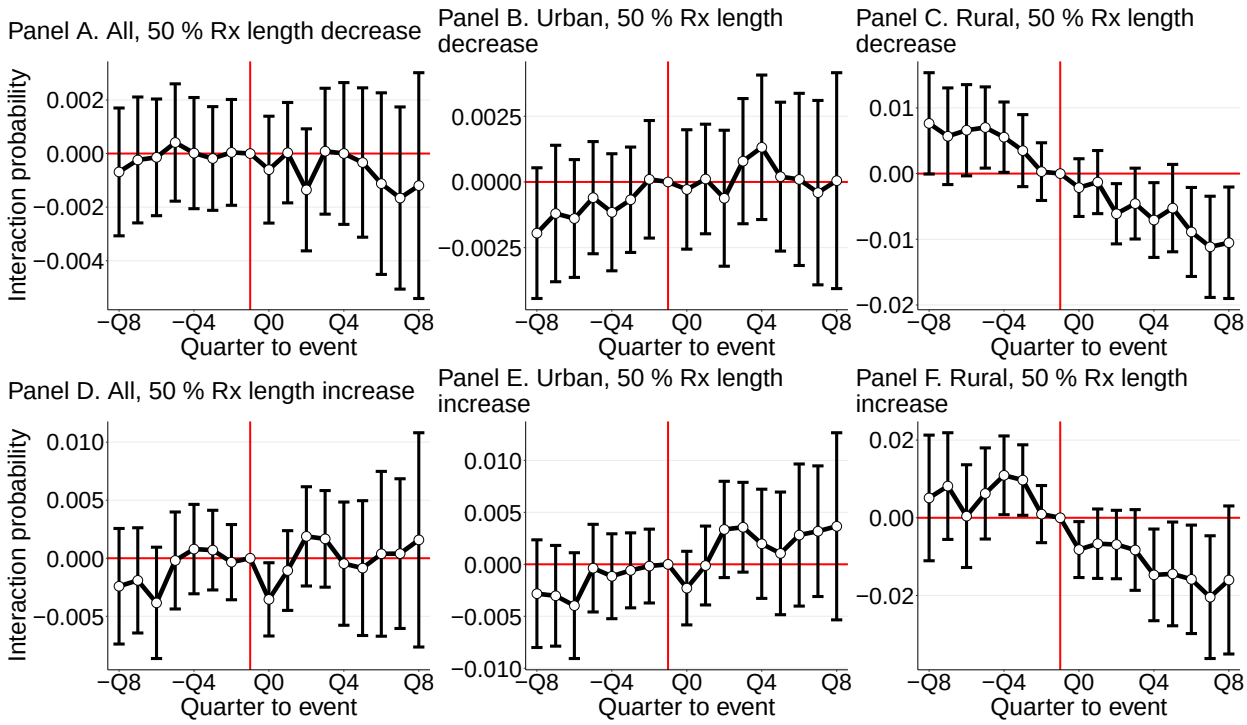

FIGURE A10: Sensitivity Test: Probability of Interaction, 50 Percent Reduction and Increase in Prescription Length

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data on warfarin patients where the amount of defined daily doses in prescriptions has decreased by 50 percent. The outcome is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. The omitted period is $-Q1$ and thus the coefficient estimates are relative to this period. The controls include municipality fixed effects, time fixed effects, age and age squared. Panel A plots the results for the whole sample of municipalities, panel B plots for urban and semi-urban municipalities, and panel C plots for rural municipalities, according to the classification by Statistics Finland. The standard errors are clustered at the municipality level.

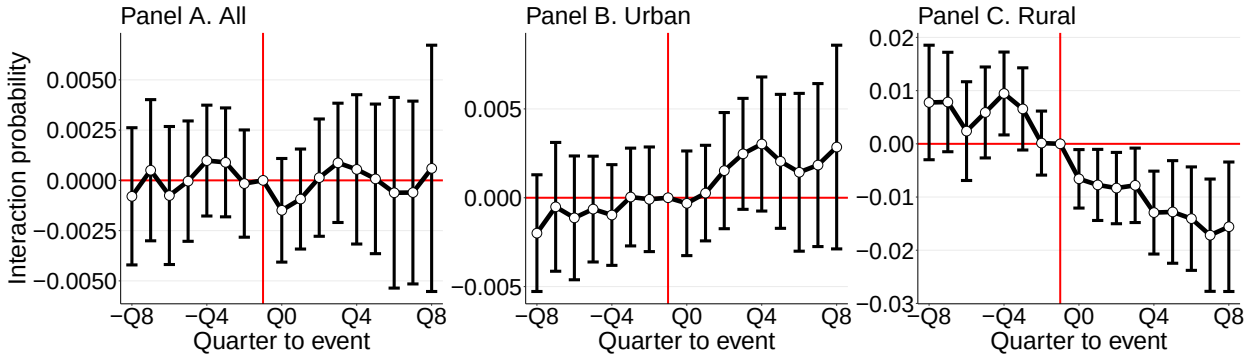

FIGURE A11: Sensitivity Test: Probability of Interaction, Interactions Under 10 Days and Over 100 Days Excluded

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data on warfarin patients where prescriptions that interact under 10 days are dropped in Panels A, B, and C, and prescriptions that interact over 100 days are dropped in Panels D, E, and F. The outcome is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. The omitted period is $-Q1$ and thus the coefficient estimates are relative to this period. The controls include municipality fixed effects, time fixed effects, age and age squared. The urban/semi-urban and rural classification is from Statistics Finland. The standard errors are clustered at the municipality level.

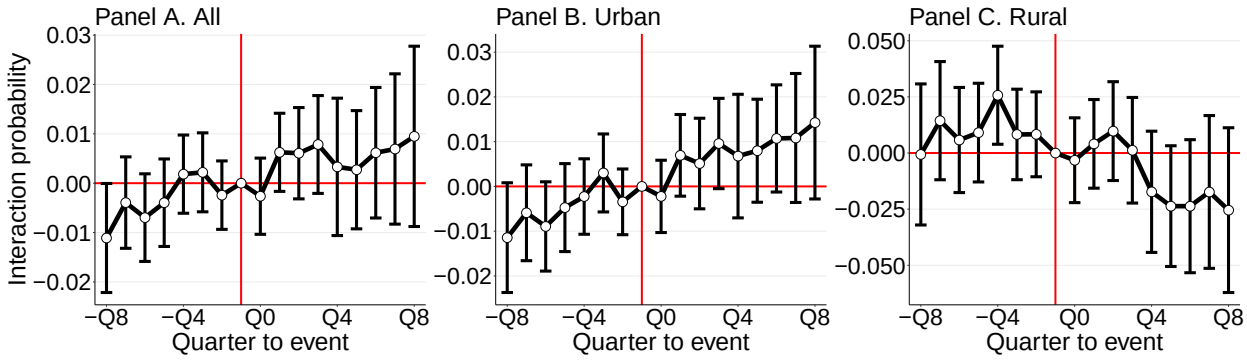

FIGURE A12: Probability of Warfarin-NSAID Interaction With Average Prescribing Intervals, by Municipality Group

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data on warfarin patients. Instead of defined daily doses, the prescription length is proxied by the patient and prescription type (warfarin or NSAID) specific average prescribing intervals. Patients that do not have at least two warfarin or NSAID prescriptions are dropped. The maximum prescription length is capped at 180 days. The outcome is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. The omitted period is $-Q1$ and thus the coefficient estimates are relative to this period. The controls include municipality fixed effects, time fixed effects, age and age squared. The urban/semi-urban and rural classification is from Statistics Finland. The standard errors are clustered at the municipality level.

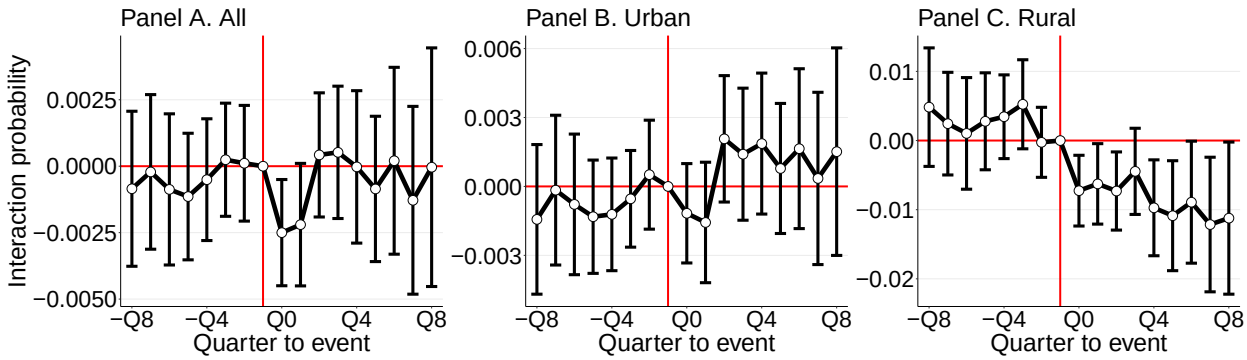

FIGURE A13: Probability of One-Way Warfarin-NSAID Interaction, By Municipality Group

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data on warfarin patients. The outcome is a dummy variable that equals one if an NSAID prescription interacts with another warfarin prescription. The omitted period is $-Q1$ and thus the coefficient estimates are relative to this period. The controls include municipality fixed effects, time fixed effects, age and age squared. Panel A plots the results for the whole sample of municipalities, Panel B plots for urban and semi-urban municipalities, and Panel C plots for rural municipalities, according to the classification by Statistics Finland. The standard errors are clustered at the municipality level.

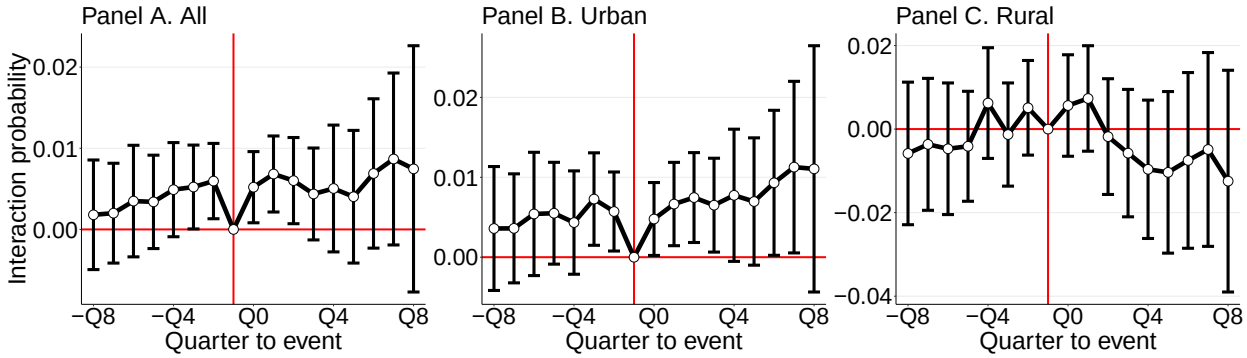

FIGURE A14: Placebo: Probability of Warfarin-Benzodiazepine Interaction, by Municipality Group

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data on warfarin patients. The outcome is a dummy variable that equals one if a warfarin (benzodiazepine) prescription interacts with a benzodiazepine (warfarin) prescription. See Figure 5 for more information on the specification of the model.

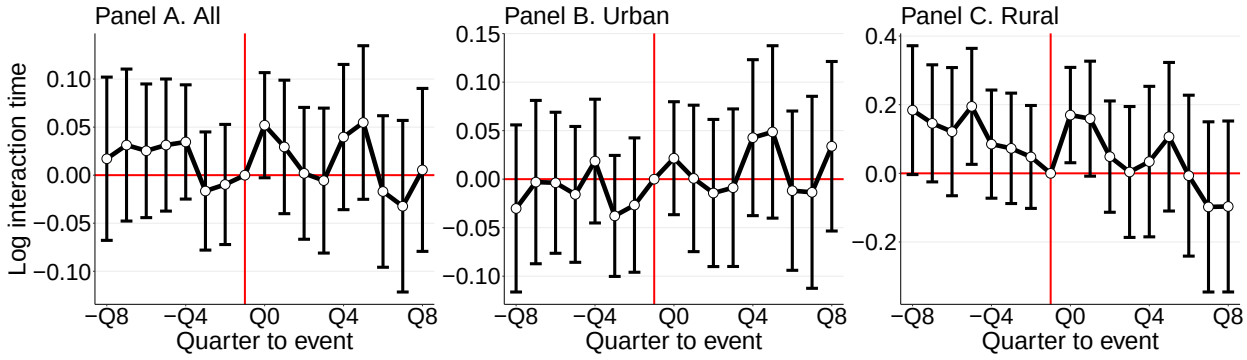

FIGURE A15: Duration of Warfarin-NSAID Interaction, by Municipality Group

Notes: These figures plot the coefficient estimates from an event study framework using the prescription-level data on interacting (wafarin and NSAID) prescriptions for warfarin patients. The outcome is the log number of days that the prescription interacts with another prescription. See Figure 5 for more information on the specification of the model.

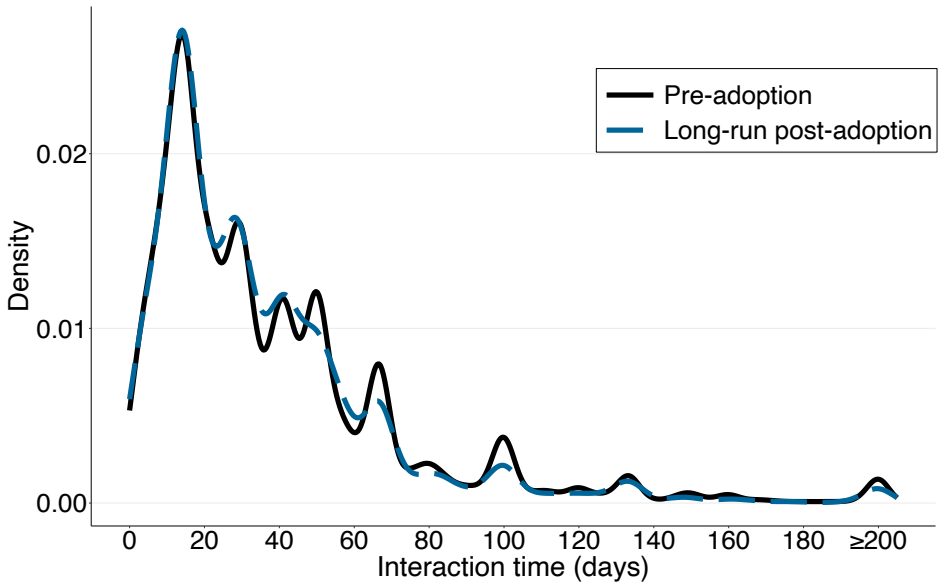

FIGURE A16: Density of Duration of Warfarin-NSAID Interaction

Notes: The figure plots the conditional density of the duration of each interacting (warfarin or NSAID) prescription, calculated in days, separately for the pre-adoption period (before 2010) and the long-run post-adoption period (at least one year after adoption). The length of warfarin and NSAID prescriptions are calculated using the number of defined daily doses of each prescription, where one day is assumed to equal to one unit of daily dose.

A.3 Tables

Table A1: Prescription Shares by Physician Speciality for Pre-Adoption Period 2007–2009

	All municipalities		Urban		Rural	
	N	Share	N	Share	N	Share
Warfarin	357,114	0.74	284,006	0.74	73,108	0.72
Unspecialized	171,165	0.48	130,632	0.46	40,533	0.55
General medicine	76,014	0.21	60,237	0.21	15,777	0.22
Internal medicine	22,346	0.06	19,183	0.07	3,163	0.04
NSAID	127,133	0.26	98,817	0.26	28,316	0.28
Unspecialized	59,796	0.47	44,758	0.45	15,038	0.53
General medicine	24,272	0.19	18,361	0.19	5,911	0.21
Internal medicine	4,005	0.03	3,381	0.03	624	0.02
Interacting Rx	34,970	0.07	26,811	0.07	8,159	0.08
Unspecialized	16,178	0.46	11,987	0.45	4,191	0.51
General medicine	6,760	0.19	4,943	0.18	1,817	0.22
Internal medicine	1,999	0.06	1,691	0.06	308	0.04

Notes: The numbers are based on patients with at least one warfarin prescription in the period of 2007–2009.

TABLE A2: Effects of E-prescribing on Warfarin-NSAID Interaction, by Municipalities' Pre-adoption Interaction Rate

	1st quartile	2nd quartile	3rd quartile	4th quartile
	(1)	(2)	(3)	(4)
Short-run	−0.001	−0.000	−0.005**	−0.011***
	(0.002)	(0.002)	(0.002)	(0.004)
Long-run	−0.001	−0.002	−0.009***	−0.015**
	(0.003)	(0.003)	(0.003)	(0.006)
Mean outcome	0.035	0.042	0.049	0.065
Observations	395,028	594,113	505,052	195,313

Notes: This table reports the coefficients from Difference-in-Differences regressions using the prescription-level data on warfarin patients. The quartiles are based on the municipalities' mean warfarin-NSAID interaction probabilites during the pre-adoption period of e-prescribing of 2007–2009. The outcome is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. Each column is estimated from a separate regression. "Short-run" refers to the first three quarters after adoption, and "Long-run" refers to all subsequent quarters. All regressions control for time and municipality fixed effects, patient's age, and square of age. The standard errors are clustered at the municipality level.

TABLE A3: Effects of E-prescribing on Warfarin-NSAID Interaction With Average Prescribing Intervals, by Municipality Group

	All municipalities	Urban	Rural
	(1)	(2)	(3)
Short-run	0.002	0.003	−0.006
	(0.004)	(0.004)	(0.008)
Long-run	−0.001	0.004	−0.031***
	(0.007)	(0.007)	(0.011)
Mean outcome	0.083	0.080	0.092
Observations	444,111	355,071	89,040

Notes: This table reports the coefficients from Difference-in-Differences regressions using the prescription-level data on warfarin patients. Instead of defined daily doses, the prescription length is proxied by the patient and prescription type (warfarin or NSAID) specific average prescribing intervals. Patients that do not have at least two warfarin or NSAID prescriptions are dropped. The maximum prescription length is capped at 180 days. The outcome is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. "Short-run" refers to the first year after adoption, and "Long-run" refers to all subsequent periods. Each column is estimated from a separate regression. All specifications include municipality fixed effects, time fixed effects, and age and age squared. The urban/semi-urban and rural classification in the columns is from Statistics Finland. The standard errors are clustered at the municipality level.

TABLE A4: Effects of E-prescribing on Warfarin-NSAID Interaction, by Municipality Group and Physician Specialty

	All municipalities (1)	Urban (2)	Rural (3)
Panel A. Unspecialized			
Short-run	−0.002	0.000	−0.012***
	(0.001)	(0.001)	(0.003)
Long-run	−0.004*	−0.001	−0.018***
	(0.002)	(0.002)	(0.005)
Mean outcome	0.043	0.042	0.047
Observations	917,214	709,548	207,666
Panel B. General medicine			
Short-run	−0.003	−0.002	−0.008
	(0.002)	(0.002)	(0.006)
Long-run	−0.004	−0.002	−0.010
	(0.003)	(0.003)	(0.007)
Mean outcome	0.040	0.038	0.049
Observations	337,702	266,726	70,976
Panel C. Internal medicine			
Short-run	−0.001	0.001	−0.023
	(0.004)	(0.005)	(0.015)
Long-run	0.001	0.004	−0.030
	(0.007)	(0.007)	(0.024)
Mean outcome	0.056	0.055	0.063
Observations	73,862	63,477	10,385

Notes: This table reports the coefficients from Difference-in-Differences regressions using the prescription-level data on warfarin patients. The outcome is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. "Short-run" refers to the first year after adoption, and "Long-run" refers to all subsequent periods. Each panel-column combination is estimated from a separate regression. All specifications include municipality fixed effects, time fixed effects, and age and age squared. Panel A uses prescriptions written by physicians without any specialization, Panel B by physicians specialized in general medicine, and Panel C by physicians specialized in internal medicine. The urban/semi-urban and rural classification in the columns is from Statistics Finland. The standard errors are clustered at the municipality level.

TABLE A5: Effects of E-prescribing on Warfarin-NSAID Interaction, Different Versus Same prescribing Physician

	All municipalities (1)	Urban (2)	Rural (3)
Short-run × same physician	0.000	0.001	−0.002
	(0.000)	(0.000)	(0.002)
Long-run × same physician	0.000	0.001	−0.004**
	(0.001)	(0.001)	(0.002)
Short-run × different physician	−0.002**	−0.001	−0.008***
	(0.001)	(0.001)	(0.003)
Long-run × different physician	−0.003**	−0.003*	−0.009**
	(0.001)	(0.002)	(0.004)

Notes: This table reports the coefficients from Difference-in-Differences regressions using the prescription-level data on warfarin patients. The outcome is a dummy variable that equals one if a warfarin (NSAID) prescription interacts with another NSAID (warfarin) prescription. "Short-run × same physician" and "Long-run × same physician" refer to the interaction between drug interactions where the prescribing physician is the same as the previous prescribing physician and, respectively, the first year after adoption and all subsequent periods after adoption. "Short-run × different physician" and "Long-run × different physician" refer to the same interactions but when the interacting prescription is written by a different physician than the prescriber of the underlying prescription. The coefficients for different physician are estimated relative to the coefficients of same physician, meaning that the total effect for different physician is the sum of coefficients of same physician and different physician. Each column is estimated from a separate regression. All specifications include municipality fixed effects, time fixed effects, and age and age squared. The urban/semi-urban and rural classification in the columns is from Statistics Finland. The standard errors are clustered at the municipality level.

TABLE A6: Intensive and Extensive Margins of Warfarin Prescriptions, by Municipality Group

	All municipalities (1)	Urban (2)	Rural (3)
Panel A. Intensive margin: Log warfarin DDDs			
Short-run	0.018**	0.016*	0.029**
	(0.008)	(0.009)	(0.012)
Long-run	0.038***	0.035**	0.056**
	(0.013)	(0.014)	(0.023)
Mean outcome	140.086	140.548	138.234
Observations	1,050,380	840,392	209,988
Panel B. Extensive margin: Log warfarin prescriptions			
Short-run	0.003***	0.003***	0.006***
	(0.001)	(0.001)	(0.002)
Long-run	0.002*	0.001	0.005
	(0.001)	(0.001)	(0.003)
Mean outcome	3.103	3.102	3.107
Observations	7,422,752	5,952,632	1,470,120

Notes: This table reports the coefficients from Difference-in-Differences regressions using the prescription-level data in Panel A and patient-quarter-level balanced data in panel B on warfarin patients. In Panel A the outcome is the log number of defined daily doses of warfarin prescriptions, and the data include only warfarin prescriptions. In Panel B, the outcome is the log number of warfarin prescriptions+1 to adjust for zeros in the balanced panel. "Short-run" refers to the first year after adoption, and "Long-run" refers to all subsequent periods. Each panel-column combination is estimated from a separate regression. All specifications include municipality fixed effects, time fixed effects, and age and age squared. The urban/semi-urban and rural classification in the columns is from Statistics Finland. The standard errors are clustered at the municipality level.

TABLE A7: Intensive Margin of Warfarin Prescriptions Without $-Q1$, by Municipality Group

	All municipalities (1)	Urban (2)	Rural (3)
Short-run	0.003	0.002	0.007
	(0.006)	(0.007)	(0.015)
Long-run	0.021*	0.021*	0.030
	(0.011)	(0.012)	(0.025)
Mean outcome	139.921	140.369	138.129
Observations	1,015,591	812,526	203,065

Notes: This table shows the intensive margin results for warfarin prescriptions with the first pre-quarter of e-prescribing, $-Q1$, dropped from the data. See Table A6 for more information on the specification.

TABLE A8: Intensive and Extensive Margins of NSAID Prescriptions, by Municipality Group

	All municipalities	Urban	Rural
	(1)	(2)	(3)
Panel A. Intensive margin: Log NSAID DDDs			
Short-run	0.000	0.003	−0.013
	(0.008)	(0.009)	(0.018)
Long-run	−0.008	0.000	−0.046
	(0.011)	(0.011)	(0.034)
Mean outcome	53.036	52.607	54.677
Observations	639,126	506,806	132,320
Panel B. Extensive margin: Log NSAID prescriptions			
Short-run	0.001	0.001	0.000
	(0.001)	(0.001)	(0.001)
Long-run	0.001	0.001	0.001
	(0.001)	(0.001)	(0.002)
Mean outcome	2.952	2.950	2.963
Observations	7,422,752	5,952,632	1,470,120

Notes: This table reports the coefficients from Difference-in-Differences regressions using the prescription-level data in Panel A and patient-quarter-level balanced data in Panel B on warfarin patients. In Panel A the outcome is the log number of defined daily doses of NSAID prescriptions, and the data include only NSAID prescriptions. In Panel B, the outcome is the log number of NSAID prescriptions+1 to adjust for zeros in the balanced panel. "Short-run" refers to the first year after adoption, and "Long-run" refers to all subsequent periods. Each panel-column combination is estimated from a separate regression. All specifications include municipality fixed effects, time fixed effects, and age and age squared. The urban/semi-urban and rural classification in the columns is from Statistics Finland. The standard errors are clustered at the municipality level.

TABLE A9: Summary Statistics for New Patients in Pre- and Post-Adoption Years

	Urban		Rural	
	Pre-adoption	Post-adoption	Pre-adoption	Post-adoption
Warfarin DDDs per patient	181.008	188.077	176.905	185.715
	(120.254)	(123.949)	(119.651)	(117.267)
Warfarin Rx per patient	1.510	1.482	1.502	1.450
	(0.748)	(0.702)	(0.769)	(0.702)
DDDs in first warfarin Rx	118.017	121.372	119.025	123.918
	(79.547)	(83.033)	(83.252)	(83.256)
NSAID DDDs per patient	18.913	18.244	20.896	19.701
	(51.600)	(51.985)	(56.474)	(56.687)
NSAID Rx per patient	0.390	0.363	0.413	0.363
	(0.815)	(0.799)	(0.899)	(0.809)
DDDs in first NSAID Rx	12.778	12.372	12.952	12.885
	(32.895)	(31.826)	(33.475)	(34.660)
Share of Rx by specialty				
Unspecialized	0.568	0.603	0.631	0.668
	(0.425)	(0.422)	(0.419)	(0.408)
General medicine	0.118	0.126	0.139	0.139
	(0.268)	(0.279)	(0.295)	(0.295)
Internal medicine	0.069	0.070	0.060	0.051
	(0.223)	(0.225)	(0.206)	(0.196)
Age	67.750	68.463	70.206	70.684
	(14.698)	(14.545)	(13.665)	(13.403)
Number of new patients	17,736	17,735	4,176	4,274

Notes: Mean values are taken over per patient values. The standard deviations are in parentheses. The table includes only those patients who have their first warfarin prescription either during the year right before or during the year right after the adoption of e-prescribing. The time of the patient's first warfarin prescription is defined as the first time a warfarin prescription is observed for the patient in the data. The urban/semi-urban and rural classification in the columns is from Statistics Finland.

TABLE A10: Extensive Margin of Warfarin Use and Interactions in Municipality

	All municipalities	Urban	Rural
	(1)	(2)	(3)
Panel A. Log number of new patients			
Short-run	0.007	−0.013	0.019
	(0.023)	(0.025)	(0.034)
Long-run	0.018	−0.001	0.027
	(0.032)	(0.034)	(0.050)
Observations	7,296	2,904	4,392
Adjusted R^2	0.872	0.921	0.572
Panel B. Log number of warfarin prescriptions			
Short-run	0.032**	0.027*	0.033
	(0.016)	(0.015)	(0.025)
Long-run	0.050*	0.034	0.056
	(0.026)	(0.023)	(0.041)
Observations	7,296	2,904	4,392
Adjusted R^2	0.945	0.972	0.827
Panel C. Log number of interactions			
Short-run	−0.054**	0.040	−0.124***
	(0.027)	(0.038)	(0.035)
Long-run	−0.056	0.126*	−0.188***
	(0.044)	(0.069)	(0.055)
Observations	9,728	3,872	5,856
Adjusted R^2	0.727	0.776	0.419

Notes: This table reports the coefficients from Difference-in-Differences regressions using municipality-quarter-level balanced data. In Panel A, the outcome is the log number of new warfarin patients. New patients are defined as those patients that have their first warfarin prescription in a given quarter in the data. In Panel B, the outcome is the log number of overall warfarin prescriptions in the municipality. In Panel C, the outcome is the log number of warfarin-NSAID interactions. In Panels A and B, because of left-censoring, those patients that have their first warfarin prescription in 2007–2009 are dropped and only data from the years 2009–2017 are used in the regressions. "Short-run" refers to the first year after adoption, and "Long-run" refers to all subsequent periods. All regressions include fixed effects for municipality and time trend. All regressions are weighted by the population size in the municipality. The urban/semi-urban and rural classification in the columns is from Statistics Finland. The standard errors are clustered at the municipality level.

Table A11: Effects of E-prescribing on Gastrointestinal Bleeding Diagnosis

	All municipalities	Urban	Rural
	(1)	(2)	(3)
Short-run	0.0003***	0.0002**	0.0005*
	(0.0001)	(0.0001)	(0.0003)
Long-run	0.0004***	0.0003**	0.0007**
	(0.0001)	(0.0001)	(0.0003)
Mean outcome	0.0020	0.0020	0.0021
Observations	7,361,632	5,920,658	1,440,974

Notes: This table reports the coefficient estimates from Difference-in-Differences regressions using patient-quarter-level balanced data from warfarin patients. The outcome is a dummy variable that equals to one if the patient has a gastrointestinal hemorrhage diagnosis in specialized health care in a given period. All regressions include municipality fixed effects, time fixed effects, age and age squared. The urban/semi-urban and rural classification in the columns is from Statistics Finland. The standard errors are clustered at the municipality level.

B Early Versus Later Treated Municipalities

Goodman-Bacon (2018) shows that, in the case of a staggered adoption of policy where the treatment occurs at different times across units, the two-way fixed effects DiD estimator is a weighted average of all possible individual two-period/two-group DiD estimators in the data. In the case of dynamic treatment effects, this could induce negative weights to later-treated groups as these units are compared to already-treated units.

We follow Goodman-Bacon (2018) to examine the potential bias in the overall DiD estimates on the quality of prescribing from the later-treated municipalities. Specifically, we perform an explicit decomposition of the summed weights and average DiD estimates for early- versus later-treated municipalities and later- versus early-treated municipalities. The shortcoming of this approach is that as such it does not allow us to partition the treatment effect into short- and long-run effects as in our main analysis.[28] To reduce the computational burden, as we have to compute all two-by-two DiD estimates separately for each municipality group (urban and rural) and adoption time, we use aggregated municipality-quarter level data and the log number of warfarin-NSAID interactions as an outcome. Thus, the estimates are not fully comparable to our baseline estimates obtained from the prescription-level data, but the results should give an idea of whether using early-treated

[28] Another shortcoming is that the approach does not allow for weights in the regressions when doing the full decomposition.

municipalities as a control group is worrisome in our setting.

The results for the municipality-level DiD estimates and the decompositions beneath them are shown in Tables A12. We find that the number of warfarin-NSAID interactions decreases by 14 percent in rural municipalities and there is no statistically significant effect in urban municipalities. Based on the decompositions, we conclude that negative weighting is not a major issue, especially in rural municipalities. Albeit not fully comparable, our conclusions regarding the effects of e-prescribing based on the aggregated data remain fairly similar to those drawn from our baseline estimates using the prescription-level data.

TABLE A12: Goodman-Bacon Analysis on the Number of Interactions in Municipality

	All municipalities (1)	Urban (2)	Rural (3)
DiD	-0.066^{**}	0.031	-0.140^{***}
	(0.029)	(0.034)	(0.042)
Observations	9,728	3,872	5,856
Adjusted R^2	0.78	0.823	0.502
Earlier vs. Later (Weight × DiD)	0.693×-0.064	0.686×0.054	0.698×-0.149
Later vs. Earlier (Weight × DiD)	0.307×-0.071	0.314×-0.019	0.302×-0.119

Notes: This table reports the coefficients from Difference-in-Differences regressions using municipality-quarter-level balanced data. The outcome is the log number of interactions in the municipality. "DiD" is the binary variable for the treatment effect and it gets the value of one after the municipality gets treated. "Earlier vs. Later" and "Later vs. Earlier" show the summed weights and the average DiD coefficients from all two-by-two decompositions of earlier and later adopting municipalities, respectively. All regressions include municipality fixed effects and time fixed effects. The urban/semi-urban and rural classification in the columns is from Statistics Finland. The standard errors are clustered at the municipality level.