Healthcare Consequences of Drug Quality Failures: Evidence from the 2012 NECC Outbreak

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Abstract

This paper studies the healthcare consequences of patient exposure to drugs with severe quality failures. I examine the shipment of contaminated sterile injectable drugs produced by the New England Compounding Center (NECC) in 2012, which triggered the largest known outbreak of disease due to drug contamination in U.S. history. Using administrative Medicare claims and NECC invoice records, I implement a difference-in-differences design to compare the outcomes of injections administered by healthcare providers that did and did not receive the implicated drugs. Potential patient exposure to the implicated drugs caused substantial changes in downstream care, including a 72 percent increase in hospital-based and post-acute care and a 25 percent increase in total healthcare spending in the 180 days after injection. The effects are consistent with both curative treatment of contamination-related illness and precautionary responses to exposure risk. I also find that changes in patterns of care emerged sharply when public health authorities announced the outbreak and issued treatment guidance, highlighting the role of centralized public health communication in raising awareness of drug quality failures and coordinating the downstream clinical responses to them.

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1 Introduction

Preventing product quality failures is a central concern in pharmaceutical markets (Conti and Wosińska, 2025; Hemel and Ouellette, 2023; Philipson and Sun, 2008; Peltzman, 1973). Regulatory institutions such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) devote substantial resources to this end: for example, they establish and enforce drug manufacturing standards, conduct on-site inspections, request recalls, and carry out laboratory testing of drug samples (Woodcock and Wosinska, 2013). Despite the importance of preventing patient exposure to unsafe drugs, there is limited empirical evidence on the downstream consequences of quality failures due to the rare nature of these high-stakes events.

This paper provides novel causal evidence on these consequences by leveraging quasi-experimental variation in potential patient exposure to contaminated steroid injections produced by the New England Compounding Center (NECC) in 2012, which sparked the largest known outbreak of infections due to drug contamination in U.S. history (Smith et al., 2013). The outbreak offers a useful empirical setting for several reasons. First, the quality failure—fungal contamination—threatened severe central nervous system infection because the implicated drug was a sterile injectable commonly administered near the spine, bypassing many of the body's natural defenses against impurities. Second, the incident provides a well-defined empirical structure. NECC invoice records identify the healthcare providers that received the implicated drugs during the known four-month contamination period, and public health communications document how providers were advised to respond to contamination risk. Third, the setting is one in which drug quality failures are especially salient because NECC belonged to a group of large-scale drug compounding firms that have attracted ongoing regulatory scrutiny due to concerns about mass production outside of FDA manufacturing standards (Watson et al., 2021; National Academies of Sciences, Engineering, and Medicine et al., 2020; Gottlieb, 2018; Woodcock and Dohm, 2017).

I complement existing research on the NECC outbreak, which documents public health investigations that linked 753 infections and 64 deaths to the contaminated drugs (Kauffman and Malani, 2016; Smith et al., 2015, 2013; Kauffman et al., 2013; Kainer et al., 2012), by examining the broader healthcare consequences of patient exposure to contamination risk. Even when the most severe outcome of mortality is averted, curative treatment of contamination-related illness and precautionary care may lead patients to undergo urgent evaluations, diagnostic testing, treatment, hospitalization, and post-acute care. While these clinical responses may enhance welfare conditional on exposure, they also serve as observable markers of excess patient burdens, reflecting additional healthcare utilization and spending relative to the counterfactual world absent the quality failure. I study these broader burdens by quantifying the downstream clinical responses to the NECC outbreak and estimating the causal effects of potential patient exposure on compre-

hensive healthcare outcomes.

To do so, I link NECC invoice records to a 20% sample of administrative Medicare claims. The invoice records identify the healthcare providers that received implicated NECC products, while the claims data identify spinal methylprednisolone acetate (MPA) injections, the procedure most closely associated with the outbreak (Smith et al., 2013). I classify injections as belonging to the treatment group if they were performed by healthcare providers that received implicated NECC drugs and as belonging to the control group if they were performed by other providers. A difference-in-differences estimation strategy is then used to compare patient outcomes in the 180-day period after injection across treated and control injections that were administered before, during, and after the circulation of contaminated NECC drugs. The key identifying variation comes from the fact that the contaminated drugs could only have been administered to patients who received injections from treatment group providers during the four-month window while those drugs were in circulation. Since Medicare claims cannot verify the administration of an implicated NECC drug at a given injection, I interpret the estimates as capturing the reduced-form impacts of potential patient exposure to drug contamination, which embed both the effects of contamination-related illness and differential precautionary responses among treatment group providers as the outbreak unfolded.[1]

This empirical design yields three main findings. First, potential exposure to the implicated NECC drugs led to substantial changes in downstream patient care. Patients who received injections from treatment group providers during the contamination period were 6.1 percentage points more likely to receive an outbreak-related infection diagnosis, as well as more likely to undergo diagnostic tests and receive prescription drugs recommended by public health guidance. They also had additional physician evaluation and management events and received fewer follow-on spinal MPA injections relative to controls.

Although I find no evidence of excess mortality, potentially-exposed patients experienced 4.2 additional unhealthy days, a composite measure capturing mortality and utilization of hospital-based care, post-acute care, and other non-routine care in the 180-day period after injection. This increase in high-intensity healthcare utilization, which is equal to 72 percent of the baseline mean, was primarily driven by inpatient hospitalizations, emergency department visits, skilled nursing facility care, and home health agency visits. Together, these changes translated to a $2,551 rise in total post-injection healthcare spending, equal to 25 percent of the baseline mean, which was borne primarily by Medicare but also reflected higher patient out-of-pocket costs.[2] Notably, the

[1]Though precautionary clinical responses among control group healthcare providers, who did not receive the implicated NECC MPA drugs, may also be part of the outbreak's aggregate downstream consequences, such responses are beyond the scope of this study.

[2]Extensive margin analyses are consistent with these effects being driven by differential curative and precautionary care across treatment and control healthcare providers, as opposed to changes in the underlying composition of

estimated effects are attenuated but remain statistically significant among injections that were not followed by an outbreak-related infection diagnosis, suggesting that the main estimates are not explained solely by the treatment of contamination-related illness, but also reflect precautionary responses by providers and patients.[3]

Second, the timing of clinical responses to the outbreak is consistent with public health communication playing a key role as an information shock that alerted healthcare providers to contamination risk. Drug contamination creates an incomplete information problem: even as patient complications arise, providers may struggle to isolate the cause due to non-specific symptoms or the presence of contemporaneous medical care (Scott Morton and Kyle, 2011). In the case of the NECC outbreak, my results suggest that routine provider surveillance alone did not generate widespread recognition of the contamination risk. Estimated effects on contamination-related diagnoses, diagnostic testing, and unhealthy days were small and statistically insignificant during the four-month period while the implicated NECC drugs were being administered but prior to mobilization of the public health response. Each of these measures then rose sharply precisely in the month when public health authorities announced the outbreak and issued clinical guidance.

Third, I find little evidence that contamination-related care was extended to patients who received injections during the post-contamination period, despite high salience of the outbreak at this time due to the active public health response and ongoing treatment of patients who received injections during the contamination window. Aside from physician evaluation and management events, which remain elevated among injections administered in the post-contamination period, I find that other changes in contamination-related care dissipated. This pattern suggests that providers closely followed public health guidelines by targeting clinical responses to patients potentially exposed to NECC drugs, rather than applying broad changes in practice styles for subsequent injections.

Taken together, my findings show that potential patient exposure to drugs implicated in the NECC outbreak generated substantial downstream clinical responses as the healthcare system mobilized to manage contamination risk. Whether due to treatment of contamination-related illness or precautionary care to mitigate potential harm, these responses provide an observable measure of excess healthcare burden caused by the upstream drug quality failure. The 25 percent increase in post-injection healthcare spending quantifies the additional resources entailed by the clinical response, and also shows that quality failures impose financial costs on patients and payers such as Medicare. Additionally, the results highlight that the consequences of contamination

patients receiving spinal MPA injections due to the outbreak.

[3]Outbreak-related infection diagnoses in claims data may be imperfect markers of true illness because care may have been provided under a working diagnosis. Conversely, patients without recorded outbreak-related infection diagnoses are less likely to have experienced clinically recognized illness from exposure, though undiagnosed illness or other serious health events cannot be ruled out.

depend not only on the biological risk posed by the affected drugs, but also on the actions of downstream public health authorities and healthcare providers, both of which were active participants in responding to the NECC outbreak. Specifically, public health authorities appear to have played an important coordinating role by raising awareness of exposure to contamination and issuing treatment guidance, which influenced both the timing and form of clinical responses. Meanwhile, the evidence suggests that healthcare providers adhered to that guidance, using the recommended diagnostic tests and treatment drugs, as well as targeting care to patients most likely to have been exposed.

This article builds on several strands of literature. First, it contributes to evidence on the consequences of patient exposure to severe drug quality failures. Existing empirical evidence has largely come from public health investigations of adverse events, such as the NECC outbreak, that document the event's epidemiology and confirmed infections and mortality (Kauffman and Malani, 2016; Smith et al., 2015, 2013; Pettit and Malani, 2015; Kauffman et al., 2013; Lockhart et al., 2013; Pettit et al., 2012; Kainer et al., 2012). I extend this literature by providing causal evidence that the broader patient care consequences of product quality failures also include sizeable increases in high-intensity healthcare utilization, which can represent patient burden even if precautionary, and measurable increases in healthcare costs borne by patients and insurers. These findings are especially relevant for policy discussions regarding the emerging role of large-scale drug compounding in pharmaceutical supply, where the NECC outbreak serves as a seminal event for understanding the safety risks of mass production outside of the FDA regulatory regime (Broughel, 2021; Watson et al., 2021; Shehab et al., 2018; Cantrell, 2016; Gudeman et al., 2013; Staes et al., 2013). Concerns about these safety risks have persisted even after federal legislation enacted in response to the outbreak placed limitations on large-scale drug compounding (Gottlieb, 2018; Woodcock and Dohm, 2017).

Second, I contribute to the growing literature on the propagation of supply chain shocks (Korovkin et al., 2024; Castro-Vincenzi et al., 2024; Balboni et al., 2023; Carvalho et al., 2021; Boehm et al., 2019; Barrot and Sauvagnat, 2016). Existing research on pharmaceutical markets has largely focused on quantity-based shocks that reduce drug access, examining how shortages impact rationing, medication errors, substitution, and healthcare spending (Liebman et al., 2023; Park et al., 2025; Blankart and Felder, 2022; Conti and Wosińska, 2025). Ironically, drug shortages are often precautionary responses to mitigate harms from quality failures: the FDA reports that 62 percent of shortages from 2013 to 2017 were rooted in supply disruptions following the discovery of product or manufacturing quality problems (FDA, 2020). For example, Liebman et al. (2023) study the welfare effects of a pediatric vaccine shortage that resulted from one of two manufacturers suspending production due to concerns about sterility assurance. This paper studies the other side of this trade-off by providing evidence on the downstream consequences of a quality-based

supply chain shock in which unsafe drugs reached downstream patients.

Third, this paper contributes to the literature on how public health communication shapes healthcare provider behavior. Prior research shows that providers tend to adhere to practice recommendations in routine care settings (Churchill and Lawler, 2025; Alalouf et al., 2024; Lawler, 2020, 2017) and to public health rationing guidelines (Liebman et al., 2023; Buchmueller and Carey, 2018). My findings indicate that this pattern extends to high-stakes emergency settings requiring non-routine patient care. In the case of the NECC outbreak, clinical responses rapidly emerged when contamination risk was communicated by public health authorities, and were narrowly targeted among patients for whom follow-up was recommended.

The remainder of the paper is organized as follows. Section 2 provides background on the NECC outbreak and its influence on drug compounding regulation. Section 3 presents the data and descriptive statistics. Section 4 presents the main estimates of the causal effects of potential patient exposure to drugs implicated in the NECC outbreak. Section 5 examines the relative roles of public health communication and routine healthcare provider surveillance in shaping these effects, and Section 6 concludes.

2 Background

2.1 The 2012 NECC Fungal Meningitis Outbreak

This paper studies the shipment of contaminated preservative-free methylprednisolone acetate (MPA) injections compounded by the New England Compounding Center (NECC) in 2012, which led to a nationwide outbreak of fungal infections. Investigations by the CDC and state health departments identified 753 infections and 64 deaths linked to the implicated drugs, making the incident the largest known outbreak of infection caused by drug contamination in U.S. history (Smith et al., 2015; Lockhart et al., 2013; FDA, 2012). The episode represents the type of high-risk quality failure that pharmaceutical regulatory oversight is intended to prevent: loss of sterility in a drug intended for administration into sterile parts of the body (Woodcock and Wosinska, 2013; Wosińska and Frank, 2023).

Laboratory testing identified evidence of *Exserohilum rostratum* fungus, the primary pathogen linked to the outbreak, across three consecutive production lots of MPA vials prepared by NECC on May 21, June 29, and August 10, 2012 (CDC, 2012b).[4] Exposure to this pathogen, a black mold, posed a severe threat to patient health because of the risk of central nervous system infection. This is because the implicated drugs were not only injectable, a route of administration that bypasses many of the body's natural defenses against impurities, but were also commonly ad-

[4]The literature indicates that infection risk was greatest in the lot produced on June 29, 2012 (Kauffman and Malani, 2016; Smith et al., 2015; Kauffman et al., 2013).

ministered near the spine for the treatment of back and joint pain, providing a potential pathway for infection to reach the spinal cord and brain (Smith et al., 2015; Pettit and Malani, 2015).

Public health authorities received the first signal of a possible contamination event on September 18, 2012, when a healthcare provider alerted the Tennessee Department of Health to a patient who died of unexplained meningitis (Pettit et al., 2012). As additional cases were identified with administration of NECC MPA as a common factor, NECC was informed of an investigation into its products and recalled the three lots eventually implicated in the outbreak on September 26, 2012 (Smith et al., 2015). The contaminated MPA drugs therefore circulated for 129 days prior to the recall. NECC invoice data indicate that the drugs were distributed widely during this period: approximately 17,500 vials were shipped to 76 healthcare facilities across 23 states (CDC, 2015).

The public health response intensified when new cases emerged in North Carolina, ruling out the possibility that infections were caused by provider-specific preparation errors at a single facility in Tennessee. Officials responded by identifying and notifying all 13,500 patients thought to have been potentially exposed to the contaminated drugs. Symptomatic patients were advised to seek immediate medical evaluation and asymptomatic patients were advised to seek follow-up in the event of future symptoms due to possible incubation time before disease onset. By October 19, 99% of potentially-exposed patients had been contacted by means of a letter, telephone call, voicemail, or home visit (Smith et al., 2013).

Public health officials also issued clinical guidance to healthcare providers. On October 3, 2012, the CDC distributed its first Health Alert publicly announcing the outbreak and providing expert diagnostic and treatment guidance (CDC, 2012a). The following day, the CDC and FDA also announced confirmed fungal contamination in unopened vials of NECC MPA (Smith et al., 2015). Guidance from public health authorities recommended a proactive approach to preventing the most severe harms associated with exposure. Providers were advised to contact all patients exposed to any of the three implicated lots, evaluate symptoms with a high degree of clinical suspicion, and conduct diagnostic testing when potentially-exposed patients exhibited even mild symptoms, such as headache.

The low threshold for diagnostic testing reflected both the severity of potential disease—standards of care for meningitis involve immediate treatment (Pettit et al., 2012)—and the difficulty of detecting infections caused by the contaminated NECC MPA. Fungal meningitis following spinal MPA injection is a rare complication, and infected patients often initially exhibited mild or nonspecific symptoms, including headache, neck stiffness, fever, nausea, neurological deficit, and falls. The subtlety of these symptoms, together with their overlap with the underlying conditions that the injections were intended to treat, created a risk that infections could be missed without prior clinical suspicion. Repeated diagnostic testing was also encouraged because no reliable, high-quality test for detecting infection was available while the outbreak was unfolding.

The CDC developed a polymerase chain reaction (PCR) assay for fungal DNA detection during the outbreak itself, which was used under research status (Lockhart et al., 2013).

Taken together, the public health response prevented additional administration of contaminated MPA by prompting the NECC recall, created widespread awareness of the nature of the contamination risk among patients and providers, and provided expert clinical guidance for diagnosing and treating potentially exposed patients. An analysis by CDC authors estimates that these responses resulted in approximately 3,150 averted injections and improved survival among exposed patients, resulting in 124 deaths avoided (Smith et al., 2015). The features of the NECC outbreak—a severe drug quality failure in which the implicated drugs circulated for a well-defined period of time, with invoice data identifying exposed healthcare providers, and clearly documented infection risk and recommended responses from public health communications—create a useful empirical setting for analyzing the downstream effects of contamination on comprehensive healthcare outcomes.

2.2 Safety Risks of Large-Scale Drug Compounding

Following the outbreak, NECC permanently shut down and established a $200 million settlement fund to compensate survivors and families of victims exposed to the contaminated drugs (NBC News, 2015). The incident also became a pivotal moment for the regulation of drug compounding in the U.S., drawing national attention to the safety risks associated with the emerging practice of large-scale drug compounding. Drug compounding plays a valuable role in pharmaceutical supply by enabling the production of drugs that are important for patient care but are unavailable in an FDA-approved form. For example, patients may be allergic to inactive ingredients contained in FDA-approved drugs, have special administration requirements, or require customized dosage strengths. By nature of being unavailable in FDA-approved form, compounded drugs are not reviewed by the agency for safety and efficacy, and their production has historically been subject to state pharmacy board standards that are less stringent than those enforced by the FDA (Watson et al., 2021; Cantrell, 2016; Douglass and Henrichs, 2015).

Compounding also plays a role in the preparation of so-called "office stock": ready-to-administer injectable drugs used in physicians' offices and hospitals. In 2013, 79% of acute care hospitals participating in Medicare reported contracting with at least one off-site compounding facility to prepare sterile injectable drugs (Office of Inspector General, 2013). Although office stock was historically produced in-house or by local retail pharmacies, large-scale compounders like NECC emerged in the 2000s by offering lower prices and expanded access through economies of scale. However, this growth raised safety concerns because these firms operated under state pharmacy board regulation while producing at volumes resembling mass manufacturers subject to FDA quality standards (Watson et al., 2021; Shehab et al., 2018; Gudeman et al., 2013; Staes et al., 2013).

The risk of production errors associated with drug compounding was therefore magnified due to the potential for exposure among large and geographically dispersed patient populations. This paper provides empirical evidence on the consequences of such risks by studying the widespread exposure to contaminated compounded drugs caused by the NECC outbreak.

Evidence from this paper is also relevant to ongoing safety concerns regarding large-scale compounding outside of FDA manufacturing standards (Gottlieb, 2018; Woodcock and Dohm, 2017). Federal policymakers responded to the NECC outbreak by passing the Drug Quality and Security Act (DQSA) in November 2013.[5] The law created the new 503B outsourcing facility designation under which compounders can produce at scale in exchange for following FDA manufacturing standards (Smith et al., 2014; Congressional Testimony, 2018). Take-up has remained limited, however, likely because the designation is voluntary and entails investment and compliance costs. Among the 7,500 pharmacies in the U.S. that specialize in drug compounding according to The American Pharmacists Association, 95 were registered as 503B outsourcing facilities at the time of writing (U.S. Food and Drug Administration, 2026; National Council on Aging, 2024). Moreover, the FDA has expressed concern that some firms that remained in the traditional 503A status intended for small-scale pharmacy compounding may be finding means to serve large, nationwide customer bases while adhering to the DQSA (National Academies of Sciences, Engineering, and Medicine et al., 2020).[6] Thus, although nearly 90% of hospitals reported purchasing compounded drugs exclusively from 503B outsourcing facilities in 2019, large-scale compounding outside of FDA oversight has likely not been eliminated (Office of Inspector General, 2019).

3 Data and Descriptive Statistics

3.1 Medicare Claims

Following Smith et al. (2013), who report that 89% of potential patient exposures to the contaminated NECC MPA drugs arose from epidural, spinal, or paraspinal injections (hereafter referred to as spinal MPA injections), I restrict my analysis to this category of injections within a 20% sample of administrative Medicare claims.[7] The data include patient demographic informa-

[5]The first infections resulting from the contaminated shipments from NECC were identified in September 2012. The DQSA was then proposed in the Senate in April 2013, approved by the House of Representatives in September 2013, and signed into law on November 27, 2013.

[6]For example, traditional compounding pharmacies may obtain similar market access benefits as 503B outsourcing facilities by acquiring pharmacy licenses in multiple states (National Academies of Sciences, Engineering, and Medicine et al., 2020).

[7]Smith et al. (2013) state that the remaining 11% of potential exposures occurred among patients receiving peripheral joint injections. Additionally, public health investigations documented by Smith et al. (2015) and Smith et al. (2013) define exposed patients as those who received an epidural, spinal, or paraspinal MPA injection from an implicated NECC production lot. Although a small number of other compounded NECC products were found to be contaminated based on laboratory testing, the CDC stated that its epidemiological and laboratory data supported evidence

tion as well as comprehensive measures of healthcare utilization and spending for fee-for-service Medicare beneficiaries during the 2010–2014 study period. Spinal MPA injections are identified as patient-date observations on which claims record both the administration of methylprednisolone acetate and an epidural, spinal, or paraspinal injection.[8,9] The main regression sample is restricted to index injections, defined as a patient's first spinal MPA injection in a rolling 90-day period, with follow-on injections studied as an outcome of potential exposure to contamination. Figure 1 plots the quarterly time series of all spinal MPA injections recorded in the Medicare claims data. Aggregate utilization remains relatively stable before and after the NECC outbreak, fluctuating around 32,500 injections per quarter.

Since the consequences of exposure to contaminated drugs occur after administration, primary outcomes are constructed using the 180-day period following injection, including the injection date. This window is intended to be sufficiently long to capture the effects of potential exposure to the implicated drugs, which could require months of curative treatment (Smith et al., 2013), while also allowing for the netting out of changes in patterns of care reflecting intertemporal substitution, such as expedited follow-up care. Robustness checks presented in appendix section A consider outcomes over the 90- and 365-day periods after injection. To ensure that outcome variables and controls for pre-injection patient characteristics are measured accurately, patients in the sample must be continuously enrolled in Medicare Parts A and B over the period spanning 6 months before to 6 months after injection.[10]

I consider three categories of post-injection outcomes. The first captures clinical responses to contamination risk by measuring the utilization of diagnostic and treatment recommendations in public health guidance. For example, lumbar punctures were recommended to diagnose central nervous system infections, MRI was recommended to diagnose spinal and joint infections, and voriconazole and liposomal amphotericin B were designated as first-line treatment drugs for patients with central nervous system infections (CDC, 2015; Smith et al., 2013). Following CDC communications, NECC outbreak-related infections are defined as meningitis, encephalitis, other central nervous system infections, and infective arthritis (CDC, 2015).[11] The second cate-

of an outbreak linked only to preservative-free methylprednisolone acetate (CDC, 2015).

[8]Methylprednisolone acetate is identified using Current Procedural Terminology (CPT) codes J1020, J1030, and J1040.

[9]Epidural and spinal injections are identified using CPT codes listed in Medicare Local Coverage Determinations. Specifically, epidural and spinal injections are identified by CPT codes 62310 and 62311 for injections without catheter insertion; 62318 and 62319 for injections with catheter insertion; and 64479, 64480, 64483, and 64484 for epidural injections into the intervertebral foramen. See the Wisconsin Physician Service Medicare Local Coverage Determination. Paraspinal injections are identified using CPT codes 64490, 64491, 64492, 64493, 64494, and 64495, which distinguish injections administered in the cervical and lumbar regions by spinal level. See, Medicare Local Coverage Determination.

[10]Deceased patients are counted as effectively continuously enrolled.

[11]Infection diagnoses are identified in the Medicare claims data by using ICD-9 diagnosis codes-to-Clinical Classifications Software (CCS) mappings developed by the Agency for Healthcare Research and Quality.

gory of outcomes captures the broader healthcare utilization implications of potential exposure to contamination. In addition to all-cause mortality, I calculate Unhealthy Days away from Home (UDAH), a measure of quality of care and population health developed by Burke et al. (2020) and Lam et al. (2021) in conjunction with the Medicare Payment Advisory Commission (MedPAC). UDAH classifies each patient-day as either "healthy" or "unhealthy," where a healthy day is one on which the patient is alive and not receiving hospital-based acute, post-acute, or other non-routine care.[12] Although patients may be in poor health even outside these settings, UDAH is designed to capture use of the most intensive components of the healthcare system. My analysis follows Burke et al. (2023) by calculating UDAH in the period following a healthcare event of interest, which in this setting is a spinal MPA injection. The third category of outcomes captures healthcare costs and spending. These outcomes are measured by aggregating across all Medicare claims linked to the patient during the 180-day period after injection, spanning the Parts A, B, D, and Carrier claims files. In this way, the measures represent comprehensive healthcare spending across all settings of care, whether or not the care was directly linked to contamination risk. To examine how these costs are distributed across payers and patients, I separately consider total reimbursements, Medicare payments, patient out-of-pocket payments, and healthcare provider-submitted charges.

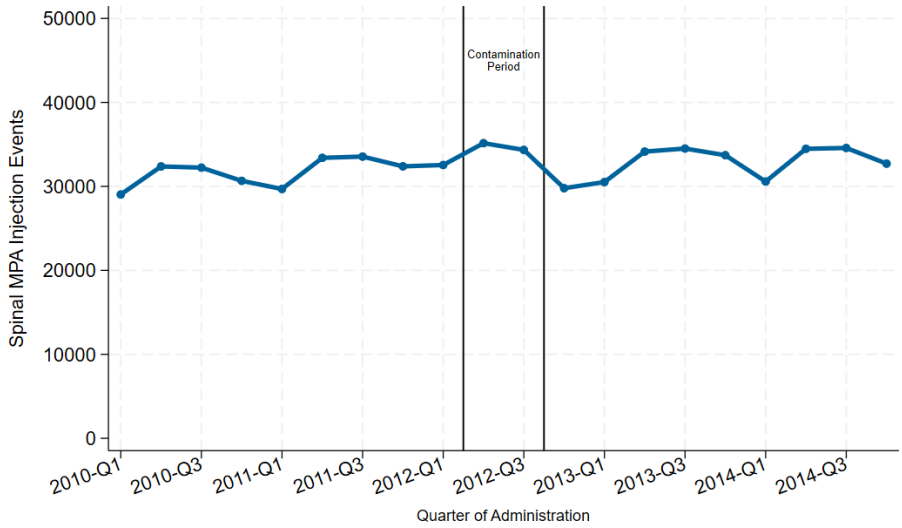


Figure 1. Time Series of Spinal MPA Injections in Medicare Claims Data

Notes: Spinal MPA injections are identified as patient-by-date combinations on which both the administration of MPA and an epidural, spinal, or paraspinal injection are recorded. Smith et al. (2013) report that 89% of potential patient exposures to the contaminated NECC MPA drugs were due to epidural, spinal, or paraspinal injections.

[12] In total, the components of unhealthy days include mortality days, inpatient hospital days, emergency department visits, observation days, skilled nursing facility days, home health agency visits, inpatient long-term care hospital days, inpatient rehabilitation hospital days, and inpatient psychiatric hospital days.

3.2 NECC Invoice Data

In general, insurance datasets like fee-for-service Medicare claims lack the detail needed to identify the utilization of compounded drugs, whether from NECC or other firms. This limitation arises because compounded drugs are not required to have National Drug Codes, the standard prescription drug identifier commonly used in healthcare research. In the case of the NECC outbreak, however, the set of healthcare providers that received implicated MPA drugs can be identified using invoice data collected and published by public health authorities to support the outbreak response.

On October 23, 2012, the FDA published a list of healthcare facilities that received products from the New England Compounding Center between May 21, 2012, and October 3, 2012. A shipment-level version of these data includes customer names, addresses, product names, quantities, and shipping dates.[13] For this study, I restrict to shipments of preservative-free methylprednisolone acetate injections in 80 mg/mL concentration, the drug produced in all three of the implicated lots.

A fuzzy matching procedure is used to link healthcare facilities recorded in the NECC invoice data to healthcare provider identifiers in the Medicare claims. Specifically, I match healthcare provider names, addresses, and phone numbers in the invoice data to organization names, business addresses, and phone numbers associated with National Provider Identifiers (NPIs) for individual healthcare practitioners. All 76 healthcare facilities recorded in the invoice data as receiving implicated MPA are matched to NPIs through this procedure. Treatment group healthcare providers are defined in the Medicare data as facilities linked to at least one NPI associated with receipt of implicated NECC MPA.[14]

This provider-level treatment definition captures whether a spinal MPA injection was administered at a facility that received implicated NECC MPA. Treatment group healthcare providers accounted for 2% of all spinal MPA injections administered while the contaminated lots were in circulation, resulting in 532 potentially-exposed patients in the 20% sample of Medicare claims. Table 1 compares the characteristics of spinal MPA injections administered by treatment and control group providers during the April 1, 2010 to May 20, 2012 pre-contamination period, where control group providers are those that did not receive the implicated drugs. Characteristics reported in the table include setting of care, patient demographics, patient unhealthy days and back

[13] These data were obtained using the Wayback Machine to access the FDA web page used to communicate updates regarding the NECC outbreak. See the NECC Customer List.

[14] Rather than defining treatment at the NPI level, treatment status is aggregated to the facility level because the NECC invoice data primarily record shipments to healthcare facilities rather than to individual practitioners. Due to the lack of formal facility identifiers in the Medicare Carrier professional services claims used to construct the sample of spinal MPA injections, I use distinct combinations of Tax ID, such as Employer Identification Numbers, and provider ZIP code as a proxy for healthcare facilities. Incorporating provider ZIP codes accounts for the possibility that a single Tax ID may be used across multi-location practices.

pain diagnoses in the three months before injection, and patient healthcare outcomes during the 180 days after injection.

The descriptive statistics show that spinal MPA injections were most commonly administered in outpatient physician office settings. During the pre-contamination period, treatment group providers were less likely to administer injections in hospital settings and more likely to administer them in physician office settings and ambulatory surgery centers relative to control group providers.[15] Patients receiving injections from treatment group providers had marginally more claims with diagnoses consistent with back pain in the three months before injection, fewer unhealthy days in the 180-day post-injection period, and fewer contamination-related infection diagnoses during the same period. These differences in baseline levels do not undermine the difference-in-differences design used in this paper, which relies on the assumption that outcomes for treatment and control group provider injections would have evolved along parallel trends absent treatment group providers receiving the implicated NECC drugs. Nevertheless, these baseline differences motivate the use of controls to account for injection setting of care and pre-injection patient characteristics, as well as the parallel pre-trend falsification test to assess the plausibility of the research design.

4 Effects of Potential Patient Exposure to Implicated NECC Drugs

4.1 Empirical Strategy

I use the 2012 NECC outbreak as a quasi-experiment that generated plausibly exogenous variation in the exposure of patients receiving spinal MPA injections to contamination risk. Specifically, I use a difference-in-differences design exploiting the fact that spinal MPA injection events could only have been physically exposed to contaminated NECC drugs if they were (1) administered by a healthcare provider recorded as receiving the implicated drugs according to NECC invoice data (2) during the 129-day period between May 21, 2012 and September 26, 2012 when those drugs circulated.

Using spinal MPA injection events in the Medicare claims data spanning April 2010 to December 2013 as my regression sample, cross-sectional variation in contamination risk therefore arises from the presence of injections performed by providers that received the implicated NECC drugs (treatment group) and injections performed by other providers (control group). Temporal variation arises from the inclusion of injections performed before, during, and after the circulation

[15] Among the 76 healthcare facilities recorded as receiving the implicated drugs, 41% were pain management clinics, 30% were ambulatory surgery centers, 11% were hospitals, 7% were outpatient facilities specializing in orthopedics, with the remaining share accounted for by other outpatient settings.

of contaminated NECC drugs.[16] Intuitively, the design compares the post-injection outcomes of injections administered by treatment and control group providers while the contaminated NECC drugs were in circulation, using the pre-contamination period to account for differences in post-injection care across treatment and control providers that are unrelated to the outbreak.[17]

Since Medicare claims do not identify the specific manufacturer of the MPA drug administered in a given injection, estimates from this comparison are interpreted as capturing the reduced-form effects of *potential* patient exposure to the implicated drugs, where potential exposure is defined as receiving a spinal MPA injection from a healthcare provider whose drug supply became contaminated due to the NECC outbreak. If treatment group providers primarily single-sourced MPA from NECC, a strategy for minimizing medication errors among sterile injectable drugs (Wosińska and Frank, 2023), the estimates approximate the effects of direct patient exposure to drugs implicated in the outbreak. If treatment group providers use multi-sourcing, the estimates instead reflect the diluted impacts of direct patient exposure plus changes in care applied to non-exposed patients among treatment group providers beyond those of control group providers. Under either interpretation, the estimates quantify the effects of contamination entering into a healthcare provider's drug supply. This is a policy-relevant object for understanding the downstream consequences of the upstream drug quality failure, embedding both providers' curative treatment of contamination-related illness and precautionary responses taken to mitigate potential harms. The relative trajectories of outcomes among injections administered after the contaminated drugs exited circulation are used to examine the persistence of differential precautionary responses across treatment and control group providers when direct exposure risk ended.

Identification of the causal effects of potential exposure to contamination relies on the assumption that, conditional on observable injection characteristics, the outcomes of patients receiving spinal MPA injections across treatment and control group providers would have evolved along parallel trends had treatment group providers not received contaminated NECC MPA. Note that this assumption permits control group providers to have responded to the outbreak, which was a high-profile event that could have updated providers' beliefs about the risks of spinal MPA injections and third-party compounded drugs. To the extent that such control group spillovers took place, the difference-in-differences estimates under parallel trends will capture the incremental causal effects of receiving an injection from a provider with contaminated drug supply

[16] I restrict the sample to each beneficiary's first spinal MPA event in a 90-day rolling period of continuous beneficiary enrollment in Parts A and B of Fee-for-Service Medicare to minimize the confounding influence of past injections.

[17] Equivalently, the difference-in-differences analysis can be conceived as comparing the outcomes of injections administered by treated healthcare providers while the contaminated lots were in circulation against those of injections performed by the same healthcare providers in the pre-contamination period, adjusted for secular trends and contemporaneous shocks unrelated to exposure as captured by the evolution of outcomes among control group providers.

beyond common changes in care caused by the outbreak, rather than relative to a state of the world in which the outbreak did not occur at all.[18]

The plausibility of parallel trends is supported by the plausibly exogenous timing of contamination risk from the perspective of healthcare providers and the narrowness of the clinical setting studied in this paper: both treatment and control group providers performed the same spinal MPA injection procedure, where some sourced MPA from NECC and others sourced MPA from different producers, including other large-scale drug compounders. The assumption is also supported by parallel pre-trends falsification tests, which show that post-injection outcomes among treatment and control providers evolved along similar trajectories prior to circulation of the contaminated NECC drugs. Finally, analyses of outbreak responses along the extensive margin of performing spinal MPA injections, presented in section 4.2, indicate stability in the observable composition of patients receiving spinal MPA injections across treatment and control group providers around the outbreak.

The causal effects of potential patient exposure to implicated NECC drugs are estimated using the difference-in-differences specification presented in equation 1:

$$\begin{aligned} Y_{i,p,t} = \alpha &+ \beta_1 \text{TreatedProvider}_p \times \text{DuringContamination}_t \\ &+ \beta_2 \text{TreatedProvider}_p \times \text{AfterContamination}_t + \delta_p + \eta_t + X_i + \varepsilon_{i,p,t} \end{aligned} \tag{1}$$

where $Y_{i,p,t}$ measures outcomes in the 180 days following spinal MPA injection i administered by provider p on date t. Provider fixed effects δ_p absorb time-invariant level differences in post-injection follow-up and patterns of care across providers. Date fixed effects η_t capture shocks to spinal MPA injection events administered on date t that are common to all providers. This includes both outbreak responses that were shared across providers and other contemporaneous shocks. To account for potential changes in the observable composition of patients receiving spinal MPA injections over time, the vector X_i controls for a rich set of observable patient and practitioner characteristics associated with each injection event, including the setting of care, specialty of the administering practitioner, patient demographics, chronic conditions, diagnoses related to back pain, and unhealthy days in the six months before injection. Standard errors are clustered at the healthcare provider level p.

The primary coefficient of interest, $\hat{\beta}_1$, estimates the difference in average post-injection outcomes across injections administered by treatment and control group providers during versus before the circulation of contaminated NECC drugs. Under the parallel trends assumption, the estimate represents the reduced-form effect of potential patient exposure to the implicated NECC drugs. From the provider perspective, the estimates can also be understood as the effects of con-

[18] Though independently interesting, responses by control group healthcare providers cannot be causally estimated due to the lack of a credible comparison group that was not impacted by the outbreak.

tamination entering into a healthcare provider's drug supply on patient care.

4.2 Extensive Margin Outbreak Responses and Their Implications

In addition to affecting post-injection care among patients who received injections from treatment group providers, the causal effects of the NECC outbreak may also operate along the extensive margin of altering providers' and patients' propensities for utilizing spinal MPA injections in the first place. Since these extensive margin responses mediate inclusion in the sample of realized injections used in the analysis described above, quantifying them provides important context for the interpretation of my main results. To the extent that extensive margin responses exist, they would only threaten the parallel trends assumption if they led to differential changes in the underlying composition of patients receiving spinal MPA injections administered by treatment and control group healthcare providers. I assess this threat in two ways, while also characterizing the independently interesting extensive margin responses to the NECC outbreak.

First, I study whether the outbreak differentially impacted the quantity of spinal MPA injections administered by treatment and control group healthcare providers. To do so, I aggregate the injection-level regression sample into a balanced provider-level panel dataset (including zeroes) and estimate a difference-in-differences model for injection volume.

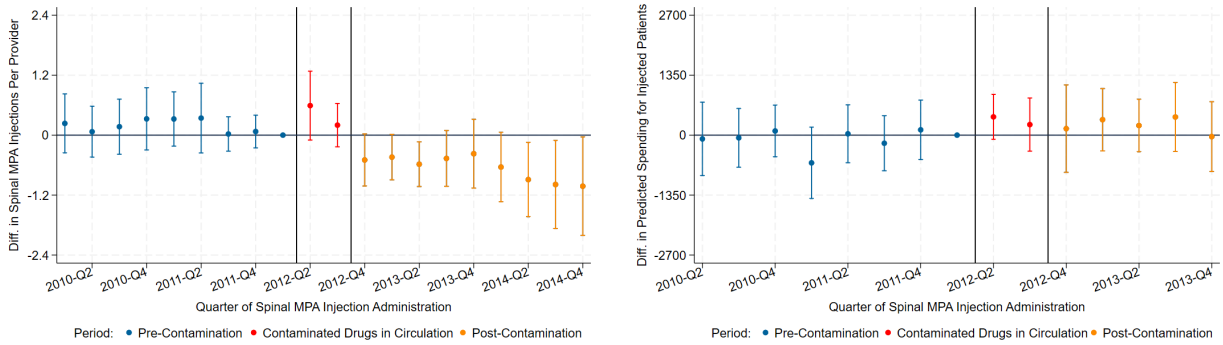
Second, I test whether the outbreak led to shifts in patient composition by examining the evolution of the observable risk profiles of patients receiving spinal MPA injections across treatment and control group providers. Specifically, I estimate the main injection-level difference-in-differences model (equation 1) using *predicted* total healthcare spending in the 180 days after injection as the outcome variable, which serves as an index summarizing patient risk.[19] The prediction is constructed with pre-contamination period injections, using a linear regression of realized total post-injection healthcare spending on the vector of observable injection-level characteristics X_i, the beneficiary's residential HRR, and a time trend. Given that X_i includes characteristics closely linked to patient risk, such as indicators for chronic conditions and recent utilization of hospital-based and post-acute care, healthcare providers responding to the outbreak by restricting spinal MPA injections to less (more) risky patients would manifest as a decline (increase) in predicted post-injection healthcare spending.

Panel (a) of Figure 2 provides strong evidence for the presence of extensive margin responses, though only after the contaminated drugs exited circulation and public health authorities announced the outbreak. During this period, treatment group providers experienced a persistent decline of 0.85 spinal MPA injections administered per month relative to control group providers, a 35 percent decrease relative to the baseline mean, as well as a 7.65 percentage point increase in the probability of performing zero monthly injections, a 12 percent increase relative to baseline

[19]The vector X_i is omitted from the regression because it is used to generate the all-cause healthcare cost prediction.

(see Table 2). The persistent decline in injection volume among treatment group providers for more than a year after the outbreak was announced is consistent with a chilling effect due to enhanced provider and patient precaution.

Panel (b) of Figure 2 shows that there is no evidence of significant changes to patient selection into receiving spinal MPA injections based on observable risk characteristics in either the contamination period or the post-contamination period, when the differential decline in spinal MPA injection volume described above materialized. Relative to the pre-contamination period, treatment group spinal MPA injections administered while the contaminated drugs circulated (i.e., potentially-exposed injections) had $303 higher predicted total healthcare spending relative to control group injections, equal to 2.9 percent of the baseline mean, which fell to $229 among injections administered after the contaminated drugs left circulation (see Table 3). Neither estimate is statistically significant at the 10% level.[20]



(a) Spinal MPA Injections Administered Per Provider **(b)** Risk Composition of Spinal MPA Injection Patients

Figure 2. Extensive Margin Responses on Utilization of Spinal MPA Injections

Notes: The figure examines patient and healthcare provider responses to the NECC outbreak along the extensive margin of spinal MPA injection utilization. Panel (a) analyzes the relative evolution of the number of spinal MPA injections administered by treatment and control group healthcare providers, reporting event study estimates from a balanced provider-by-month panel. The sample includes all providers who performed at least one spinal MPA injection during the study period. Standard errors are clustered at the healthcare provider level. Panel (b) examines the relative evolution of the observable risk profile of patients receiving spinal MPA injections from treatment and control group providers. Specifically, the figure reports estimates from a dynamic event study version of the main injection-level regression specification (see equation 1) using predicted total healthcare spending in the 180 days after injection as the outcome. Predicted healthcare spending is based on the sample of pre-contamination period spinal MPA injections, using a linear regression of realized total 180-day healthcare spending on observable injection characteristics X_i, the beneficiary's residential HRR, and a monthly time trend. Error bands represent 95% confidence intervals. Injection events are indexed by the date of administration, meaning that estimates for Q2-2012 and Q3-2012 correspond to injections administered during the contamination period.

Together, these findings support the plausibility of the parallel trends assumption for iden-

[20]The 95% confidence intervals rule out increases in predicted total healthcare spending in the 180 days after injection of more than 6.8 percent and 5.3 percent during the contamination and post-contamination periods, respectively.

tifying the causal effects of potential patient exposure to the implicated NECC drugs on post-injection healthcare outcomes using equation 1. The lack of any detectable extensive margin responses while the contaminated NECC drugs were in circulation, neither on injection volume nor on observable patient risk, highlights that the quasi-experiment created by comparing the outcomes of realized spinal MPA injections between the contamination and pre-contamination periods (i.e., $\hat{\beta}_1$) is especially compelling. One possible interpretation for this finding, explored further in section 5, is that patients and healthcare providers were largely unaware of contamination risk prior to public health action, by which time the contaminated drugs had already been removed from circulation.

Despite the differential decline in the quantity of spinal MPA injections administered in the post-contamination period, null effects on observable patient risk profiles across treatment and control providers during this time also support the parallel trends assumption. Post-contamination period injections therefore serve as an informative comparison group for measuring the persistence of changes in practice styles among treatment group providers after the contaminated drugs exited circulation and the risk of patient exposure to the implicated NECC drugs ended. Although changes in patient composition along unobserved characteristics cannot be ruled out, these results nevertheless reduce concerns that the main difference-in-differences estimates are driven by underlying changes in the types of patients receiving injections rather than the causal effects of potential exposure to contaminated drug supply.

4.3 Results

This section presents the main difference-in-differences estimates of the downstream consequences of potential exposure to contaminated NECC MPA, which reflect the reduced-form effects of receiving a spinal MPA injection from a treatment group healthcare provider relative to receiving one from a control group provider. The main results are organized into two sets of outcomes. First, I examine whether potentially-exposed patients received care consistent with the clinical responses most proximate to contamination risk. These outcomes include diagnoses with infections associated with the NECC outbreak, guideline-recommended diagnostic tests, prescription fills for guideline-recommended treatment drugs, physician evaluation and management events, and follow-on spinal MPA injections. Second, I examine the broader burden caused by potential patient exposure by examining outcomes that capture healthcare activity more comprehensively, including mortality, unhealthy days, and healthcare spending.

Across these outcomes, the estimates show that potentially-exposed patients experienced substantial changes in post-injection care relative to other recipients of spinal MPA injections, including economically large and statistically significant increases in utilization of high-intensity care and healthcare spending. The effects are temporally concentrated among injections admin-

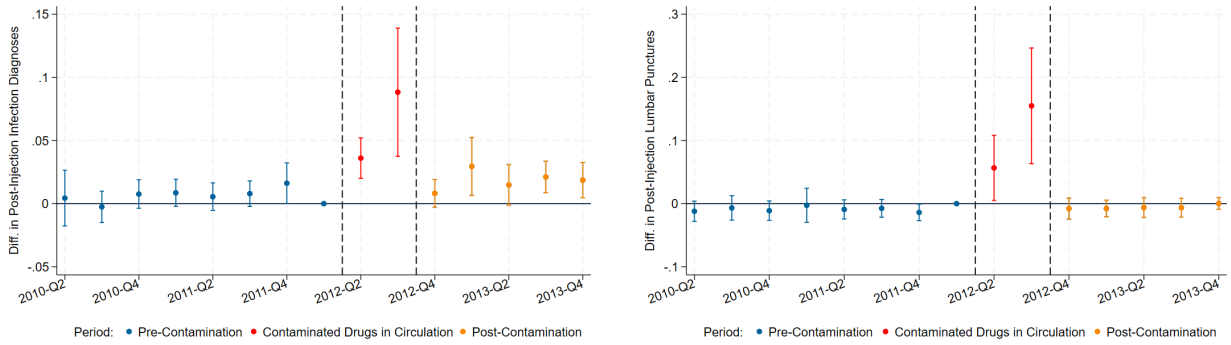
istered while the contaminated NECC drugs were in circulation, without extending to subsequent injections administered while the outbreak and its associated safety risks were most salient.

4.3.1 Contamination-Related Care

Table 4 reports difference-in-differences estimates for outcomes most directly linked to clinical responses to NECC contamination risk in the 180-day period after injection. Each of the outcomes reported in the table—spanning follow-up, evaluation, and treatment—moves in the direction consistent with management of contamination risk. The largest increases are reflected in diagnoses and diagnostic testing. Potentially-exposed patients experienced a 6.1 percentage point (pp) increase in diagnoses associated with contamination-related infection, representing an increase of nearly seven times the baseline mean among injections administered by treatment group healthcare providers. The magnitude of the increase in contamination-related diagnoses is similar to the 5.5% attack rate, defined as confirmed infections per potential exposure, reported in the public health literature (Smith et al., 2013). Potentially-exposed patients also received 0.13 additional lumbar punctures, the diagnostic test recommended for detecting nervous system infection, representing a rise of more than 20 times the baseline mean. The large increases in these outcomes in percentage terms reflect both their rarity in the absence of contamination risk, as well as the scale of the clinical response to contamination risk.

Figure 3 plots the differential evolution of contamination-related diagnoses and lumbar punctures across injections administered by treatment and control group providers by quarter of injection administration. The estimates show evidence of parallel trends in the quarters before the contamination period, indicating that post-injection outcomes were not varying differentially across treatment and control group providers among injections administered at baseline. Both outcomes then increase sharply beginning with injections administered in Q2-2012, corresponding to the onset of potential exposure after the first contaminated NECC production lot entered circulation on May 21, 2012. The effects then peak among injections administered in Q3-2012 before returning to comparatively small and statistically insignificant levels for those administered in Q4-2012, by which time the implicated NECC drugs had been recalled and the public health authorities had announced the outbreak. This timing is consistent with the underlying trajectory of potential contamination risk, as Q3-2012 nearly fully overlapped with the circulation of implicated NECC drugs and public health research indicates that the lots produced during this period were the most heavily contaminated (Smith et al., 2013).

The remaining difference-in-differences outcomes in Table 4 show that treatment effects extended to several other patterns of care consistent with clinical responses to contamination risk. Upper-body MRI scans, another diagnostic test recommended in public health guidance, increased by 0.11 scans, more than doubling relative to the baseline mean. Prescriptions for voricona-



(a) Contamination-Related Infection Diagnoses **(b)** Diagnostic Lumbar Punctures

Figure 3. Responses to Contamination Risk Following Potential Exposure to Implicated NECC Drugs

Notes: figures report event study estimates of clinical responses to NECC contamination risk among patients potentially exposed to the implicated NECC drugs. Estimates are based on a dynamic version of the main injection-level difference-in-differences specification in equation 1, which compares changes in outcomes during the 180 days following injection across injections administered by treatment and control group healthcare providers. The outcome in panel (a) is an indicator for whether the patient recorded any healthcare claims with a diagnosis of meningitis, encephalitis, other central nervous system infection, or infective arthritis during the 180-day period after injection. The outcome in panel (b) is the number of diagnostic lumbar punctures performed over the same period. Standard errors are clustered at the healthcare provider level, and error bands represent 95% confidence intervals. Injection events are indexed by the date of administration, meaning that estimates for Q2-2012 and Q3-2012 correspond to injections administered during the contamination period.

zole and amphotericin B, which were recommended as front-line treatments for fungal meningitis, increased by 0.11 prescriptions in the 180-day post-injection period.[21] The appearance of these drugs among injections administered during the contamination period is especially notable because they were not recorded in the post-injection period following any treatment group spinal MPA injections at baseline.

Consistent with follow-up care, patients potentially exposed to the implicated drugs also had 2.9 additional evaluation and management events in the 180 days after injection, an 18 percent increase relative to the baseline mean. These events capture additional time spent by healthcare providers managing patient care through consultations and office visits. Finally, potentially-exposed patients received 0.23 fewer follow-on spinal MPA injections, a 20 percent decline consistent with precautionary responses while providers and patients navigated complications and heightened concerns about the safety of spinal MPA injections.

Like contamination-related infection diagnoses and lumbar punctures, the increases in other diagnostic testing, treatment drug prescriptions, and the reduction in follow-up injections are concentrated among injections administered while contaminated NECC drugs were in circula-

[21]Prescription drug utilization is captured using Medicare Part D prescription fills and outpatient claims data. A limitation of these data is that they may incompletely capture prescription drug use in inpatient care, skilled nursing facilities, and outpatient claims that do not require detailed reporting of drug utilization.

tion, with limited persistent impacts on injections performed in the post-contamination period. The primary exception is in evaluation and management events, which remain elevated among injections administered by treatment group healthcare providers even after the risk of direct exposure to NECC contamination ended. This persistence is suggestive of heightened precaution among healthcare providers whose drug supply became contaminated by NECC drugs, albeit without broader impacts on other contamination-related patterns of care.

Taken together, the results provide clear evidence that potentially-exposed patients experienced substantial and targeted changes in post-injection care consistent with clinical management of contamination risk. The additional healthcare utilization implied by these patterns of care—including additional follow-up, diagnostics, and monitoring—is therefore a component of the downstream consequences of potential patient exposure to the NECC drug quality failure.

4.3.2 Broader Healthcare Consequences

Given the severity of the diseases associated with contaminated NECC drugs, most notably central nervous system infections, I next study the broader healthcare consequences of the NECC outbreak on potentially-exposed patients. I begin with mortality, which is the most extreme and unambiguous measure of patient harm. Table 5 shows a statistically insignificant but economically large rise in all-cause mortality in the 180 days after injection. The estimated 0.84pp increase among potentially-exposed patients represents a 68 percent increase relative to the baseline mean. As a result, though the 95 percent confidence interval cannot rule out large increases in mortality, the results do not provide evidence of excess deaths among patients potentially exposed to the implicated NECC drugs.

Unhealthy Days By capturing only the most severe margin of patient harm, mortality may miss less severe dimensions of healthcare outcomes that also influence patient well-being. In particular, potential exposure to contaminated drugs may also burden patients by increasing their utilization of time-consuming, intensive, and disruptive healthcare, such as inpatient hospitalizations, emergency department visits, skilled nursing facility stays, and home health agency care. I therefore construct a measure of unhealthy days away from home, hereafter referred to as unhealthy days, a patient-centered measure of quality of care defined as the number of days in the 180 after injection during which the patient is deceased or receives acute hospital care, post-acute care, or other non-routine care (see Section 3 for a more detailed discussion of unhealthy days).

Table 5 shows that patients potentially exposed to drugs implicated in the NECC outbreak experienced 4.2 additional unhealthy days, a highly statistically significant rise representing a 72 percent increase relative to the baseline mean. Event study estimates, plotted in Figure 4, show little evidence of differential pre-trends in unhealthy days among injections administered prior

to the contamination period, followed by a sharp rise concentrated among injections administered by treatment group healthcare providers in Q3-2012. This is the same quarter in which contamination risk was plausibly at its highest, and in which healthcare providers exhibited the greatest increases in clinical responses closely linked to contamination risk. Estimates of excess unhealthy days among injections administered by treatment group providers are modestly elevated but statistically insignificant after the contaminated NECC drugs left circulation beginning in Q4-2012.

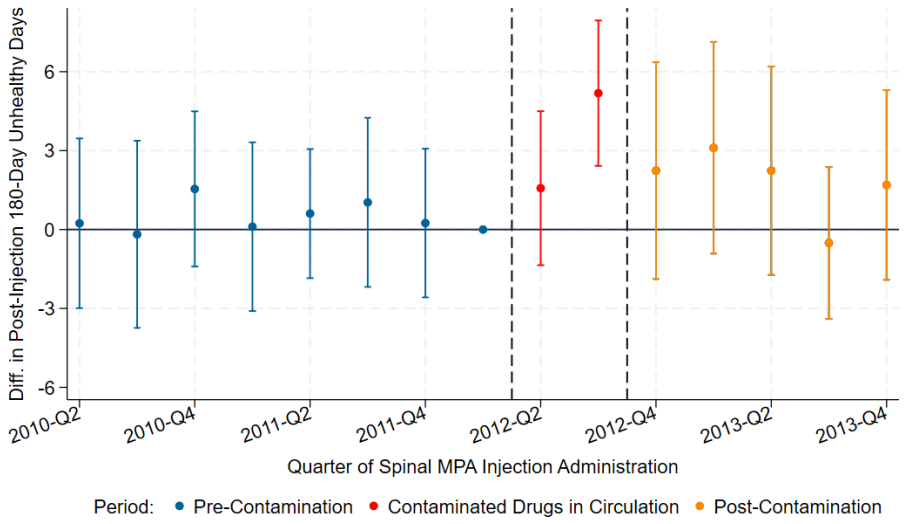


Figure 4. Unhealthy Days Following Potential Exposure to Implicated NECC Drugs

Notes: figure reports dynamic difference-in-differences estimates of the effect of potential patient exposure to the implicated NECC drugs on unhealthy days. Unhealthy days are defined as the number of days during the 180-day period following injection in which the patient received care in hospital-based, post-acute care, or other non-routine care settings. Estimates are based on a dynamic version of the main injection-level specification in equation 1, which compares changes in outcomes across injections administered by treatment and control group healthcare providers. Standard errors are clustered at the healthcare provider level, and error bands represent 95% confidence intervals. Injection events are indexed by the date of administration, meaning that estimates for Q2-2012 and Q3-2012 correspond to injections administered during the contamination period.

The increase in unhealthy days reflects greater utilization of both hospital and non-hospital care settings. Potentially-exposed patients spent 0.73 additional days receiving inpatient hospital care, a 53 percent increase relative to the baseline mean, and had 0.14 additional emergency department visits, a 23 percent increase. They also spent 2.47 more days receiving post-acute and non-routine care, driven primarily by skilled nursing facilities and home health agencies.

Regarding interpretation, it is worth noting that due to the absence of significant mortality effects, the rise in unhealthy days is not definitive evidence of adverse health effects due to contamination-related illness. Although increases in acute hospital care along with clinical responses to contamination risk documented in section 4.3.1 are consistent with deteriorating

patient health, a portion of these results may also reflect proactive, precautionary responses to reduce the probability of severe harms. Nevertheless, this ambiguity does not diminish the importance of the finding of additional unhealthy days as a downstream consequence of potential exposure to contamination. Potentially-exposed patients spent significantly more time interacting with the most intensive elements of the healthcare system and underwent additional follow-up care and invasive testing relative to patients receiving spinal MPA injections. The time and effort associated with these interactions, with many involving healthcare settings or procedures that are likely burdensome even when precautionary, represent components of the downstream consequences of the NECC drug quality failure.

Total Healthcare Spending Finally, I examine healthcare spending, which provides a direct measure of the financial burden caused by potential exposure to the contaminated NECC drugs. The preceding results presented in sections 4.3.1 and 4.3.2 show that potentially-exposed patients received care consistent with clinical responses to contamination risk and experienced increased utilization of the high-intensity healthcare settings captured by unhealthy days. Spending measures the additional resources associated with these responses.

Table 6 shows that potentially-exposed patients experienced large and statistically significant increases in total reimbursements, Medicare payments, patient out-of-pocket costs, and provider-submitted charges. Total reimbursements, which are my preferred measure of healthcare spending because they capture realized payments for healthcare services, increased by $2,551 in the 180 days after injection, representing a 25 percent increase relative to the baseline mean. Within this rise, Medicare program payments increased by $2,452, a 27 percent increase relative to baseline, while patient out-of-pocket payments increased by $174, equal to 20 percent of the baseline. As a result, though both Medicare and patients bore additional financial burden, the vast majority of the measured rise in healthcare spending accrued to the Medicare program.

Event study estimates plotted in Figure 5 exhibit a similar timing pattern to unhealthy days. Healthcare spending evolves along a trajectory consistent with parallel pre-trends among injections administered in the pre-contamination period, then rises sharply among potentially-exposed injections administered in Q3-2012. Spending effects then become smaller and statistically insignificant after the contaminated drugs exited circulation. Results are qualitatively similar when considering the log transformation of total healthcare spending plus unity, which indicate a 17% rise in spending following injections potentially exposed to the implicated NECC drugs.

Figure 6 decomposes the $2,551 increase in 180-day healthcare spending by type of healthcare claim. More than half of the increase is driven by inpatient hospital care, which is consistent with the resource-intensity of this type of care, which entails continuous monitoring, room and board,

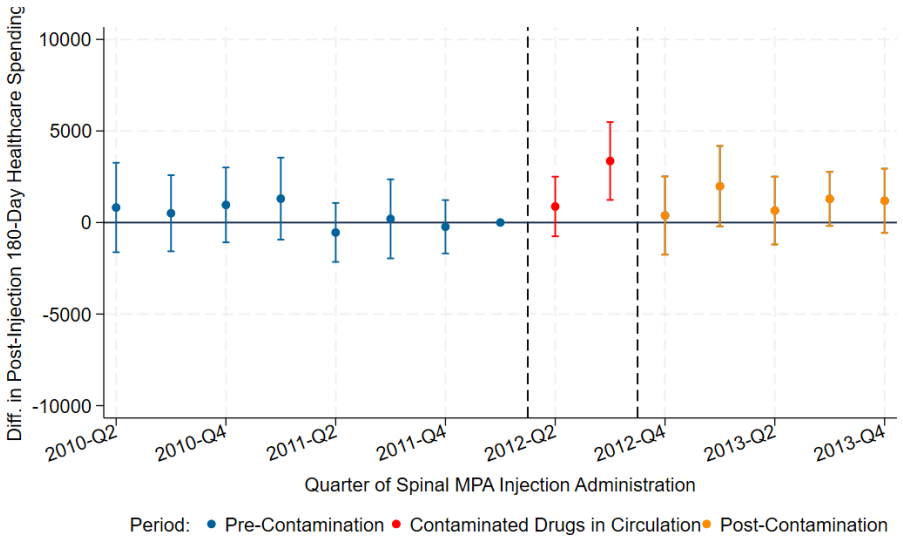


Figure 5. Total Healthcare Spending Following Potential Exposure to Implicated NECC Drugs

Notes: figure reports dynamic difference-in-differences estimates of the effect of potential patient exposure to the implicated NECC drugs on total healthcare spending. Total healthcare spending is defined as the sum of realized provider reimbursements across all healthcare claims for care received by the patient in the 180 days after injection. Estimates are based on a dynamic version of the main injection-level specification in equation 1, which compares changes in outcomes across injections administered by treatment and control group healthcare providers. Standard errors are clustered at the healthcare provider level, and error bands represent 95% confidence intervals. Injection events are indexed by the date of administration, meaning that estimates for Q2-2012 and Q3-2012 correspond to injections administered during the contamination period.

and specialized providers and technologies. Skilled nursing facility care, physician and professional services, Part D prescription fills, and home health care each account for approximately 10% of the total increase. Finally, outpatient facility care and hospice care each account for less than 5% of the increase.

A back-of-the-envelope calculation multiplying the estimated $2,551 increase in total healthcare spending among the 2,660 potentially-exposed Medicare beneficiaries implies that potential exposure to the implicated drugs resulted in $6.8 million in additional healthcare spending. If the estimates are generalized to the full set of potentially-exposed patients reported by public health authorities, including patients outside the Medicare claims data, the implied increase in total healthcare spending is $33.9 million. Though such an extrapolation should be interpreted with caution due to differences between the Medicare population and those covered by other insurers, this exercise illustrates how a 25 percent increase in healthcare spending per patient can translate into substantial aggregate costs when exposure to contamination risk is increasingly widespread.

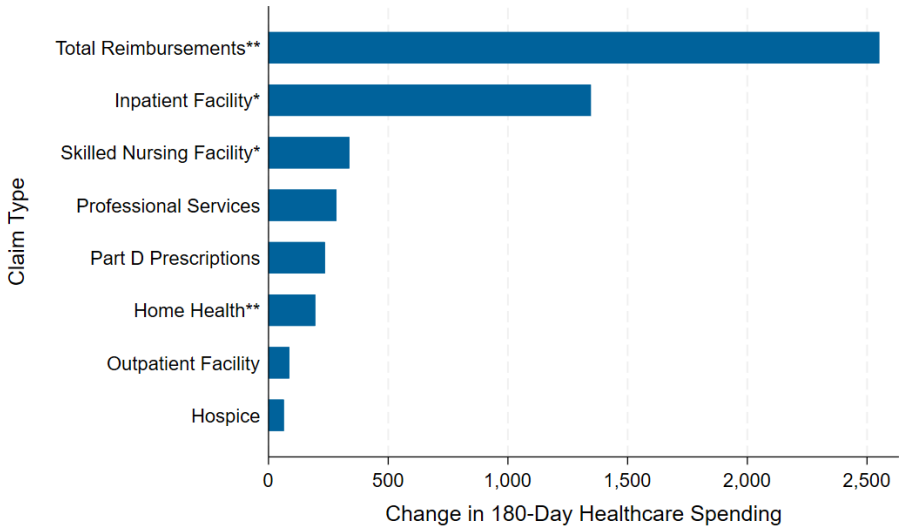


Figure 6. Decomposition of Increased Healthcare Spending by Claim Category

Notes: figure decomposes the estimated increase in total healthcare spending shown in Table 6 and Figure 5 by category of healthcare claim. Claim categories include institutional inpatient claims, institutional outpatient claims, skilled nursing facility claims, home health agency claims, hospice claims, professional services carrier claims, and Part D prescription drug claims. Bars report the magnitude of the Treated Provider × DuringContamination difference-in-differences estimate capturing the effect of potential patient exposure to the implicated NECC drugs from separate regression specifications that use category-specific healthcare spending as the outcome variable. Statistical significance is denoted with stars on the claim category labels on the vertical axis (* 5%, ** 1%).

Suggestive Evidence of Precautionary Responses To examine the role of precautionary responses, Table 7 reports difference-in-differences estimates when restricting the sample to spinal MPA injections that were not followed by an outbreak-related infection diagnosis in the 180 days after injection (see Table 8 shows qualitatively and quantitatively similar results from a heterogeneity-style rather than sample restriction version of this analysis).[22] In this sample, which is composed of patients whose care is unlikely to reflect curative treatment of contamination-related illness, I find attenuated but statistically significant changes in care consistent with precautionary responses. Potentially-exposed patients experienced a 2.7-day increase in unhealthy days, driven primarily by utilization of non-hospital settings like skilled nursing facilities, a 0.07-unit increase in number of diagnostic lumbar punctures, a 1.3-unit increase in evaluation and management events, and a 0.22-unit decrease in follow-on spinal MPA injections. The decline in follow-on spinal MPA injections is especially notable because it is nearly identical in magnitude to the main difference-in-differences estimate, suggesting that patients and healthcare providers may have sought to limit further contamination risk by foregoing spinal MPA injections even

[22]Since infection diagnoses themselves are an endogenous outcome of potential exposure to the implicated NECC drugs and may depend on provider follow-up behavior, these estimates should be interpreted as descriptive and suggestive in nature.

among patients who did not develop contamination-related illness. The $727 rise in total healthcare spending in this sample is about one-fourth of the size of the main estimate, and is not statistically significant at the 10% level. Taken together, these results provide suggestive evidence that the main difference-in-differences estimates are not driven solely by the mechanical effects of treating contamination-related illness, but also reflect precautionary care in response to contamination risk.

4.3.3 Discussion

Taken together, the results provide evidence of broad downstream healthcare consequences among patients potentially exposed to the drugs implicated in the NECC outbreak. The largest effects occur for outcomes that are most proximate to the management of contamination risk, such as diagnostics and treatment recommended by public health guidance. Importantly, however, the effects also extend to more comprehensive measures of healthcare activity, including unhealthy days and total healthcare spending in the 180 days after injection. These findings are qualitatively and quantitatively unchanged when using a regression specification without the vector of observable controls for patient and practitioner characteristics associated with each injection (see Appendix Table A.1). Appendix section A further demonstrates the robustness of the main difference-in-differences estimates to considering outcomes constructed with 90- and 365-day post-injection time horizons and to defining treatment at the level of Hospital Referral Regions, which capture market-level rather than provider-level exposure. Since the excess clinical activity observed among potentially-exposed patients would not have occurred had treatment group healthcare providers not received the implicated drugs, quantifying these responses yields a measurable component of the broader burden caused by the NECC drug quality failure. Although the respective portions of this burden attributable to curative treatment of contamination-related illness versus precautionary care cannot be isolated, the results are consistent with both channels contributing to the consequences of drug quality failures.

It is also noteworthy that these downstream consequences were concentrated among injections administered during the contamination period, peaking when contamination risk was plausibly greatest before largely shrinking towards levels that are statistically indistinguishable from zero among injections administered as soon as Q4-2012, the first quarter after the implicated drugs exited circulation. That the public health response began during this quarter implies that these injections were administered while the outbreak was highly salient to both patients and healthcare providers. Yet, I find no evidence that patterns of care associated with contamination risk were extended to these patients as a precaution. A limitation of this finding is that it cannot rule out the possibility that both treatment and control group providers made uniform changes to post-injection care during the post-contamination period. Nevertheless, the results signal that

differential clinical responses were concentrated among patients who could have been physically exposed to contamination, without broader changes in care applied to patients receiving injections after NECC contamination risk ended.

5 Role of the Public Health Response

Next, to distinguish between the relative roles of routine provider surveillance after injection and centralized public health action in shaping the clinical responses to the NECC outbreak, I examine the precise timing when treatment effects among potentially-exposed patients initially emerged. Pharmaceutical drugs are credence goods whose quality cannot be easily observed after administration (Scott Morton and Kyle, 2011). Quality failures can therefore create an incomplete information problem. Even when contamination causes complications, providers may struggle to recognize contaminated drug supply as the cause because symptoms may be difficult to disentangle from the patient's underlying condition or from the effects of contemporaneous medical care. Public health communication may therefore play an important role in shaping downstream care by alerting providers to potential exposures and issuing treatment guidance. The evidence presented in section 4.2 shows that extensive margin responses in the utilization of spinal MPA injections did not emerge until after the public health announcement of the outbreak. This section analyzes whether a similar pattern holds for post-injection care among patients who received injections during the contamination period.

5.1 Empirical Strategy

Given that the contaminated drugs circulated for the 129-day period spanning May 21, 2012 to September 26, 2012, while public health authorities announced the outbreak and issued treatment guidance on October 3, 2012, the timing when treatment effects emerged among potentially-exposed patients provides a useful distinction between the two mechanisms. If changes in patterns of care were driven by routine provider surveillance, treatment effects should emerge gradually after the contaminated production lots entered circulation, reflecting the diffuse timing of injection administration and development of complications. To the extent that contamination-related illness was clinically detectable within four months of administration, these effects should begin to appear prior to public health action (i.e., June, July, August, or September 2012). By contrast, sharp treatment effects coinciding with the October 2012 mobilization of the public health response would indicate that the announcement and treatment guidance acted as key information shocks affecting providers' beliefs about patient exposure and optimal care.

To identify when differential treatment effects emerged, I estimate a patient-level version of my main difference-in-differences regression analysis. Rather than aggregating patients' out-

comes over the 180-day post-injection window to capture the cumulative impacts of potential exposure as in equation 1, I instead use balanced patient panels reflecting outcomes separately for each month before and after spinal MPA injections.

The regression sample is composed of two cohorts of patients that received spinal MPA injections. The primary cohort consists of patients who received injections while the contaminated NECC drugs were in circulation between May 21 and September 26, 2012. This panel, referred to as the contamination cohort, includes both potentially-exposed patients whose injections were administered by treatment group providers and patients receiving injections from control group providers. Mirroring the difference-in-differences design used in section 4, which compares treatment and control group differences during versus before the contamination period, I also construct an analogous panel using the cohort of patients that received spinal MPA injections one year earlier, between May 21 and September 26, 2011. This placebo cohort accounts for dynamic differences in follow-up care across treatment and control providers that are unrelated to receiving NECC drugs implicated in the outbreak.

For each patient-by-cohort unit, the panel spans a cohort-specific time horizon: beginning with the event time 6 months before the start of the cohort's spinal MPA injection window and ending at the event time corresponding to 6 months after the mobilization of the public health response in the contamination cohort. In calendar time, the contamination cohort panel spans October 2011 to April 2013, while the placebo cohort panel spans October 2010 to April 2012. Using event time defined at the cohort level, rather than relative to each patient's own injection date, means that the public health response is mobilized at a common event time within the contaminated cohort. This allows the analysis to test for both the emergence of differential outcomes during the four event months while the injections were being administered and prior to the public health response, as well as for the sharpness of treatment effects once it was mobilized.[23]

I use a triple-differences model to compare the dynamic evolution of healthcare outcomes across patients who received spinal MPA injections from treatment and control group providers during the contamination period, using the placebo cohort treatment versus control group difference as a baseline. The identifying assumption is that, in the absence of potential exposure to the implicated NECC drugs in the contamination cohort, differences in the monthly outcomes of treatment and control group patients would have evolved in parallel across the contamination and placebo cohorts. To confound this mechanisms analysis, violations of parallel trends would need to emerge sharply in the event time coinciding with the public health response, despite this event time corresponding to a range of different lags since injection administration among patients within a given cohort. The plausibility of this assumption is supported by parallel pre-

[23]This event horizon means that the outcomes in the placebo cohort panel dataset do not extend into the period when contaminated NECC drugs were in circulation, meaning its outcomes cannot be impacted by the outbreak.

trends falsification tests.

As in the main analysis, treatment effects from this comparison should be interpreted as the reduced form impacts of potential patient exposure to the implicated NECC drugs, which embed the effects of contamination-related illness and precautionary responses. In this case, the object of interest is not *whether* treatment effects emerged, but *when* they emerged relative to the public health response. Since there is no variation in the timing of the public health response relative to cohort-specific event time, I estimate the stacked triple-differences regression model presented in equation 2

$$Y_{b,p,t,\tau} = \sum_{r=-7, r\neq -1}^{12} \beta_r \text{TreatedProvider}_p \times \text{ContaminatedCohort}_\tau \times \mathbf{1}\left\{\text{CohortEventTime} = r\right\}_{t,\tau} + \delta_{b,\tau} + \gamma_{p,r} + \eta_{r,\tau} + \varepsilon_{b,p,t,\tau} \quad (2)$$

where $Y_{b,p,t,\tau}$ measures the outcomes of beneficiary b in month t, who was treated by healthcare provider p in cohort window τ, where r represents cohort-specific event time. Beneficiary-by-cohort fixed effects $\delta_{b,\tau}$ absorb time-invariant level differences in outcomes across individual patients that are specific to each cohort, healthcare provider-by-event time fixed effects $\gamma_{p,r}$ capture provider-specific variation in care around spinal MPA injection events, and cohort-by-event time fixed effects $\eta_{r,\tau}$ capture shocks that are common to all beneficiaries at each cohort-specific event time. The coefficients of interest, $\hat{\beta}_r$, trace the relative monthly evolution of outcomes across patients receiving injections from treatment and control group healthcare providers during the contamination period relative to the treatment versus control difference at the same event time in the placebo cohort. Standard errors are clustered at healthcare provider level p (Wing et al., 2024).

5.1.1 Results

Figure 7 plots the triple-differences event study estimates showing the monthly evolution of clinical responses to contamination risk before and after public health action. Panels (a) and (b) plot contamination-related infection diagnoses and lumbar punctures, respectively. The estimates show no evidence of differential pre-trends among potentially-exposed patients and other patients in the months leading up to injection. Estimated coefficients also remain statistically insignificant during event months 0 through 4, when the contaminated injections were being administered to contamination cohort patients but before the public health response had mobilized. This evidence suggests that although contamination risk existed during this period, as patients were receiving injections of the implicated NECC drugs, the risk remained latent. To the extent that providers observed symptoms among patients who received contaminated injections,

it appears they lacked the information to conduct the appropriate diagnostic tests or arrive at contamination-related infection diagnoses via alternative means.

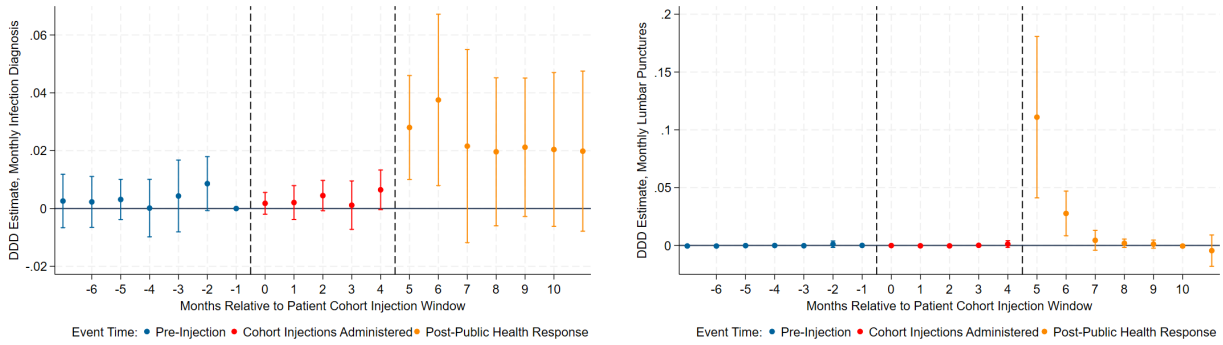
Instead, contamination-related infection diagnoses and lumbar punctures rose sharply among potentially-exposed patients in event month 5, corresponding to the October 2012 mobilization of the public health response. Potentially-exposed patients were 0.6pp more likely to receive a contamination-related infection diagnosis relative to control group patients in the month immediately preceding the public health announcement of the outbreak. This difference increased to 2.8pp and 3.8pp in the first two months after the announcement, respectively. The increase in lumbar punctures was especially pronounced in the month of the announcement, as potentially-exposed patients went from being 0.1pp more likely to undergo this diagnostic test in the month before the public health response to 11.1pp more likely in the month when it mobilized.

Figure 8 examines whether the broader healthcare consequences of potential patient exposure follow a similar timing pattern. Panels (a) and (b) plot the evolution of monthly unhealthy days and total healthcare spending, respectively. Both outcomes evolve along parallel trends across potentially-exposed and control group patients in the pre-injection period. Estimated treatment effects also remain statistically insignificant between event months 0 and 4, when the contaminated drugs were administered but before the public health response. Thus, although healthcare providers did not exhibit clinical responses to contamination risk prior to the public health response, the evidence indicates that potential exposure did not generate complications severe enough to result in systematic increases in unhealthy days or spending that were missed or misattributed during this period.

Unhealthy days and healthcare spending then rose beginning around the mobilization of the public health response. There are small, statistically insignificant increases in event month 4, corresponding to September 2012, which may suggest that some contamination-related complications had begun to appear before the formal public health announcement. However, increases are concentrated in the following months, which coincide with the sharp rise in contamination-related infection diagnoses and lumbar punctures. Unhealthy days, for example, peaked at 0.5 additional days per month among potentially-exposed patients precisely in October 2012, a statistically significant increase at the 5% level, before gradually decreasing towards zero in the following event months.

5.1.2 Discussion

Taken together, these results show that care linked to NECC contamination risk emerged among potentially-exposed patients sharply when the public health response began, rather than during the months when contaminated injections were being administered. This timing suggests that the public health response played an influential role in raising provider awareness of con-



(a) Contamination-Related Infection Diagnosis **(b)** Diagnostic Lumbar Puncture Tests

Figure 7. Timing of Clinical Responses to Contamination Risk Following Potential Exposure to Implicated NECC Drugs

Notes: figures examine when clinical responses to NECC contamination risk initially emerged among patients potentially exposed to the implicated drugs. The figure reports triple-differences event study estimates using a patient-by-month panel dataset composed of two stacked patient cohorts. The first stack is the contamination cohort, which consists of patients who received a spinal MPA injection while the implicated NECC drugs were in circulation, and the second stack is the placebo cohort, which consists of patients who received a spinal MPA injection during the same calendar window one year earlier. The triple-differences estimates compare the monthly evolution of outcomes for patients receiving injections from treatment and control group healthcare providers in the contamination cohort, using the corresponding treatment versus control difference in the placebo cohort as a baseline capturing differential post-injection follow-up care unrelated to the NECC outbreak. Panel (a) reports estimates for a monthly indicator equal to 1 if patients recorded any contamination-related infection diagnosis, and Panel (b) reports estimates for the monthly number of diagnostic lumbar punctures performed. Monthly event time is indexed to the cohort-specific injection window: event months 0–4 correspond to May through September, when patients in each cohort were administered spinal MPA injections. For the contamination cohort, event month 5 corresponds to October 2012, when public health authorities announced the outbreak and issued clinical guidance. Standard errors are clustered at the healthcare provider level, and error bands represent 95% confidence intervals.

tamination risk and in shaping the timing, form, and intensity of clinical responses. The evidence points to a comparatively limited role for routine provider surveillance, consistent with a lack of widespread awareness of the risk prior to public health action. While my results cannot speak to what would have occurred in the absence of the public health response, they suggest that, to the extent that healthcare providers would have detected contamination through independent routine surveillance, they did not do so within the first four months of exposure risk.

Due to variation in the time between injection and clinical responses being confounded by the likelihood that injections administered closer to the public health response involved more heavily contaminated production lots, it is challenging to quantify the public health response's efficacy. Nevertheless, this mechanism analysis highlights that the downstream consequences of drug quality failures depend not only on the biological severity and reach of the failure, but also on the process through which providers and patients recognize and respond to that risk. The work entailed in detecting contamination, identifying and alerting exposed patients, and developing

and communicating clinical guidance is therefore itself part of the downstream burden created by the upstream quality failure. As such, this finding also underscores the importance of public health capacity: when contamination enters the drug supply, public health systems can play an important role in coordinating responses that may mitigate adverse outcomes.

6 Conclusion

This paper studies the healthcare consequences of patient exposure to severe drug quality failures by leveraging evidence from the distribution of contaminated sterile injectable drugs produced by the NECC in 2012. My findings highlight that drug quality failures do not unfold in a vacuum against a passive healthcare system. Instead, they can trigger downstream clinical responses as healthcare providers and public health authorities mobilize to mitigate patient harm. I quantify the comprehensive healthcare utilization and spending effects associated with these clinical responses, finding that potential exposure to the implicated drugs resulted in a 72 percent increase in unhealthy days and a 25 percent increase in total healthcare spending in the 180-day period after injection. Consistent with drug quality failures creating an incomplete information problem due to difficulties in detection, changes in patterns of care consistent with contamination risk did not emerge during the initial 4-month period while the contaminated drugs were in circulation, but instead rose sharply when public health authorities announced the outbreak and issued treatment guidance.

In addition to the 64 deaths attributed to the NECC outbreak in public health investigations, the estimates of excess healthcare utilization and spending among potentially-exposed patients serve as a marker of the scale of additional burden borne by these patients relative to comparable controls, and represent an important component of the outbreak's broader downstream consequences. The clinical responses documented in this paper would not have occurred absent the upstream quality failure, were costly for patients and insurers, and likely imposed meaningful patient burden whether through illness requiring curative treatment or precautionary care following potential exposure.

While these downstream healthcare consequences are of first-order importance because they capture treatment effects among patients at risk of being physically administered the implicated drugs, high-profile quality failures like the NECC outbreak may also affect patients and providers who were not directly exposed. For example, patients and providers may have responded to news of the outbreak by updating their beliefs about the safety risks of spinal MPA injections or procedures involving compounded drugs more generally. Future research could estimate these spillover effects on spinal MPA injection utilization and precautionary care, including among providers that procured non-implicated drugs from NECC and among other providers performing

spinal MPA injections. Future research could also leverage variation in access to compounded drugs arising from policy responses to the NECC outbreak, including temporary state restrictions on large-scale drug compounding prior to the implementation of new federal legislation. Such evidence would help clarify the trade-offs posed by the emerging large-scale drug compounding sector, which promises to improve efficiency and access through economies of scale but may raise the risk of low-probability, high-stakes quality failures with broad downstream consequences for patients and the healthcare system.

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7 Additional Tables and Figures

Table 1. Characteristics of Spinal MPA Injections Administered During Pre-Contamination Period

	Injection Characteristics by Healthcare Provider Type		
	Treatment	Control	P-value of Difference
Providers (N)	71	5016	
Spinal MPA Injections (N)	2628	127629	
Patient Characteristics			
Age	70.7	70.7	.966
	(12.4)	(12.5)	
Female	.65	.64	.645
	(.48)	(.48)	
Unhealthy Days (1–3 Months Pre)	2	2.1	.501
	(7.2)	(7.8)	
Back Problem Diagnosis Claims (1–3 Months Pre)	3.4	3.1	.009**
	(3.4)	(3.6)	
Injection Setting of Care			
Office	.71	.61	.17
	(.45)	(.49)	
Hospital	.18	.35	.001**
	(.38)	(.48)	
Ambulatory Surgery Center	.09	.02	.152
	(.28)	(.14)	
Other	.03	.03	.889
	(.17)	(.16)	
Outcomes in 180 Days After Injection			
Mortality	.01	.01	.217
	(.11)	(.12)	
Unhealthy Days	5.8	6.8	.028*
	(18)	(20.5)	
Outbreak-Related Infection Diagnosis	.01	.01	.041*
	(.09)	(.11)	
Total Reimbursements	10381	10777	.369
	(14879)	(18072)	
Follow-On Spinal MPA Injections	1.2	1	.48
	(1.4)	(1.2)	
Evaluation & Management Events	16.4	15.3	.229
	(14.2)	(15.4)	

Notes: The table reports summary statistics of spinal MPA injections administered by treatment and control group healthcare providers during the pre-contamination period, defined as April 1, 2010 through May 20, 2012, including the characteristics of patients receiving injections, setting of care in which the injection was administered, and outcomes over the 180-day period after injection. Standard deviations are reported in parentheses. P-values are derived from univariate regressions of each characteristic on an indicator variable for whether the injection was administered by a treatment group provider, with standard errors clustered at the provider level and statistical significance denoted by * 5%, ** 1%.

Table 2. Extensive Margin Responses: Provider-Level Spinal MPA Injections Administered

	(1)	(2)
	Spinal MPA Injection Volume	$\mathbf{1}\{\text{Monthly Volume} = 0\}$
Treated Provider × DuringContamination	0.1816	−0.0213
	(0.2115)	(0.0345)
Treated Provider × AfterContamination	−0.8467**	0.0765**
	(0.3363)	(0.0375)
N	481,560	481,560
R^2	0.7139	0.4430
Provider FEs	✓	✓
Month FEs	✓	✓
Dep. Var. Treated Pre-Mean	2.43	0.61
Ind. Var. Mean	0.01	0.01

* 5%, ** 1%

Notes: the table reports difference-in-differences estimates comparing the evolution of spinal MPA injection volume between treatment group and control group healthcare providers. The sample is a balanced provider-by-month panel composed of all providers who performed at least one spinal MPA injection during the study period. DuringContamination refers to provider-month observations between June through September 2012, AfterContamination period refers to provider-month observations in October 2012 or later, and the omitted period spans April 2010 through May 2012. Standard errors are clustered at the healthcare provider level.

Table 3. Extensive Margin Responses: Risk Composition of Patients Receiving Spinal MPA Injections

	(1)	(2)
	Predicted 180-Day Healthcare Spending	Log(Predicted 180-Day Healthcare Spending)
Treated Provider × DuringContamination	302.9875	0.0302
	(213.0437)	(0.0191)
Treated Provider × AfterContamination	229.3956	0.0233
	(170.8634)	(0.0197)
N	237,310	237,310
R^2	0.1382	0.1973
Provider FEs	✓	✓
Date FEs	✓	✓
Dep. Var. Treated Pre-Mean	10,647.45	8.66
Ind. Var. Mean	0.02	0.02

* 5%, ** 1%

Notes: the table reports difference-in-differences estimates of the observable risk profiles of patients receiving injections administered by treatment and control group healthcare providers. Estimates are based on the main injection-level regression specification (see equation 1). The outcome variable capturing patient risk composition is predicted total healthcare spending during the 180 days following injection. Predicted spending is constructed using the sample of pre-contamination spinal MPA injections, using a linear regression of realized total 180-day healthcare reimbursements on observable injection characteristics, the beneficiary's residential HRR, and a time trend. DuringContamination refers to injections performed between May 21, 2012 and September 26, 2012, AfterContamination refers to injections performed between September 27, 2012 and December 31, 2013, and the omitted period spans April 1, 2010 to May 20, 2012. Standard errors are clustered at the healthcare provider level.

Table 4. Difference-in-Differences Estimates of Clinical Responses to Contamination Risk Following Potential Patient Exposure to Implicated NECC Drugs

	(1)	(2)	(3)	(4)	(5)	(6)
	Outbreak Infection	Lumbar Punctures	Upper Body MRI	Outbreak Prescriptions	Spinal MPA Injections	E&M Events
Treated Provider × DuringContamination	0.0608**	0.1315**	0.1140*	0.1105*	−0.2299**	2.9403**
	(0.0162)	(0.0382)	(0.0496)	(0.0536)	(0.0814)	(0.8060)
Treated Provider × AfterContamination	0.0111	−0.0004	−0.0024	0.0210	−0.1083	1.3437**
	(0.0088)	(0.0052)	(0.0187)	(0.0131)	(0.1073)	(0.4894)
N	234,688	234,688	234,688	234,688	234,688	234,688
R^2	0.0446	0.0541	0.0502	0.0291	0.2086	0.2333
Provider FEs	✓	✓	✓	✓	✓	✓
Date FEs	✓	✓	✓	✓	✓	✓
Dep. Var. Treated Pre-Mean	0.01	0.01	0.10	0	1.16	16.36
Ind. Var. Mean	0.02	0.02	0.02	0.02	0.02	0.02

* 5%, ** 1%

Notes: table reports difference-in-differences estimates of the effects of potential patient exposure to implicated NECC drugs on clinical responses to NECC contamination risk in the 180-day period after injection. The estimates are based on equation 1, which compares the evolution of outcomes across injections administered by treatment and control group healthcare providers before, during, and after the contamination period. Outcomes include an indicator for diagnosis with an outbreak-related infection (defined using Clinical Classifications Software for meningitis, encephalitis, other central nervous system infection, or infective arthritis); the number of diagnostic lumbar punctures performed; the number of upper body MRIs performed; prescription fills for guideline-recommended treatment drugs; follow-on spinal MPA injections; and physician evaluation and management events. DuringContamination refers to injections administered between May 21, 2012 and September 26, 2012, AfterContamination refers to injections administered between September 27, 2012 and December 31, 2013, and the omitted period spans April 1, 2010 through May 20, 2012. Standard errors are clustered at the healthcare provider level.

Table 5. Difference-in-Differences Estimates of Unhealthy Days Following Potential Patient Exposure to Implicated NECC Drugs

	(1)	(2)	(3)	(4)	(5)	(6)
	Unhealthy Days	All-Cause Mortality	Inpatient Days	ED Visits	SNF Days	Home Health Visits
Treated Provider × DuringContamination	4.1971**	0.0084	0.7345**	0.1378*	1.8429**	0.6928*
	(1.2097)	(0.0058)	(0.2626)	(0.0634)	(0.5462)	(0.3180)
Treated Provider × AfterContamination	1.2863	0.0033	0.0321	−0.0259	0.9002	0.1633
	(0.7419)	(0.0044)	(0.1179)	(0.0462)	(0.5027)	(0.2084)
N	234,688	234,688	234,688	234,688	234,688	234,688
R^2	0.2090	0.0519	0.1372	0.2107	0.1093	0.2859
Provider FEs	✓	✓	✓	✓	✓	✓
Date FEs	✓	✓	✓	✓	✓	✓
Dep. Var. Treated Pre-Mean	5.85	0.01	1.38	0.59	1.15	1.76
Ind. Var. Mean	0.02	0.02	0.02	0.02	0.02	0.02

* 5%, ** 1%

Notes: table reports difference-in-differences estimates of the effect of potential patient exposure to implicated NECC drugs on the number of unhealthy days during the 180 days after injection. The estimates are based on equation 1, which compares the evolution of outcomes across injections administered by treatment and control group healthcare providers before, during, and after the contamination period. Unhealthy days are defined as the number of days during the 180 following injection in which the patient received care in a hospital-based, post-acute care, or other non-routine setting. The table also reports estimates for related outcomes and selected components of unhealthy days, including all-cause mortality, inpatient hospitalization days, ED visits, skilled nursing facility days, and home health agency visits. DuringContamination refers to injections administered between May 21, 2012 and September 26, 2012, AfterContamination refers to injections administered between September 27, 2012 and December 31, 2013, and the omitted period spans April 1, 2010 through May 20, 2012. Standard errors are clustered at the healthcare provider level.

Table 6. Difference-in-Differences Estimates of Healthcare Spending and Costs Following Potential Patient Exposure to Implicated NECC Drugs

	(1)	(2)	(3)	(4)
	Total Spending	Medicare Payments	Patient OOP	Total Charges
Treated Provider × DuringContamination	2,551.1124**	2,452.7565**	173.5777*	8,416.6334**
	(926.1321)	(836.2127)	(81.7470)	(2,809.4458)
Treated Provider × AfterContamination	752.8775	628.5822	39.6990	876.6598
	(473.7682)	(456.1896)	(47.5830)	(1,886.4156)
N	234,688	234,688	234,688	234,688
R^2	0.1176	0.1259	0.1578	0.1269
Provider FEs	✓	✓	✓	✓
Date FEs	✓	✓	✓	✓
Dep. Var. Treated Pre-Mean	10,383.12	8,941.94	861.95	33,189.76
Ind. Var. Mean	0.02	0.02	0.02	0.02

* 5%, ** 1%

Notes: table reports difference-in-differences estimates of the effect of potential patient exposure to implicated NECC drugs on healthcare spending in the 180-day period after injection. The estimates are based on equation 1, which compares the evolution of outcomes across injections administered by treatment and control group healthcare providers before, during, and after the contamination period. Total healthcare spending is defined as the sum of provider reimbursements across all healthcare claims for care received by the patient in the 180 days after injection. The table also reports estimates for payments made by Medicare, patient out-of-pocket payments, and total provider charges submitted. Provider charges submitted refer to the list prices for healthcare services rendered, rather than realized reimbursements. DuringContamination refers to injections administered between May 21, 2012 and September 26, 2012, AfterContamination refers to injections administered between September 27, 2012 and December 31, 2013, and the omitted period spans April 1, 2010 through May 20, 2012. Standard errors are clustered at the healthcare provider level.

Table 7. Difference-in-Differences Estimates of Healthcare Outcomes Following Potential Exposure to Implicated NECC Drugs, Among Injections Not Resulting in Contamination-Related Infection Diagnosis

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
	Unhealthy Days	Inpatient Days	ED Visits	Post-Acute Care Days	Lumbar Punctures	E&M Events	Spinal MPA Injections	Total Spending
Treated Provider × DuringContamination	2.6939*	0.1488	0.0615	1.4114*	0.0658*	1.3211*	−0.2201*	726.9631
	(1.1287)	(0.1555)	(0.0631)	(0.6379)	(0.0303)	(0.5419)	(0.0868)	(724.6712)
Treated Provider × AfterContamination	0.8016	−0.1592	−0.0488	0.7387	−0.0023	0.8607	−0.1096	255.9932
	(0.7510)	(0.1031)	(0.0482)	(0.5534)	(0.0022)	(0.5046)	(0.1096)	(465.4375)
N	231,643	231,643	231,643	231,643	231,643	231,643	231,643	231,643
R^2	0.2082	0.1374	0.2092	0.2719	0.0603	0.2360	0.2089	0.1150
Provider FEs	✓	✓	✓	✓	✓	✓	✓	✓
Date FEs	✓	✓	✓	✓	✓	✓	✓	✓
Dep. Var. Treated Pre-Mean	5.77	1.36	0.58	3.02	0	16.26	1.16	10,326.26
Ind. Var. Mean	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02

* 5%, ** 1%

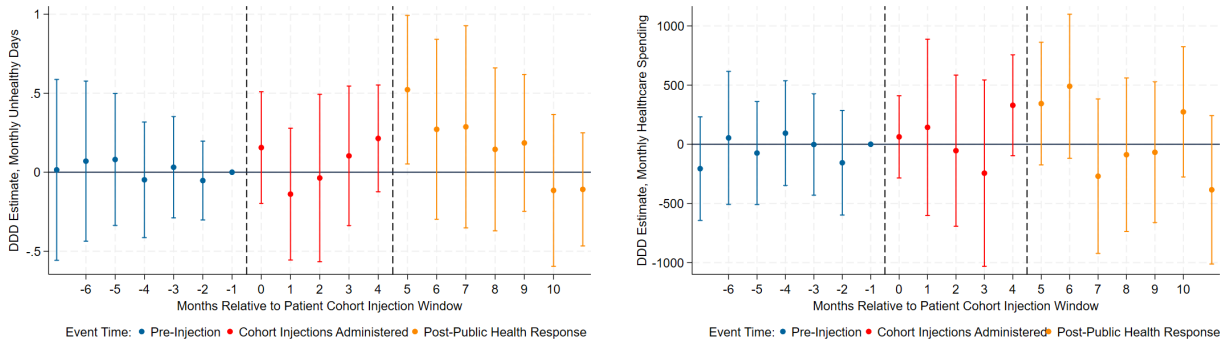
Notes: table provides suggestive evidence of precautionary responses to potential patient exposure to the implicated NECC drugs by reporting estimates from the main difference-in-differences specification from equation 1 when restricting the regression sample to spinal MPA injections that were not followed by an NECC outbreak-related diagnosis in the 180 days after injection. DuringContamination refers to injections administered between May 21, 2012 and September 26, 2012, AfterContamination refers to injections administered between September 27, 2012 and December 31, 2013, and the omitted period spans April 1, 2010 through May 20, 2012. Standard errors are clustered at the healthcare provider level.

Table 8. Heterogeneity Analysis: Difference-in-Differences Estimates of Healthcare Outcomes Following Potential Exposure to Implicated NECC Drugs, by Post-Injection Contamination-Related Infection Diagnosis

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
	Unhealthy Days	Inpatient Days	ED Visits	Post-Acute Care Days	Lumbar Punctures	E&M Events	Spinal MPA Injections	Total Spending
Treated Provider, No Infection × DuringContamination	2.7626*	0.1640	0.0633	1.4597*	0.0626*	1.3485*	−0.2221*	784.7629
	(1.1334)	(0.1533)	(0.0630)	(0.6404)	(0.0303)	(0.5440)	(0.0866)	(728.1083)
Treated Provider, Infection Diagnosis × DuringContamination	21.9659**	7.3347**	1.1347**	13.2810**	0.8333**	19.6110**	−0.3714	23,573.1698**
	(7.3824)	(2.8330)	(0.2097)	(5.1457)	(0.2597)	(7.2885)	(0.2092)	(5,858.5141)
Treated Provider, No Infection × AfterContamination	0.8537	−0.1314	−0.0480	0.7460	−0.0021	0.8828	−0.1090	250.5810
	(0.7381)	(0.1009)	(0.0478)	(0.5447)	(0.0028)	(0.5031)	(0.1093)	(478.1770)
Treated Provider, Infection Diagnosis × AfterContamination	20.5334*	6.9503*	1.0023**	9.7468	−0.1609	19.7894*	−0.0871	22,345.2131**
	(8.3038)	(3.4503)	(0.2289)	(5.5643)	(0.1765)	(8.2021)	(0.2317)	(7,402.2148)
N	234,688	234,688	234,688	234,688	234,688	234,688	234,688	234,688
R^2	0.2092	0.1380	0.2108	0.2684	0.0663	0.2338	0.2086	0.1181
Provider FEs	✓	✓	✓	✓	✓	✓	✓	✓
Date FEs	✓	✓	✓	✓	✓	✓	✓	✓
Dep. Var. Treated Pre-Mean	5.85	1.38	0.59	3.09	0.01	16.36	1.16	10,383.12
Ind. Var. Mean	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02

* 5%, ** 1%

Notes: table provides suggestive evidence of precautionary responses to potential patient exposure to the implicated NECC drugs by reporting estimates from the main difference-in-differences specification from equation 1 when using a categorical version of the provider-level treatment variable that separates treatment group injections by whether they were followed by an NECC outbreak-related infection diagnosis in the 180 days after injection. DuringContamination refers to injections administered between May 21, 2012 and September 26, 2012, AfterContamination refers to injections administered between September 27, 2012 and December 31, 2013, and the omitted period spans April 1, 2010 through May 20, 2012. Standard errors are clustered at the healthcare provider level.



(a) Unhealthy Days

(b) Total Healthcare Reimbursements

Figure 8. Timing of Excess Unhealthy Days and Healthcare Spending Following Potential Exposure to Implicated NECC Drugs

Notes: figure examines the emergence of changes in high-intensity healthcare utilization and healthcare spending among patients potentially exposed to the implicated NECC drugs. The figure reports triple-differences event study estimates using a patient-by-month panel dataset composed of two stacked patient cohorts. The first stack is the contamination cohort, which consists of patients who received a spinal MPA injection while the implicated NECC drugs were in circulation, and the second stack is the placebo cohort, which consists of patients who received a spinal MPA injection during the same calendar window one year earlier. The triple-differences estimates compare the monthly evolution of outcomes for patients receiving injections from treatment and control group healthcare providers in the contamination cohort, using the corresponding treatment versus control difference in the placebo cohort as a baseline capturing differential post-injection follow-up care unrelated to the NECC outbreak. Panel (a) reports estimates for unhealthy days, which is defined as the number of days in the month in which the patient received care in hospital-based, post-acute, or other non-routine healthcare settings. Panel (b) reports estimates for total healthcare spending, which is defined as the sum of provider reimbursement across all healthcare claims for care received by the patient in the month. Monthly event time is indexed to the cohort-specific injection window: event months 0–4 correspond to May through September, when patients in each cohort were administered spinal MPA injections. For the contamination cohort, event month 5 corresponds to October 2012, when public health authorities announced the outbreak and issued clinical guidance. Standard errors are clustered at the healthcare provider level, and error bands represent 95% confidence intervals.

A Robustness

This section presents analyses assessing the robustness and sensitivity of the main difference-in-differences estimates of the effects of potential patient exposure on healthcare utilization and spending. Appendix Table A.2 shows that the estimates are robust to measuring outcomes over the 90 and 365 days after injection, rather than over the 180-day horizon used in the main analysis. The estimated effects of potential exposure to the implicated NECC drugs on unhealthy days are positive and statistically significant across all time horizons, increasing from 1.6 days in the 90-day window to 4.2 days in the main 180-day window and 6.9 days in the 365-day window after injection. The components of unhealthy days attributable to hospital-based and post-acute care are similar in magnitude between the 180- and 365-day horizons, with the additional increase over the longer time horizon being driven by a statistically insignificant increase in mortality-related unhealthy days. The concentration of additional hospital and post-acute care within 180 days after injection, without evidence of long-term increases in morbidity, is supported by Appendix Table A.3, which separately estimates effects over days 91 through 180 and days 181 through 365 after injection. Estimated effects on healthcare spending are statistically significant in the 90-day post-injection window. The 365-day spending estimates are similar in magnitude to the main 180-day estimates but are not statistically significant, consistent with greater noise in spending outcomes over longer time horizons.

Appendix Table A.4 shows that the main results are also robust to defining treatment at the level of Hospital Referral Regions (HRRs).[24] I consider both an indicator for whether the HRR received any shipments of the implicated NECC drugs, and a continuous measure equal to the ratio of MPA volume shipped to the HRR in the NECC invoice data to total MPA volume administered by injection in Medicare claims during the contamination period. Rather than capturing the effects of potential patient exposure to the implicated drugs, as in the main provider-level specifications, estimates from these HRR-level specifications should be interpreted as capturing the market-level effects of exposure to the implicated NECC drugs. This broader interpretation reflects that HRR-level treatment allows for potential spillover effects among control group healthcare providers, who did not receive the implicated drugs, to the extent that such responses to the NECC outbreak were proportional to market-level exposure to the contaminated drugs. Estimates using the continuous HRR-level treatment measure are qualitatively and quantitatively similar to the main provider-level difference-in-differences estimates. Estimates using the HRR treatment indicator are attenuated because treatment group providers accounted for only a small share of spinal MPA injections within treated HRRs, implying that a correspondingly small share

[24] The treatment status of Hospital Referral Regions is based on linking the addresses of healthcare facilities that received the implicated drugs in the NECC invoice data to HRRs. The linking uses a mapping of 5-digit ZIP codes to HRRs provided by the Dartmouth Atlas.

Table A.1. Difference-in-Differences Estimates of Healthcare Outcomes Following Potential Patient Exposure to Implicated NECC Drugs, No Controls for Injection Characteristics

	(1)	(2)	(3)	(4)	(5)
	Unhealthy Days	All-Cause Mortality	Hospital Days	Post-Acute Days	Healthcare Spending
Treated Provider × DuringContamination	4.3862**	0.0084	0.9073**	2.5967**	2,795.0302**
	(1.2900)	(0.0057)	(0.2589)	(0.8530)	(885.2250)
Treated Provider × AfterContamination	1.0745	0.0028	0.1001	0.7305	933.9932
	(0.8621)	(0.0047)	(0.1639)	(0.5891)	(526.2439)
N	234,688	234,688	234,688	234,688	234,688
R^2	0.0419	0.0285	0.0372	0.0514	0.0403
Provider FEs	✓	✓	✓	✓	✓
Date FEs	✓	✓	✓	✓	✓
Dep. Var. Treated Pre-Mean	5.85	0.01	1.79	3.09	10,383.12
Ind. Var. Mean	0.02	0.02	0.02	0.02	0.02

* 5%, ** 1%

Notes: table reports the results of the main difference-in-differences specification estimating the effect of potential patient exposure to implicated NECC drugs when excluding controls for observable patient and practitioner characteristics associated with each spinal MPA injection event. DuringContamination refers to injections administered between May 21, 2012 and September 26, 2012, AfterContamination refers to injections administered between September 27, 2012 and December 31, 2013, and the omitted period spans April 1, 2010 through May 20, 2012. Standard errors are clustered at the healthcare provider level.

of injections in these markets were at risk of direct exposure to the implicated NECC drugs. Nevertheless, it is notable that statistically significant effects persist when treatment is aggregated to the HRR level. Patients receiving spinal MPA injections in treated HRRs during the contamination period had a 0.8 pp higher probability of receiving a contamination-related infection diagnosis, experienced 0.57 additional unhealthy days, including a 0.16-day increase in inpatient hospital days, and incurred $426 higher total healthcare spending relative to patients receiving injections in untreated HRRs. The ratio of additional unhealthy days to contamination-related infection diagnosis is qualitatively similar between the provider-level and HRR-level treatment variables, which is consistent with small spillover effects on patients not potentially exposed to the implicated NECC drugs.

Table A.2. Difference-in-Differences Estimates of Healthcare Outcomes Following Potential Patient Exposure to Implicated NECC Drugs, 90- and 365-Day Periods After Injection

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
	90 Days After Injection					**365 Days After Injection**				
	Unhealthy Days	All-Cause Mortality	Hospital Days	Post-Acute Days	Healthcare Spending	Unhealthy Days	All-Cause Mortality	Hospital Days	Post-Acute Days	Healthcare Spending
Treated Provider × DuringContamination	1.5845**	0.0072	0.5019*	0.8327*	1,391.4730*	6.8669**	0.0146	0.8307*	2.9294**	1,924.1446
	(0.5129)	(0.0048)	(0.2033)	(0.3420)	(545.7031)	(2.2928)	(0.0095)	(0.3852)	(0.9692)	(1,571.3894)
Treated Provider × AfterContamination	0.2723	0.0045	−0.0201	0.3072	187.5039	2.5625	0.0045	−0.1688	1.7585	758.4863
	(0.3418)	(0.0024)	(0.0901)	(0.2795)	(265.7727)	(1.7706)	(0.0080)	(0.3197)	(0.8979)	(952.7170)
N	237,249	237,249	237,249	237,249	237,249	230,400	230,400	230,400	230,400	230,400
R^2	0.2237	0.0408	0.1293	0.2697	0.1052	0.1996	0.0780	0.2190	0.2860	0.1705
Provider FEs	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Date FEs	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Dep. Var. Treated Pre-Mean	2.48	0.01	0.88	1.38	5,282.71	15.53	0.03	3.66	7.33	20,819.55
Ind. Var. Mean	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02

* 5%, ** 1%

Notes: table reports difference-in-differences estimates of the effects of potential patient exposure to implicated NECC drugs on healthcare outcomes when considering the 90-day and 365-day periods after injection, rather than the 180-day period used in the main results. Estimates are based on equation 1, which compares the evolution of outcomes across injections administered by treatment and control group healthcare providers before, during, and after the contamination period. DuringContamination refers to injections administered between May 21, 2012 and September 26, 2012, AfterContamination refers to injections administered between September 27, 2012 and December 31, 2013, and the omitted period spans April 1, 2010 through May 20, 2012. Standard errors are clustered at the healthcare provider level.

Table A.3. Difference-in-Differences Estimates of Healthcare Outcomes Following Potential Patient Exposure to Implicated NECC Drugs, 91-180 and 181-365-Day Periods After Injection

	(1)	(2)	(3)	(4)
	Unhealthy Days (91–180)	Unhealthy Days (181–365)	Healthcare Spending (91–180)	Healthcare Spending (181–365)
Treated Provider × DuringContamination	2.6134**	2.5384	1,177.0855	−649.1788
	(0.7999)	(1.5369)	(617.9212)	(906.1630)
Treated Provider × AfterContamination	0.9985*	1.2031	563.6974*	−33.4899
	(0.4430)	(1.2699)	(255.3968)	(737.7150)
N	234,688	230,400	234,688	230,400
R^2	0.1469	0.1537	0.0666	0.1229
Provider FEs	✓	✓	✓	✓
Date FEs	✓	✓	✓	✓
Dep. Var. Treated Pre-Mean	3.35	9.63	5,087.80	10,394.26
Ind. Var. Mean	0.02	0.02	0.02	0.02

* 5%, ** 1%

Notes: To provide additional detail on the timing of outbreak-related care after injection, the table reports difference-in-differences estimates of the effects of potential patient exposure to implicated NECC drugs on healthcare outcomes when considering the time horizon from 91 to 180 and 181 to 365 days after injection. Estimates are based on equation 1, which compares the evolution of outcomes across injections administered by treatment and control group healthcare providers before, during, and after the contamination period. DuringContamination refers to injections administered between May 21, 2012 and September 26, 2012, AfterContamination refers to injections administered between September 27, 2012 and December 31, 2013, and the omitted period spans April 1, 2010 through May 20, 2012. Standard errors are clustered at the healthcare provider level.

Table A.4. Difference-in-Differences Estimates of Healthcare Outcomes Following Injection Using HRR Market-Level Exposure to Implicated NECC Drugs

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
	Outbreak Infection	Outbreak Infection	Lumbar Punctures	Lumbar Punctures	Unhealthy Days	Unhealthy Days	Healthcare Spending	Healthcare Spending
Treated HRR × DuringContamination	0.0080**		0.0203*		0.5755*		426.7010	
	(0.0027)		(0.0080)		(0.2715)		(246.9600)	
HRR Treatment Intensity × DuringContamination		0.0270*		0.0832		2.5882*		2,584.0077**
		(0.0131)		(0.0475)		(1.1345)		(779.9346)
Treated HRR × AfterContamination	0.0019		0.0022*		0.0122		293.1068*	
	(0.0011)		(0.0011)		(0.1630)		(145.2211)	
HRR Treatment Intensity × AfterContamination		0.0077		0.0016		0.3909		359.6472
		(0.0045)		(0.0034)		(0.6724)		(438.1133)
N	236,182	236,182	236,182	236,182	236,182	236,182	236,182	236,182
R^2	0.0187	0.0187	0.0147	0.0149	0.1906	0.1906	0.0964	0.0964
HRR FEs	✓	✓	✓	✓	✓	✓	✓	✓
Date FEs	✓	✓	✓	✓	✓	✓	✓	✓
Dep. Var. Treated Pre-Mean	0.01	0.01	0.01	0.01	7.29	7.29	11,140.05	11,140.05
Ind. Var. Mean	0.36	0.05	0.36	0.05	0.36	0.05	0.36	0.05

* 5%, ** 1%

Notes: table reports difference-in-differences estimates of the effect of market-level exposure to implicated NECC drugs when using treatment variables defined at the level of Hospital Referral Regions (HRRs). Specifically, HRR treatment status is defined by mapping healthcare facilities recorded as receiving the implicated drugs based on NECC invoice data to HRRs using a 5-digit ZIP code to HRR mapping provided by the Dartmouth Atlas. Treated HRR refers to an indicator variable for whether the HRR received any shipments of the implicated NECC drugs. HRR Treatment Intensity is a continuous measure equal to the ratio of MPA volume shipped to the HRR in the NECC invoice data to total MPA volume administered by injection in Medicare claims during the contamination period. The estimates are based on equation 1, which compares the evolution of outcomes across injections administered across HRRs with different treatment statuses before, during, and after the contamination period. DuringContamination refers to injections administered between May 21, 2012 and September 26, 2012, AfterContamination refers to injections administered between September 27, 2012 and December 31, 2013, and the omitted period spans April 1, 2010 through May 20, 2012. Standard errors are clustered at the HRR level.