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When the Big One Came: A Natural Experiment on Demand Shock and Market Structure in India's Influenza Vaccine Markets

Arzi Adbi
INSEAD, Singapore, arzi.adbi@insead.edu

Chirantan Chatterjee
Indian Institute of Management, Ahmedabad, India, chirantanc@iima.ac.in

Matej Drev
School of Public Policy, Georgia Institute of Technology, Atlanta, Georgia, USA, matej.drev@pubpolicy.gatech.edu

Anant Mishra*
Carlson School of Management, University of Minnesota, Minneapolis, Minnesota, USA, mish0049@umn.edu

This study examines the relationship between exogenous demand shock and market structure in India's influenza vaccine markets. Using a novel dataset of detailed purchasing information for vaccines in India, and exploiting the 2009–10 global H1N1 pandemic as an exogenous demand shock, we provide evidence of heterogeneous responses to the shock by domestic and multinational vaccine manufacturers in the influenza vaccine market relative to our control group of all other vaccine markets. We find that such a shock results in a reversal of the market structure for influenza vaccines in India, with a decline in the market share of multinational vaccine manufacturers and significant gains in the market share of domestic vaccine manufacturers. This reversal of the market structure is driven by increased efforts at new product introduction among domestic vaccine manufacturers, the effects of which persist even after the pandemic has ended. Our results remain robust to the use of alternative controls, synthetic control method, coarsened exact matching method, and other relevant estimation methodologies. These results provide new evidence on the role of a pandemic-induced demand shock in the context of an emerging economy by creating differential incentives for domestic and multinational vaccine manufacturers to bring new products to market. We also conduct additional analysis to explore the impact of targeted policy instruments on the new product introduction efforts of domestic vaccine manufacturers. Finally, we discuss the implications of our findings and offer insights into the role of policy on pandemic preparedness in emerging markets facing adverse welfare effects from pandemics.

Key words: demand shocks; influenza; new product development; emerging economy; public policy; natural experiment
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1. Introduction

> "When we think of the major threats to our national security, the first to come to mind are nuclear proliferation, rogue states and global terrorism. But another kind of threat lurks beyond our shores, one from nature, not humans – an avian flu pandemic" (Obama and Lugar 2005).
>
> "The big one is coming, and it's going to be a flu pandemic" (Gupta 2017).

Infectious disease outbreaks pose significant challenges to societies, firms, and governments globally (Deo and Corbett 2009, Yamin and Gavious 2013). For example, following its emergence in December 2013 in West Africa, the Ebola virus claimed more than 11,000 lives;[1] the Zika virus, after its outbreak in Brazil in early 2015, spread to affect nearly 43,000 individuals across the United States.[2] While similar outbreaks continue to affect countries with astonishing regularity, limited solutions are in the offing from either vaccine manufacturers or governments (Fineberg 2014, Tebbens and Thompson 2009). The threat of infectious disease outbreaks is particularly acute in emerging economies, where the bulk of the world population resides and where public and private spending on vaccinations remains disproportionately limited (Partridge and Kieny 2013). Two important questions that require attention from researchers and

policymakers alike arise in this context. First, *how do vaccine manufacturers, both domestic and multinational, respond to pandemic-induced demand shocks in emerging economies?* Second, *do targeted policy instruments—specifically, advanced market commitments (AMCs) in response to pandemic-induced demand shocks—incentivize domestic vaccine manufacturers in emerging economies to bring new products to market?*

We examine the above questions in India's vaccine markets using the 2009–10 H1N1 pandemic as an exogenous demand shock. Our study uses aggregate purchasing data from more than 750,000 private chemists and retailers on 280 vaccine stock keeping units (SKUs) sold in India between 2007 and 2013. We conduct a difference-in-differences analysis to estimate and document the impact of exogenous demand shock on the market structure for multinational and domestic vaccine manufacturers in the influenza vaccine market relative to other vaccine markets in the country. Our unit of observation is at the product-market and month level; the treated group is the influenza vaccine market affected by the pandemic, and the control group is all other vaccine markets not affected by the pandemic.

Our analysis indicates that multinational market share[3] —calculated as the share of revenues earned by multinational vaccine manufacturers relative to total revenues—decreased from around 90% in the pre-pandemic period in India's influenza vaccine market to just above 60% at the time the H1N1 pandemic ended. In contrast, in all other (i.e., non-influenza) vaccine markets, multinational market share rose to almost 60% from 50% in the pre-pandemic period. Further, we find that this significant shift toward domestic manufacturers in the structure of India's influenza vaccine market is driven by their new product introductions in response to pandemic-induced demand shock. This shift is present even in the post-pandemic period, highlighting the persistent benefits of the knowledge and experience domestic vaccine manufacturers gained by investing in a specific technology area (e.g., Cockburn and Henderson 1994, Macher and Boerner 2006)—that is, the development and production of influenza vaccines. These findings remain robust to the use of alternative controls, synthetic control method, and difference-in-differences analysis on a coarsened exact matching (CEM) sample instead of the full sample.

Additional exploratory investigation reveals that government-issued AMCs did not have a distinctive impact in facilitating the development efforts of select domestic vaccine manufacturers following the pandemic. A plausible explanation for this finding could be that the pandemic shock significantly reduced the uncertainty in market demand, providing a sufficient incentive for domestic vaccine manufacturers to bring new products to market and thereby substituting away the benefits of AMCs. Further investigation is needed to understand whether AMCs may be more useful as part of proactive rather than reactive effort by governments in emerging economies.

To summarize, our findings contribute in three ways. First, we demonstrate that in an emerging economy, domestic and multinational vaccine manufacturers differ greatly in their response to pandemic-induced demand shocks, with effects that persist beyond the period of the shock. That is, such shocks reduce demand uncertainty associated with emerging economy vaccine markets and stimulate domestic vaccine manufacturers to bring new products to market and compete with multinational vaccine manufacturers. In this regard, our study complements prior operations management (OM) research on vaccine supply chains, which has largely focused on the production challenges associated with seasonal influenza vaccines in emerging economy settings (e.g., Arifoglu et al. 2012, Deo and Corbett 2009). Second, we build upon the prior work that examines the relationship between demand shocks and new product development efforts in the pharmaceutical industry (e.g., Acemoglu et al. 2006, Dubois et al. 2015). While there is a need for careful identification strategy in this literature that exploits the exogenous occurrence of temporary demand shifters, this research gap is particularly salient in the context of emerging economies. Our study represents an effort to address this gap. Finally, the lack of empirical support for the impact that AMCs have in incentivizing domestic vaccine manufacturers raises important questions for researchers and policymakers alike about the conditions under which such policy instruments may prove effective in stimulating pandemic preparedness in emerging economies and about the timing of such instruments. We discuss potential implications for governments in emerging markets regarding their efforts to incentivize domestic vaccine manufacturers to develop vaccines in advance of a public health crisis.

The remainder of the study is organized as follows. In section 2, we provide the background for the research context, which includes a discussion of the influenza vaccine development process, specific characteristics of India's vaccine markets, and the 2009–10 H1N1 pandemic. We provide an overview of prior OM research on vaccine supply chains and briefly touch upon work on demand shocks and new product development efforts relating to our study. Section 3 presents the hypotheses and is followed by section 4, which describes the data and the model specifications. Section 5 describes the empirical results and estimates from various robustness checks. Finally, section 6 concludes the study with a

discussion of the key findings, the theoretical and policy implications, and the limitations of the study.

2. Research Context

2.1. The Influenza Vaccine Development Process

Vaccination is the primary avenue in the prevention and control of the influenza virus. The virus has multiple strains and is known to evolve over time through antigenic drifts and shifts (CDC 2011). Antigenic drift refers to gradual changes in influenza virus antigens, necessitating yearly updates to the composition of influenza vaccines. Influenza vaccines developed in response to antigenic drifts are referred to as seasonal vaccines. In contrast, antigenic shift refers to a dramatic transformation in influenza virus antigens, rendering existing seasonal vaccines ineffective and giving rise to a pandemic (e.g., the H2N2 pandemic in 1957–1958, the H3N2 pandemic in 1968–1969, and the H1N1 pandemic in 2009–10). In light of the occurrence of antigenic drifts and shifts, the development of influenza vaccines requires continuous surveillance of influenza cases and their global patterns of spread (Cho 2010, Treanor 2004). This surveillance is conducted by the World Health Organization (WHO) via a global network of government agencies, laboratories, and collaboration centers.

Once a specific influenza virus strain of a seasonal or pandemic nature has been identified, the vaccine development process typically spans a 6–8 month period. As shown in Table 1, this process follows a sequence of steps that starts with preparing the virus strain, understanding its growth conditions, developing and manufacturing the product prototype, conducting clinical trials, and procuring regulatory approval; the process ends with packaging and shipping (WHO 2009). Much of the development process is focused on the seasonal influenza virus strain that is expected to be prevalent in North America and Europe. The majority of influenza vaccine manufacturing units therefore are located in these continents and account for nearly 90% of global influenza vaccine production (Jadhav et al. 2009). Their extensive experience in developing seasonal influenza vaccines (e.g., understanding the epidemiology of virus strains, determining effective virus cultivation techniques, and identifying mechanisms for delivering vaccine antigens) ensures these manufacturers keep their place at the forefront of scientific development. In addition, it endows them with expertise in regulatory, manufacturing, and logistical processes for delivering vaccines to large populations, even beyond their domestic borders to emerging economies like India.

2.2. India's Vaccine Markets and the 2009–10 H1N1 Pandemic

The procurement of vaccines from multinational vaccine manufacturers and domestic manufacturers in India is carried out through two channels: public and private. Under the public procurement channel, the Government of India (GoI) runs the Universal Immunization Program (UIP), wherein it purchases vaccines for selected preventable diseases (e.g., tuberculosis, diphtheria, tetanus, and poliomyelitis) in bulk from vaccine manufacturers and makes them available to the public free of cost. The private procurement channel comprises vaccines not covered under UIP, such as recurrent optional vaccines for influenza and typhoid and one-time optional vaccines for diseases prevalent in the developing world, such as cholera. Industry reports suggest that private purchases of vaccines in India exceed public purchases, accounting for approximately 55% of total vaccine purchases (Frost & Sullivan 2013). Despite this fact, India's vaccine markets were quite small and significantly under-penetrated when compared to its global peers

Table 1 Summary of Influenza Vaccine Development Process

Steps in influenza vaccine development	Description of steps
Step 1: Virus Strain Preparation and Validation (1.5 months)	Once the seasonal or the pandemic virus strain is identified, it is prepared and validated for bulk manufacturing at WHO collaboration centers and provided to vaccine manufacturers globally
Step 2: Determining Virus Growth Conditions (1 month)	The vaccine manufacturer uses the strain to identify the optimal growth conditions for producing the virus in embryonated hen's eggs
Step 3: Manufacturing (1 month)	The manufacturing process begins with the virus strain being injected into thousands of embryonated eggs and incubated for 2–3 days where it multiplies. Subsequently, the egg white which includes millions of viruses of the identified strain is harvested and the viruses are separated from the egg white. The viruses are treated with chemicals to inactivate it and refined to generate the antigen (i.e., the virus protein) that is the active ingredient in a vaccine. Finally, the antigen is quality-tested in batches
Step 4: Clinical Trials and Regulatory Approval (3 months)	The vaccine passes through multiple stages (stages I, II, and III) of clinical trials for regulatory approval
Step 5: Packaging and Shipping (1 month)	Following regulatory approval, the vaccine is packaged and shipped

Source: WHO (2009).

in the years leading up to the 2009–10 H1N1 pandemic (Bhadoria et al. 2012).

Once the 2009–10 H1N1 strain of influenza virus struck, it rapidly expanded in scope from its initial outbreak in Veracruz, Mexico, on 12 April 2009; its final global impact reached more than 200 countries by August 2010. India was among the countries affected in the initial months of the outbreak. Three months into the outbreak, the WHO raised its alert to the level of *pandemic* (i.e., phase 6, the highest alert level), accompanied by public requests for vaccines to address the global H1N1 pandemic. By July 2010, the WHO was able to deliver 78 million doses to countries that were eligible to receive donated vaccines. However, India was not eligible to receive donated vaccines because eligibility was based on two factors: (i) the absence of domestic vaccine production capabilities, and (ii) the inability to purchase vaccines on the commercial market (WHO 2010). Specifically, India already had robust public and private-sector manufacturing facilities geared toward producing UIP vaccines (Madhavi 2005), and the GoI had historically demonstrated the capability of purchasing vaccines in large scale on the commercial market when it was deemed necessary (e.g., GoI purchases of poliomyelitis, rotavirus, and pneumococcal conjugate vaccines on a large scale over the previous three decades) (Lahariya 2014). India's ineligibility to receive donated vaccines from the WHO thus presented a substantial market opportunity for multinational and domestic vaccine manufacturers alike.

The H1N1 vaccine development process of domestic vaccine manufacturers began in June 2009, with the Serum Institute of India (SII) among the first few to secure a sublicense from the WHO to develop the vaccine (Dhere et al. 2011). In July–August 2009, sublicenses were secured by two other domestic vaccine manufacturers, Panacea Biotec and Bharat Biotech, for the same purpose (BioSpectrum 2010). The ensuing regulation of vaccine development—as well as production and sales—was carried out by the Drug Controller General of India (DCGI), the chief regulatory organization in India responsible for evaluating the effectiveness of clinical trial results and for ensuring that appropriate scientific and ethical standards were followed in conducting the trials (Gupta et al. 2013). The domestic vaccine manufacturers conducted phase I, II, and III trials and submitted their results to the DCGI for approval, following which they shifted focus to vaccine production.

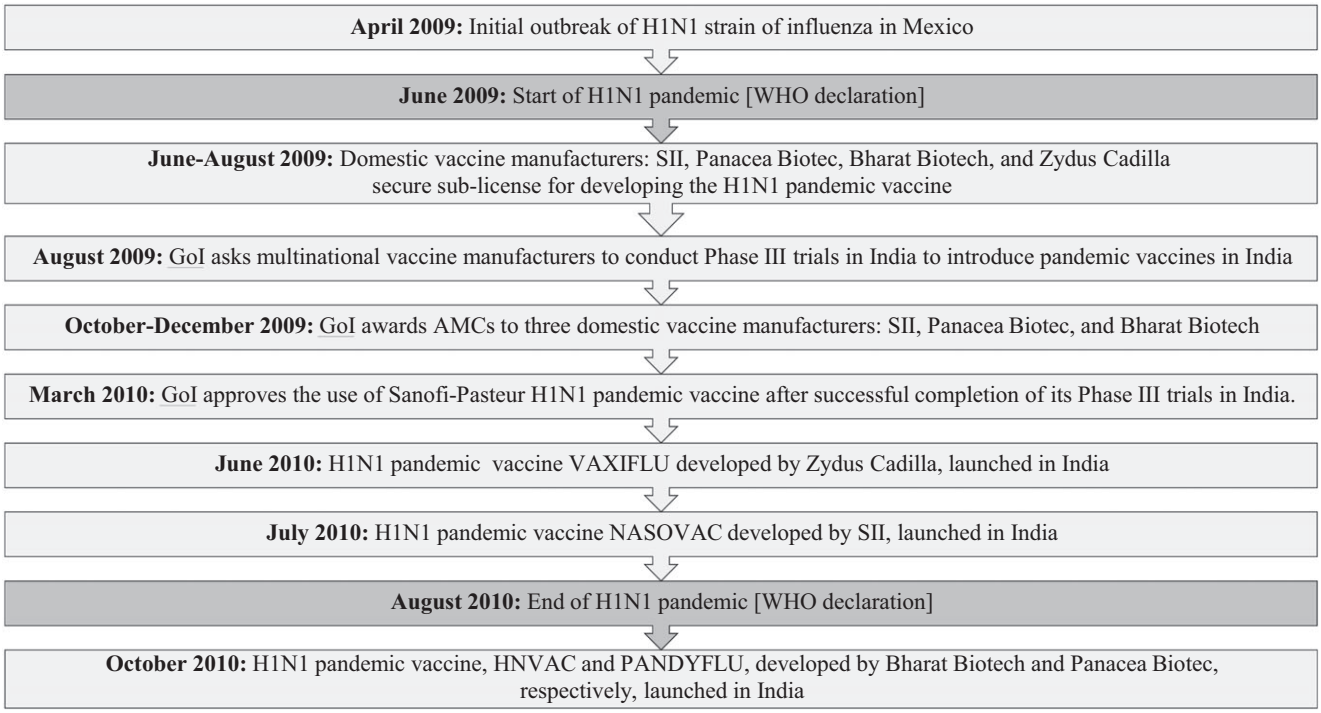
While the regulatory process for vaccines, leading up to their final release to the market, can span anywhere from 5 to 8 years in the case of chronic disease (DiMasi et al. 2016), this process is expedited across countries when a specific disease is accorded pandemic status by the WHO. Despite the expedited nature of the regulatory process, the DCGI rigorously enforced evaluation standards for both multinational and domestic vaccine manufacturers (Dhere et al. 2011). That is, domestic manufacturers were required to undergo the entire clinical trial process, and multinational manufacturers that had successfully developed a vaccine outside India were asked to conduct a phase III clinical trial[4] in India to demonstrate the efficacy of the vaccine in the Indian population (as mentioned in Section 2.4(a), Schedule Y, Drugs and Cosmetics Act 1940 and Rules 1945) (BioSpectrum 2010). In January 2010, following the successful completion of phase III clinical trials in India, the GoI imported 1.5 million doses of the 2009–10 H1N1 pandemic vaccine from Sanofi-Pasteur, a France-based multinational vaccine manufacturer, to be made available to high-risk individuals (e.g., health workers, emergency service personnel) (Khanna and Gupta 2010). Subsequently, in June 2010, Zydus Cadilla became the first domestic vaccine manufacturer to develop a 2009–10 H1N1 pandemic vaccine, followed by SII in July 2010 and Bharat Biotech and Panacea Biotec in October 2010. Figure 1 provides a timeline representing some of the major events associated with the 2009–10 H1N1 pandemic in India's context.

2.3. Prior Literature

The OM literature on vaccine supply chains can be broadly characterized along two lines: one focusing on *supply-side* challenges, such as vaccine shortages and distribution challenges, and the second focusing on *yield uncertainty* challenges associated with vaccine production. For example, focusing on supply-side challenges, Chick et al. (2008) examined the role of contract types (e.g., cost-sharing contracts, pay-back contracts) in incentivizing a vaccine manufacturer to optimize production volumes, while Mamani et al. (2013) focused on the role of the incentives and subsidies the central government provides to vaccine manufacturers to help achieve optimal vaccine coverage. Focusing on yield uncertainty challenges, Deo and Corbett (2009) found that limited levels of yield uncertainty may make the industry attractive to vaccine manufacturers due to upward adjustment of prices, while Cho (2010) investigated vaccine composition as an important driver of yield uncertainty in vaccine production. More recently, Arifoglu et al. (2012) analyzed how government interventions in the form of partial centralization can reduce supply chain inefficiencies that arise from yield uncertainty and self-interested consumers.

Although operational challenges relating to production volumes or yield levels persist, vaccine manufacturers have generally been successful in producing effective seasonal influenza vaccines. However, research on the role of pandemic shocks on

Figure 1 Timeline of Major Events Associated with the 2009–10 H1N1 Pandemic in India's Context



vaccine supply chains is limited, and current methods appear insufficient to produce large amounts of vaccine rapidly enough to combat a pandemic (Fineberg 2014). Because accurate identification of the next pandemic strain cannot be assured in advance, vaccine stockpiling may not prove effective. In this regard, research on firm and government responses to pandemics requires greater attention; this is a key area of focus in this study and one of its main contributions. Our review of the OM literature also indicates that research on vaccine supply chains is based on developed countries, with limited attention paid to emerging economies, where the threat of a pandemic is more salient (Chen et al. 2014). Further, empirical research in this space is largely nonexistent; this can be attributed to the fact that publicly available data on vaccine supply chains remain sparse, more so in the context of emerging economies (Jonas 2014). Compounding this difficulty of access to data is the fact that pandemic shocks are rare events. As such, a longitudinal examination of vaccine supply chains across multiple time periods (before the shock, during the shock, and after the shock) presents a challenge for researchers. Our study attempts to address these gaps in the OM literature.

Our study also builds upon and extends prior research on the link between demand shocks and new product development in the pharmaceutical industry (e.g., Acemoglu et al. 2006, Blume-Kohout and Sood 2013, Branstetter et al. 2014, Dubois et al. 2015, Finkelstein 2004). For example, Finkelstein (2004) finds that the passage of specific US government policies designed to stimulate the usage of preexisting vaccines resulted in a significant increase in the number of clinical trials for new vaccines. Similarly, Blume-Kohout and Sood (2013) found that the passage of the Medicare prescription drug coverage plan (or Medicare Part D) in the United States has had a positive effect on pharmaceutical product development in the therapeutic classes that are primarily prescribed to Medicare beneficiaries. While market size may be crucial in understanding the pace and trajectory of new product development in the pharmaceutical industry, much of this literature has focused on secular/permanent shifts in demand. Yet, exogenous demand shocks, even if temporary, such as pandemics are of considerable interest to public policy and have been known to generate substantive, quasi-permanent effects in regional markets (Parman 2013, Sands et al. 2016). How heterogeneous firms (e.g., multinationals and domestic vaccine manufacturers) respond to the temporary increases in market size that are introduced by pandemic-driven demand shocks remains an open question.

3. Hypothesis Development

3.1. Demand Shock and Market Structure

While the 2009–10 H1N1 pandemic facilitated the increased availability of influenza vaccines in the Indian market, we argue that production responses to the pandemic will differ across multinational and

domestic vaccine manufacturers, with the latter driving the increase in the influenza vaccine supply. We identify the following in support of this argument.

First, heterogeneity in production responses is attributable to differences in production costs across multinational and domestic vaccine manufacturers. Vaccine manufacturing is capital intensive. Firms incur significant fixed costs in creating the production infrastructure (e.g., laboratories, manufacturing facilities, equipment, and compliance with Good Manufacturing Practices)[5] and in acquiring the technical and managerial resources necessary to produce vaccines on a large scale (Pisano 2006). In addition, the costs of developing the distribution channels for handling, storing, and delivering such vaccines to health care providers and pharmacies are significantly high. While multinational vaccine manufacturers attempt to recover fixed costs through entry into newer markets, they may not have the distribution infrastructure in such markets that domestic vaccine manufacturers often already have for their existing products (Khanna and Palepu 2006, Vachani and Smith 2008). As a result, multinational vaccine manufacturers may have needed to make significant additional investments to create the necessary distribution infrastructure for market entry in response to the H1N1 pandemic. Further, the high costs of vaccine development are compounded for multinational vaccine manufacturers in emerging economy markets, where they encounter the "liability of foreignness" (e.g., Hymer 1976, Lamin and Livanis 2013, Zaheer 1995) due to their limited understanding of (i) the emerging economy market environment and within-market/regional variations in vaccination preferences, (ii) the demographic attributes of the emerging economy population, their genetic characteristics, and how these elements affect immune and safety responses, and (iii) regulatory requirements and how they are applied during the vaccine development and clinical trial process. In contrast, while domestic vaccine manufacturers may not find market entry to be attractive enough to recover their fixed costs prior to a pandemic (given that influenza vaccines are optional and are not part of the national vaccination programs in emerging economies),[6] a pandemic shock can generate a marked increase in demand for influenza vaccines that may be sufficient to offset the fixed costs. Coupled with domestic vaccine manufacturers' existing distribution infrastructure and lower variable costs (e.g., raw material and labour costs)[7] in their home markets relative to multinational vaccine manufacturers, we anticipate that the former will be more active in responding to the pandemic shock.

Second, production responses may differ across multinational and domestic vaccine manufacturers due to differences in the opportunity costs. Compared to domestic vaccine manufacturers in an emerging economy, multinational vaccine manufacturers face increased global demand for influenza vaccines, including in their own home markets, which have customers with higher willingness to pay. Additionally, the goals and targets of the average multinational vaccine manufacturer may not vary with events at the level of the local market because global opportunities take precedence over local demand potential (Pisano 2006). This adds to the opportunity costs faced by the multinational firm, which typically manufactures its products closer to its headquarters in controlled settings, outside India. Given that the 2009–10 H1N1 pandemic had global ramifications, we expect multinational vaccine manufacturers to pay less attention to the Indian market, which comprises customers with a lower willingness to pay, and to instead focus on developed markets, which comprise customers with a higher willingness to pay (Khanna and Palepu 2006).

Finally, the multinational vaccine manufacturers' attention to addressing global demand is also drawn by inter-governmental and multilateral agencies (e.g., the WHO), which often require these manufacturers to pledge a portion of their production volumes to the least-developed countries (WHO 2012, Yamada 2009).[8] As a consequence, multinational vaccine manufacturers might face more inelastic supply conditions compared to domestic vaccine manufacturers that have relatively limited supply engagements with inter-governmental and multilateral agencies; they may cede Indian market expansion opportunities to the latter. To summarize, these arguments lead us to propose the following hypothesis:

HYPOTHESIS 1. *The increase in supply of influenza vaccines in India* ***during*** *the* 2009–10 *H1N1 pandemic period relative to pre-pandemic period will be greater for domestic vaccine manufacturers compared to multinational vaccine manufacturers.*

3.2. Persistence of Effects of Demand Shock on Market Structure

Did the 2009–10 H1N1 pandemic foster knowledge acquisition in domestic vaccine manufacturers such that their gains in market share during the shock spilled over to persist beyond the shock? In raising this possibility, we take a closer look at the organizational learning literature (e.g., March 1991) and industry studies pertaining to the pharmaceutical sector (e.g., Danzon et al. 2005, Macher and Boerner 2006) that examine how firms learn from experience in specific technological areas. Specifically, March (1991) argued that as firms develop competency in an area and are rewarded by the market for such competence,

they are more likely to adapt their organizational processes to further develop such competencies. Similarly, Macher and Boerner (2006) contended that the experience of engaging in knowledge production activities in a given technological area in pharmaceutical drug development—ranging from R&D to development, regulatory, and commercialization activities—enables firms to learn from previous mistakes and prior successes, which can be further leveraged in development activities within the same technological area. Highlighting further the path-dependent nature of firm R&D in the pharmaceutical industry, Cockburn and Henderson (1994), and more recently Banerjee and Seibert (2017), contended that a firm's future R&D investments in a given technological area are driven by its previous year's investments in the technological area. Additionally, past experience in a given technological area can enable firms to gain inter-temporal economies of scope and develop more efficient organizational approaches toward knowledge production activities in the same area (Helfat and Eisenhardt 2004, Kaul 2012). For example, Kaul (2012) found that technological innovations induce firms to reconfigure their product portfolio, redeploying resources to areas of new opportunity while divesting from marginal businesses.

Building upon the insights from these studies, we argue that domestic vaccine manufacturers' investments in significant managerial attention and resources during the 2009–10 H1N1 pandemic provided them with important working knowledge and "know how" associated with influenza vaccine development. To that end, Dhere et al. (2011) noted that influenza vaccine manufacturers often need to experiment with various virus cultivation techniques and identify the technique most suitable to their specific environment. Similarly, the experience of navigating the regulatory process provides domestic vaccine manufacturers with a deeper understanding of regulatory protocols and tacit knowledge of various regulatory agencies. This in turn is likely to benefit their ex post operations and enable them to engage in new product introduction efforts in the post-pandemic period. In contrast, the liability of foreignness that multinational vaccine manufacturers typically face when operating in an emerging market setting (e.g., Lamin and Livanis 2013, Zaheer 1995) is likely to increase further in the presence of competition from domestic vaccine manufacturers, particularly as such manufacturers seek to utilize the benefits of production capacity enhancements made during the pandemic period. To this end, evidence from proceedings in the Indian Parliament (Lok Sabha 2010) indicate that the GoI attempted to encourage the indigenous development of influenza vaccines that were geared toward the needs of the local population by issuing AMCs and soft loans[9] to select domestic vaccine manufacturers. We therefore propose the following hypothesis:

HYPOTHESIS 2. *The increase in supply of influenza vaccines in India* ***after*** *the* 2009–10 *H1N1 pandemic period relative to pre-pandemic period will be greater for domestic vaccine manufacturers compared to multinational vaccine manufacturers.*

3.3. Impact of Government-Issued AMCs on Domestic Vaccine Manufacturers

Recent research efforts in OM (e.g., Arifoglu et al. 2012) and in healthcare policymaking (e.g., Berndt and Hurvitz 2005, Berndt et al. 2007, Glennerster et al. 2006) have begun to examine the role of government in encouraging firms to undertake costly investments in R&D and capacity building to develop vaccines. For example, Berndt et al. (2007) noted that government-issued AMCs (i.e., binding contracts offered by governments to vaccine manufacturers that guarantee a viable market for a vaccine) may play a critical role in the development of new products, especially for neglected diseases such as malaria and tuberculosis. By serving as a tool for reducing demand uncertainty (Rangan et al. 2006), AMCs allow firms to recover some of the costs associated with vaccine R&D above and beyond what can be recovered by operating in free markets. Additionally, because AMCs include a specific price that is underwritten into a legally binding contract, they reduce the risk that a vaccine manufacturer will be subjected to price pressure by the government following development of the vaccine (Glennerster et al. 2006). Notwithstanding the theoretical arguments in support of the benefits of AMCs, empirical research on its efficacy remains scarce in the academic literature. More recently, a 2015 study by a collaboration of the GAVI alliance and Boston Consulting Group (BCG) assessed the extent to which a pilot AMC, launched in 2007 (to reduce morbidity and mortality from pneumococcal disease by accelerating the development of pneumococcal conjugate vaccines), achieved its objectives. The study presents mixed findings on the effects of AMCs—while the AMC contributed to the acceleration of supply availability by encouraging recipient vaccine manufactures to invest in capacity expansion, it did not succeed in accelerating the development timelines of vaccine manufacturers with earlier-stage candidates.[10]

The scarcity of empirical studies on the impact of AMCs and the mixed findings of the GAVI Alliance-BCG evaluation raise a fundamental question about the efficacy of AMCs issued by the GoI to domestic vaccine manufacturers (who were in the early stages of vaccine development) after the 2009–

10 H1N1 pandemic. Specifically, three domestic vaccine manufacturers—the SII, Panacea Biotec, and Bharat Biotech—entered into AMC agreements and received 100 million rupees (approximately $1.5 million) each.[11] We conduct an exploratory analysis in our context to examine whether AMCs played a distinctive role in stimulating a greater supply of influenza vaccine from these domestic vaccine manufacturers in the mid-pandemic and post-pandemic periods compared to other domestic vaccine manufacturers.

4. Research Design

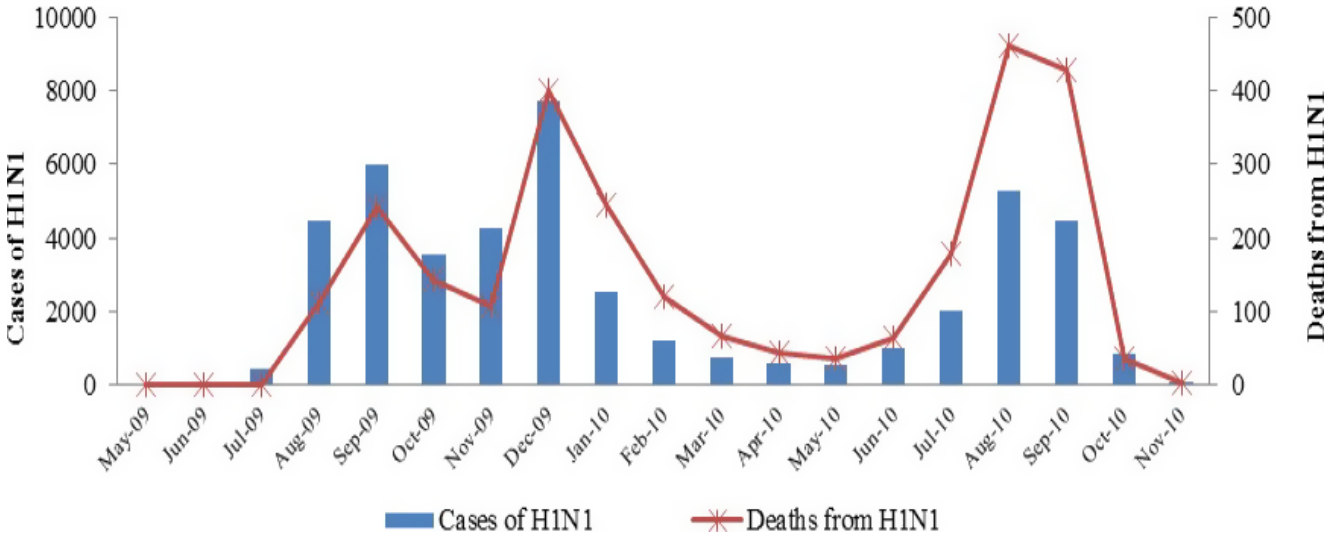
4.1. Data

The data for this study come from the All India Organization of Chemists and Druggists, the largest nodal organization of chemists, pharmacists, and retailers in India, comprising more than 750,000 such entities across the country. Having been employed in recent research (Bhaskarabhatla et al. 2016, McGettigan et al. 2015), the data range monthly from April 2007 to February 2013 and are composed of 280 vaccine SKUs sold in 24 state-regions in India by 31 vaccine manufacturers, of which eight are multinational in nature. Overall, our sample comprises of 20 vaccine product markets with each product market containing multiple vaccine SKUs sold across the different state-regions in India. The data provide information on revenues and the quantity of vaccine SKUs sold at the retailer or pharmacist level (i.e., private procurement) across India.

We identify the exogenous demand shock due to the 2009–10 H1N1 pandemic using official declarations made (and corresponding timelines released) by the WHO. Using the WHO declarations, we identified the onset of the pandemic as June 2009 and the end as August 2010. This allows us to observe the immediate effects of the shock during the pandemic period (the *during_shock* period), as well as the effects after the pandemic ended (the *after_shock* period). There are 26 months of market data prior to the shock, 15 months of data in the *during_shock* period, and 30 months of data in the *after_shock* period. Official statistics from the GoI, as shown in Figure 2, indicate that during the pandemic period, India registered 46,064 officially recorded cases of H1N1 and 2694 deaths.

In our analysis, we define the *treatment* group (i.e., the market segment affected by the demand shock) as comprising all influenza vaccines (seasonal and pandemic vaccines), while the control group comprises all other vaccines.[12] We include all influenza vaccines in the treatment group for the following reasons. First, the 2009–10 H1N1 pandemic virus strain is a specific variation of the influenza virus, and development and manufacturing of the pandemic vaccine follows the same procedure as that of other seasonal vaccines. Further, because the pandemic lasted more than a year and overlapped with the seasonal influenza season across India, we anticipate that the public awareness of influenza vaccination brought about by the 2009–10 H1N1 pandemic also affected the sales of seasonal influenza vaccines. To that end, the US Center for Disease Control (CDC) reported that the 2009–10 influenza season was "very unusual," requiring two vaccines for protection against circulating virus strains: "*one to prevent seasonal influenza viruses that were anticipated to spread and another to prevent influenza caused by the newly emerged 2009 H1N1 virus.*" (CDC 2011). In addition, our conversations with several

Figure 2 Impact of 2009–10 H1N1 Pandemic in India [Color figure can be viewed at wileyonlinelibrary.com]



Source: Ministry of Health and Family Welfare, Government of India.

doctors in Bangalore, India, indicated that seasonal influenza vaccines were often used by doctors during the 2009–10 influenza season to treat patients who reported pandemic influenza symptoms.[13]

4.2. Model Specification: Difference-in-Differences Approach

The identification strategy of this study analytically leverages the role of the 2009–10 H1N1 pandemic as an exogenous demand shock that affected the influenza vaccine market but did not affect the non-influenza vaccine market, thus setting it up as a natural experiment. Although we have data available from various state-regions in India, efforts in controlling the spread of the pandemic within the country, effectively responding to pandemic cases in the country, and ensuring the availability of vaccines in the country were primarily spearheaded by the GoI (also confirmed by the authors in conversations with K. Sujatha Rao, Union Health Secretary of the GoI at the time of the 2009–10 pandemic). Importantly, our theoretical arguments and hypotheses are focused on multinational vs. domestic market share at the national level and do not distinguish across states. Therefore, we aggregate these data up to the national level with our unit of analysis being *product-market-month*.[14]

Because the data are longitudinal, the analyses make use of the data before, during, and after the shock. We use a difference-in-differences estimation approach to estimate the impact of the 2009–10 H1N1 pandemic shock on the market structure in India's vaccine markets, following estimation approaches similar to those employed in recent OM (e.g., Gray et al. 2015, Kumar and Telang 2011) and economics (e.g., Bertrand et al. 2004, Khwaja and Mian 2008) literature.

The functional relationship among the outcome of interest, the existence of the demand shock, the treatment group (reference category is the control group), and control variables are specified as follows:

$$y_{it} = \alpha + \beta_1 shock_t + \beta_2 influenza_i + \beta_3 shock \times influenza_{it} + \beta_4 X_{it} + \sigma_t + \mu_i + \varepsilon_{it} \quad (1)$$

In this equation, the unit of observation is a product-market i (e.g., influenza, polio, measles) in month t at the national level in India; *shock* represents a set of dummy variables to indicate whether the observation was made during the pandemic (i.e., *during_shock*) or after the pandemic (i.e., *after_shock*) relative to the pre-pandemic period; *influenza* represents a dummy variable to identify the treatment group (i.e., the affected product-market segment); and *shock* × *influenza* examines the effects of the demand shock on the outcome of interest for the treatment group relative to the control group (as predicted by Hypotheses 1 and 2). Thus, the interaction terms—*during_shock* × *influenza* and *after_shock* × *influenza*—are the main coefficients of interest as they are the difference-in-differences estimators that provide an estimate of the changes in the outcome of interest in the treatment group relative to the control group in the period "during" and "after" the pandemic compared to the period "before" the pandemic shock.

As product markets may differ in a number of ways, we control for such differences through μ_i, which represents a time-invariant measure of unobserved heterogeneity at the product-market level (i.e., product-market fixed effects). Additionally, we control for time-varying unobserved heterogeneity, σ_t, by including time dummies; X_{it} controls for product-market-and-time varying characteristic (i.e., product–market size). The standard errors are clustered at the panel (i.e., product–market) level to minimize concerns regarding underestimation of standard errors due to auto-correlation among repeated observations at the panel level (Bertrand et al. 2004, Wooldridge 2003).

The outcome variable of interest, y_{it}, is operationalized in terms of two distinct measures of multinational market share in the product–market—that is, multinational market share as a share of overall revenues in the product–market and multinational market share as a share of overall quantities sold in the product–market. Thus, a statistically significant negative coefficient of the difference-in-differences estimator, *during_shock* × *influenza*, would indicate support for Hypothesis 1. Similarly, a statistically significant negative coefficient of the difference-in-differences estimator, *after_shock* × *influenza*, would indicate support for Hypothesis 2. Given that the measures of multinational market share are constrained between 0 and 1, to test the robustness of our results we estimate a generalized linear model (GLM) fractional logit specification in addition to our baseline ordinary least squares (OLS) fixed-effects regression specifications. Table 2 lists the descriptions of key variables used in this study, and Table 3 shows the descriptive statistics and correlations. As expected, the measures of multinational market share in terms of revenues and quantity in Table 3 are highly correlated ($\rho = 0.94$, $p < 0.05$). We also see a positive significant correlation of *influenza* with both revenue ($\rho = 0.20$, $p < 0.05$) and quantity ($\rho = 0.25$, $p < 0.05$) measures, indicating that the multinational market share for influenza vaccines during the period of our study was higher than non-influenza vaccines. A review of the descriptive statistics indicates that the multinational market share by revenues and quantities in all vaccines markets for the entire observation period was non-trivial, averaging around 52% and 45%, respectively.

Table 2 Description of Variables

Variables	Description
Dependent variables	
Multinational_Market_Share_Revenues	Measured as a ratio of multinational vaccine manufacturers' product–market revenues to the total product–market revenues of both multinational and domestic vaccine manufacturers
Multinational_Market_Share_Quantity	Measured as a ratio of multinational vaccine manufacturers' product–market quantities to the total product–market quantities of both multinational and domestic vaccine manufacturers
Independent variables	
during_shock	The period affected by global H1N1 pandemic. It is equal to 1 for months from June 2009 to August 2010 and 0 otherwise
after_shock	The period after the end of global H1N1 pandemic. It is equal to 1 for months from September 2010 to February 2013 (last month in our observation period) and 0 otherwise
influenza	The affected product–market segment, that is, influenza vaccines. It is equal to 1 for influenza vaccines and 0 for other vaccines
during_shock × *influenza*	It indicates the interaction of variables during_dummy and influenza. It is equal to 1 for influenza vaccines from June 2009 to August 2010 and 0 otherwise
after_shock × *influenza*	It indicates the interaction of variables after_dummy and influenza. It is equal to 1 for influenza vaccines from September 2010 to February 2013 and 0 otherwise
Control variables	
Time dummies	Dummy variables for each month *t*
Product–market fixed effects	Fixed effect for each product-market *i*
Product–market size (in rupees)	Total revenues of product–market *i* in month *t*

Table 3 Descriptive Statistics and Correlation

	Variables	Mean	SD	Min	Max	*1*	*2*	*3*	*4*	*5*	*6*
1	Multinational_Market_Share_Revenues	0.52	0.36	0	1	1					
2	Multinational_Market_Share_Quantity	0.45	0.38	0	1	0.94*	1				
3	during_shock	0.21	0.41	0	1	−0.06*	−0.05*	1			
4	after_shock	0.44	0.50	0	1	0.14*	0.12*	−0.45*	1		
5	influenza	0.05	0.22	0	1	0.20*	0.25*	0.00	0.00	1	
6	Product–market size (in rupees)	2.43×10^7	3.70×10^7	535	19.5×10^7	0.09*	0.10*	−0.02	0.12*	−0.08*	1

Notes: $N = 1365$ observations. Unit of analysis is at the product-market and month level. $^*p < 0.05$.

5. Results

5.1. Effect of Pandemic Shock on Indian Vaccine Market

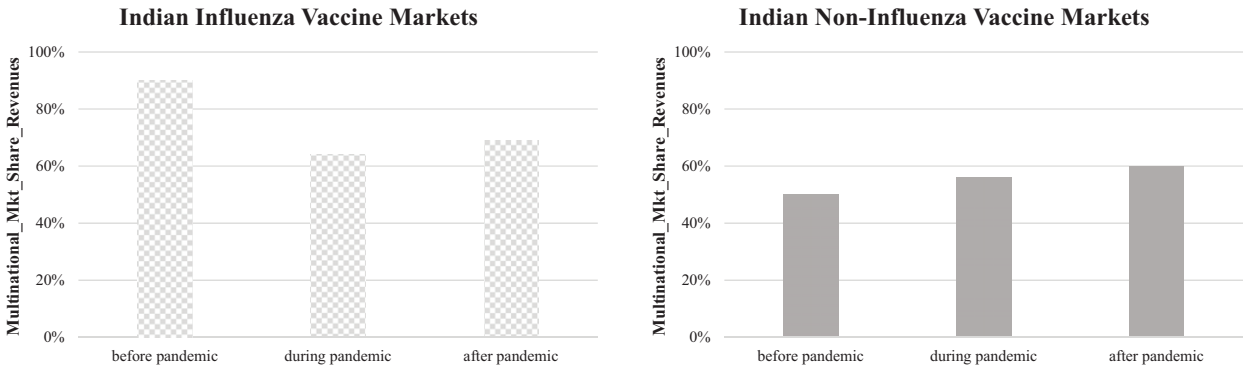
Prior to estimating Equation (1), we first examine whether the pandemic facilitated the increased availability of influenza vaccines in India. We find a sixfold increase in monthly sales quantities of influenza vaccine SKUs in the period during and after the H1N1 pandemic ($\bar{X}_{during\_and\_after\_shock} = 26{,}214$, $SD_{during\_and\_after\_shock} = 19{,}814$, $N = 45$) compared to the sales in the period before the H1N1 pandemic ($\bar{X}_{before\_shock} = 4312$, $SD_{before\_shock} = 3978$, $N = 26$). This difference is statistically significant ($t = 5.56$, $df = 69$, $p < 0.001$). This difference is also robust to the use of monthly revenues (in '000 rupees)[15] and to the use of a two-sample *t*-test with unequal variances applying either Satterthwaite's or Welch's approximation.

Subsequently, we carry out a descriptive analysis of the responses of multinational and domestic vaccine manufacturers to the H1N1 pandemic in Figure 3, as witnessed through the products these manufacturers sold in the market. In June 2009, during the start of the H1N1 pandemic, domestic vaccine manufacturers were selling only one product (measured by the number of SKU-types sold) in the Indian influenza vaccine market, but this had reached four by August 2010, when the end of the pandemic was officially declared. Given the slight lag in bringing products to the influenza vaccine market, this number reached an all-time high of seven around October 2010. By the time the panel ended, domestic vaccine manufacturers were selling three products in the market. The numbers at corresponding time points for multinational manufacturers were three, three, four, and five. In contrast, other vaccine markets in India did not exhibit such a dramatic rise in domestic vaccine manufacturer activity during the same period, as seen in Figure 3. Extending these findings, Figure 4 shows multinational market share as a share of overall revenues in the product market. This share was approximately 90% before the pandemic but declined to just above 60% in the Indian influenza vaccine market after the pandemic. In contrast, one can witness a secular increase in multinational shares, from approximately 50% before the pandemic to almost 60% after the pandemic, in other vaccine product markets in our sample.

Figure 3 New Products and Domestic vs. MNC Firms in Indian Influenza vs. Non-Influenza Vaccine Markets [Color figure can be viewed at wileyonlinelibrary.com]

Source: All India Organization of Chemists and Druggists.

Figure 4 Reversal of Market Structure in Indian Influenza Vaccine Markets



Next, we formalize our descriptive findings by examining the results of the difference-in-differences analysis in Table 4. The inclusion of monthly time dummies to account for unobserved time-varying heterogeneity results in the dropping of some of the month dummies (specifically, two) to avoid multicollinearity while still providing the estimates of *during_shock* and *after_shock*. The coefficients of *influenza* are not additionally estimated in OLS fixed-effects regression as they are already accounted for by the product–market fixed effects. The results point to a dramatic reshaping of the Indian influenza vaccine market during and after the H1N1 pandemic, relative to the country's other vaccine markets. As seen from the OLS fixed-effects estimation results presented in Column 1, the revenue share of multinational firms in the influenza vaccine market fell by 13.5% during the pandemic ($\beta_{during\_shock,\ revenues} + \beta_{during\_shock \times influenza,\ revenues} = -0.135$). The difference-in-differences estimator is both economically and statistically

Table 4 Decline in Multinational Market Share in Indian Influenza Markets During and After 2009–10 H1N1 Pandemic

	Dependent variable: Multinational_Market_Share_Revenues		Dependent variable: Multinational_Market_Share_Quantity	
Independent variables	OLS FE (1)	GLM-fractional Logit (2)	OLS FE (3)	GLM-fractional Logit (4)
during_shock	0.048	0.333	0.008	0.062
	(0.06)	(0.40)	(0.06)	(0.51)
after_shock	0.144*	1.020*	0.096	0.977*
	(0.08)	(0.56)	(0.07)	(0.56)
influenza	–	4.238***	–	5.980***
	–	(0.21)	–	(0.25)
during_shock × influenza	−0.183***	−1.917***	−0.147**	−1.803***
	(0.05)	(0.33)	(0.05)	(0.38)
after_shock × influenza	−0.320***	−2.777***	−0.287***	−2.769***
	(0.05)	(0.31)	(0.04)	(0.33)
Constant	0.453***	−1.258***	0.408***	−2.736***
	(0.06)	(0.32)	(0.05)	(0.37)
Observations	1365	1365	1365	1365
R^2	0.094		0.096	
Log Pseudo Likelihood		−428.6		−377.1
Time dummies	Y	Y	Y	Y
Product–market fixed effects	Y	Y	Y	Y
Number of product-markets	20	20	20	20

Notes: Robust clustered standard errors at the product–market level in parentheses; ***$p < 0.01$, **$p < 0.05$, *$p < 0.1$.
These results indicate a decrease in multinational activity in Indian influenza vaccine market during and after the 2009–10 H1N1 pandemic. The fixed effects OLS estimation results in Column 1 show that the revenue share of multinational firms in the Indian influenza vaccine market fell by 13.5% during the pandemic ($\beta_{during\_shock,\ revenues} + \beta_{during\_shock \times influenza,\ revenues} = -0.135$, $p < 0.01$) compared to before pandemic and 17.6% in the period after the pandemic subsided ($\beta_{after\_shock,\ revenues} + \beta_{after\_shock \times influenza,\ revenues} = -0.176$, $p < 0.01$) compared to before pandemic. Importantly, both the difference-in-differences estimators (i.e., the interaction terms) are economically and statistically significant. The results are qualitatively consistent with GLM-Fractional Logit regression presented in Column 2, and also when we use an alternative measure of multinational market share in terms of the quantities sold (Columns 3 and 4). Note that the coefficient of *influenza* will not be additionally estimated in the fixed effects OLS estimation as product–market fixed effects are already employed.

significant ($\beta_{during\_shock \times influenza,\ revenues} = -0.183$, $p < 0.01$). Similarly, we observe that the revenue share of multinational firms in the influenza vaccine market fell by 17.6% after the pandemic ($\beta_{after\_shock,\ revenues} + \beta_{after\_shock \times influenza,\ revenues} = -0.176$). The difference-in-differences estimator is again both economically and statistically significant ($\beta_{after\_shock \times influenza,\ revenues} = -0.320$, $p < 0.01$). These results are qualitatively consistent with the GLM regression results presented in Column 2. The results when using an alternative multinational market share measure based on quantities of products sold present a similar inference, as shown in Column 3 of Table 4. Specifically, we find the quantity share of multinational firms in the influenza vaccine market dropped by 13.9% during the pandemic ($\beta_{during\_shock,\ quantities} + \beta_{during\_shock \times influenza,\ quantities} = -0.139$), followed by a 19.1% drop in the period after the pandemic subsided ($\beta_{after\_shock,\ quantities} + \beta_{after\_shock \times influenza,\ quantities} = -0.191$); both difference-in-differences estimators (i.e., the interaction terms) are economically and statistically significant.[16]

To summarize, we find strong support for Hypothesis 1, which posits that the greater availability of influenza vaccines in India following the 2009–10 H1N1 pandemic is driven by domestic vaccine manufacturers relative to multinational vaccine manufacturers. In addition, this trend in market structure persists beyond the shock, as evidenced by the continued decline in multinational market share in the after-pandemic period, providing support for Hypothesis 2.[17]

5.2. Exploratory Analysis— Effect of AMCs on Domestic Vaccine Manufacturers

Beyond the main results, we conduct additional exploratory analysis to examine whether the increased supply of influenza vaccines by domestic vaccine manufacturers in response to the 2009–10 H1N1 pandemic was driven primarily by those manufacturers who had received government-issued AMCs during the pandemic. We find that the monthly revenues (in '000 rupees) of non-AMC-supported influenza vaccines from domestic vaccine manufacturers ($\bar{X}_{non\_AMC} = 4609$, $SD_{non\_AMC} = 7377$, $N = 44$) was about three-fold higher than that of AMC-supported influenza vaccines from domestic vaccine manufacturers ($\bar{X}_{AMC} = 1529$, $SD_{AMC} = 2974$, $N = 19$). This difference is statistically significant ($t = 1.75$, $df = 61$, $p < 0.10$). Further, this difference is

robust to the use of monthly sales quantity[18] as well as the use of the same comparison time periods (i.e., 19 time periods for which the AMC-supported influenza vaccine sales were observed); consistent results are found when using a two-sample *t*-test with unequal variances applying either Satterthwaite's or Welch's approximation.

Subsequently, we carry out a regression analysis using the sample of domestic vaccine manufacturers' products within the influenza vaccine market. Because AMCs were awarded for specific products (i.e., SKUs), using SKU-month as the unit of analysis, we can examine whether the AMCs had positive effects on the monthly revenues and sales quantity of influenza vaccines from domestic vaccine manufacturers. We estimate an OLS fixed-effects regression with SKU fixed-effects, while controlling for monthly time dummies. The results from this analysis are shown in Table 5. To minimize skewness, we log-transformed the monthly revenues and sales quantity measures in our analysis. Column 1 of Table 5 indicates that, compared to the before-pandemic period, domestic vaccine manufacturers' influenza vaccine sales by revenue increased substantively in the during-pandemic period ($\beta = 8.570$, $p < 0.05$) and in the after-pandemic period ($\beta = 4.72$, $p < 0.05$). However, as the interaction terms reveal, there is no statistically significant effect of AMCs in either the during-pandemic period or after-pandemic period. Similar patterns are observed if sales are measured by quantity (Column 2) instead of by revenue. Taken together, results suggest that AMCs may not have played a distinctive role in stimulating a greater supply of influenza vaccines from domestic vaccine manufacturers.

While the lack of support for AMC effects is interesting, we cautiously interpret this finding as preliminary in nature requiring greater replication. It is plausible that the following factors specific to our study context may have had a bearing on the above finding. First, the financial incentives AMCs provided to recipient domestic vaccine manufacturers could have been insufficient ($1.5 million over two years) given the high costs of vaccine development. Further, our interviews with AMC-recipient domestic vaccine manufacturers suggest that the AMCs were difficult to execute, often leading to legal arbitration issues.[19] This points toward the possibility that legal and economic issues relating to contract design (especially in an emerging economy context) are of first-order importance and may determine the efficacy of AMCs (Berndt and Hurvitz 2005). Second, only three products— Nasovac™ by the SII, HNVAC™ by Bharat Biotech, and Pandyflu™ by Panacea Biotec— were launched in response to AMCs, and these products captured only a fraction of the market share in influenza vaccine markets in India. This points toward the possibility that, though there might be a compelling theoretical case for how AMCs could spur development efforts in vaccine manufacturing, practical issues that need further empirical examination remain. Third, given that AMCs are policy instruments that can spur development activity among vaccine manufacturers through the mechanism of reducing uncertainty (Rangan et al. 2006) in market demand, it is possible that the presence of a pandemic shock (which serves as an alternative channel for uncertainty reduction in market demand) may have substituted away some of their distinctive effects. In sum, given these reasons and the preliminary nature of our findings, the effects of AMCs on the extensive margin should potentially be more carefully examined to understand whether such support may generate positive externalities and push domestic vaccine manufacturers to engage in R&D during public health emergencies.

Table 5 Effect of AMCs on Sales of Influenza Vaccines by Domestic Vaccine Manufacturers

Product-market	Influenza SKU_Sales_Value (Log) OLS FE	Influenza SKU_Sales_Qty (Log) OLS FE
Independent variables	(1)	(2)
during_shock	8.570**	4.724**
	(3.479)	(1.968)
after_shock	4.969*	2.345
	(2.688)	(1.354)
during_shock X AMC	−2.773	−1.216
	(2.015)	(1.110)
after_shock X AMC	−2.102	−1.243
	(2.248)	(1.158)
Constant	−0.000	−0.000
	(1.139)	(0.593)
Observations	568	568
R^2	0.400	0.399
Time Dummies	Y	Y
SKU Fixed Effects	Y	Y
Number of SKUs	8	8

Notes: Robust clustered standard errors at the SKU level in parentheses; ***$p < 0.01$, **$p < 0.05$, *$p < 0.1$.

We document whether government-issued AMCs had positive effects on monthly revenues and quantity sales of influenza vaccines of domestic vaccine manufacturers. To minimize skewness, we log-transformed the monthly revenues and quantity sales measures in our analysis. The fixed effects OLS results in Column 1 indicate that compared to before-pandemic period, domestic vaccine manufacturers' influenza vaccine sales by revenues increased substantively in the during-pandemic period ($\beta = 8.570$, $p < 0.05$) and also in the after pandemic period ($\beta = 4.72$, $p < 0.05$). However, as the interaction terms reveal, there is no statistically significant effect of AMCs in either the during-pandemic period or after-pandemic period. Similar pattern of results are observed if sales are measured by quantity (Column 2) instead of by revenues.

5.3. Robustness Checks

We extend our empirical analysis by performing relevant robustness tests, as discussed below.[20]

5.3.1. An Assessment of the Parallel Trends Assumption. A potential concern with the difference-in-differences estimation approach is that the treatment group and the control group may have been on different trends even prior to the H1N1 pandemic demand shock. Following Angrist and Pischke (2009) and prior studies (e.g., Singh and Agarwal 2011), we employed a standard econometric procedure to examine whether or not the trends between treatment group and control group show divergence in the pre-pandemic period. Table A1 in Appendix A shows the results from this analysis. In this table, each period is defined as one year, except for the last period (i.e., period 6, which has data for 11 months).[21] Periods 1 and 2 are before the occurrence of the H1N1 pandemic. As Period 1 serves as the omitted reference category in the regression analyses, a statistically significant coefficient of *period 2 × influenza* would indicate a violation of the parallel trends assumption. However, in both Columns 1 and 2 of Table A1, the coefficients of *period 2 × influenza* reveal no indication of diverging trends for multinational vaccine manufacturers' share (in revenues or in quantities) between influenza and non-influenza vaccines in the pre-pandemic period.

5.3.2. Alternative Control Group that Excludes UIP Vaccines. Given that some vaccines in India are primarily procured by the GoI under UIP, a question may arise regarding whether or not they should be considered a part of the control group. It is plausible that government support lends UIP vaccines a unique characteristic in terms of their market structure when compared to non-UIP vaccines, indicating that the latter may represent a sharper control group in our analysis given that influenza is a non-UIP vaccine. We therefore conduct additional analysis with an alternative control group that excludes the UIP vaccines. This reduces the number of product–markets from 20 to 15 and the number of observations from 1365 to 1010. Despite the exclusion of the UIP vaccines from the control group, the results of this analysis shown in Columns 1 and 5 of Table 6 remain qualitatively similar to those of the main analysis.

5.3.3. Analysis Using a Synthetic Control Group. The synthetic control method for making causal inferences has received increasing attention in the recent business literature (e.g., Conti and Valentini 2018, Tirunillai and Tellis 2017), following the seminal work by Abadie et al. (2010, 2015). In this method, using data on outcomes in the pre-treatment period, the control group is constructed as a weighted average of the available control units (i.e., all 19 non-influenza vaccine panels in our research setting). Weights are assigned to all available control units to create the synthetic control group by using an optimization procedure that minimizes the root mean squared prediction error on pre-treatment outcomes.

Although the intuition of the synthetic control method is similar to matching techniques (e.g., propensity score matching, CEM) that aim to develop

Table 6 Robustness Checks

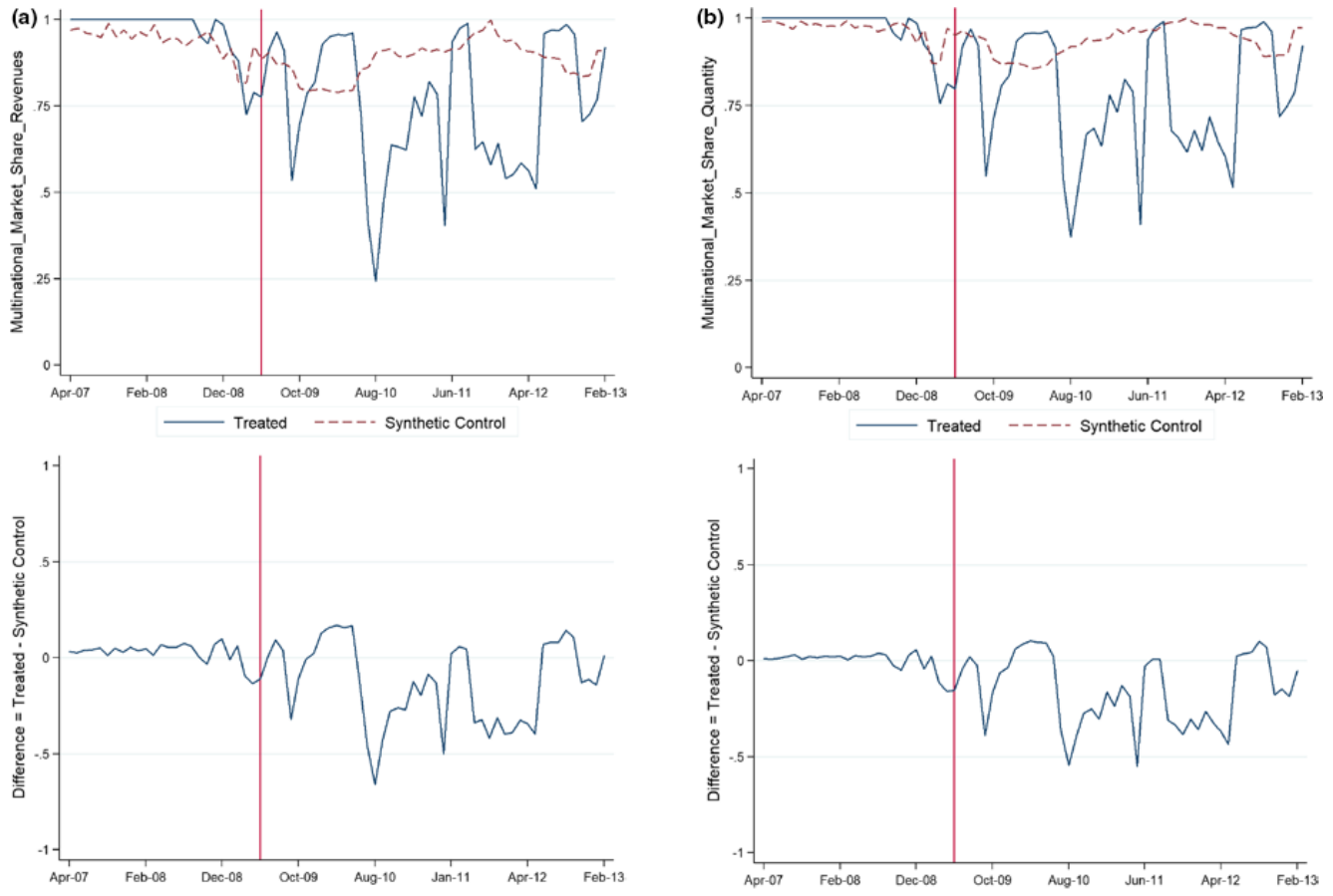
	Dependent variable:				Dependent variable:			
	Multinational_Market_Share_Revenues				Multinational_Market_Share_Quantity			
Independent variables	OLS FE Alternative control (1)	OLS FE Synthetic control (2)	OLS FE Coarsened exact matching (3)	OLS FE Excl. AMC products (4)	OLS FE Alternative control (5)	OLS FE Synthetic control (6)	OLS FE Coarsened exact matching (7)	OLS FE Excl. AMC products (8)
during_shock	0.018	−0.313	−0.291	0.053	−0.022	−0.246	−0.241	0.013
	(0.07)	(0.29)	(0.28)	(0.07)	(0.06)	(0.21)	(0.23)	(0.06)
after_shock	0.191**	−0.109	0.073	0.084	0.098	−0.104	0.063	0.039
	(0.09)	(0.08)	(0.10)	(0.07)	(0.06)	(0.07)	(0.09)	(0.06)
during_shock × influenza	−0.364**	−0.072***	−0.176***	−0.165***	−0.302**	−0.066***	−0.143***	−0.122**
	(0.13)	(0.00)	(0.06)	(0.05)	(0.13)	(0.00)	(0.05)	(0.05)
after_shock × influenza	−0.447***	−0.199***	−0.227***	−0.310***	−0.369***	−0.178***	−0.206***	−0.276***
	(0.08)	(0.00)	(0.04)	(0.05)	(0.07)	(0.00)	(0.03)	(0.04)
Constant	0.550***	0.985***	1.020**	0.452***	0.529***	0.987***	1.018**	0.408***
	(0.07)	(0.01)	(0.02)	(0.06)	(0.05)	(0.01)	(0.02)	(0.05)
Observations	1010	142	142	1365	1010	142	142	1365
R^2	0.195	0.629	0.752	0.092	0.169	0.639	0.754	0.094
Time dummies	Y	Y	Y	Y	Y	Y	Y	Y
Product–market fixed Effects	Y	Y	Y	Y	Y	Y	Y	Y
Number of product-markets	15	2	2	20	15	2	2	20

Notes: Columns 1, 4, 5, and 8 show robust clustered standard errors at the product-market level in parentheses. ***$p < 0.01$, **$p < 0.05$, *$p < 0.1$.

an appropriate control group for comparison against a treatment group, it offers three key advantages over matching techniques (Doudchenko and Imbens 2017, Tirunillai and Tellis 2017). First, the data-driven procedure used in the construction of a synthetic control group minimizes researcher discretion and guards against the creation of extreme counterfactuals for making comparisons. This is in contrast to matching techniques where the selection of covariates can be a subjective process that is influenced in part by the researcher's knowledge and discretion, and can result in the creation of biased control groups. Second, the synthetic control uses a combination of control units to serve as a comparison group in contrast to matching techniques which find a single control unit for each treatment unit when using a stringent matching procedure. Third, the synthetic control method creates control groups that are matched on both observed covariates and unobserved time-varying factors, compared to matching techniques that generate control groups predominantly based on observed covariates. As such, the synthetic control method can reduce endogeneity concerns related to omission of unobserved time-varying factors in the selection of control groups (Conti and Valentini 2018). Given these advantages, we use the synthetic control method to test the robustness of our main results.

Using the data from the pre-pandemic period on multinational vaccine manufacturers' share by revenues as the outcome of interest, a synthetic control group is constructed as the weighted average of all 19 non-influenza vaccine panels in our research setting.[22] Next, we compare the multinational market share by revenues in the treatment group with that in the synthetic control group in the during-pandemic and after-pandemic periods. As seen in Figure 5a, prior to the pandemic shock, the multinational market share by revenues is almost identical in the treated group and the synthetic control group. However, after the pandemic shock (denoted by the red vertical line), we see a substantive reduction in this measure in the treated group compared to the synthetic control group with the reduction averaging around −25% in the during- and post-pandemic periods. The top and bottom panels of Figure 5b show similar plots for the multinational vaccine manufacturers' share by quantity. Subsequently, consistent with Peri and Yasenov (2017), we also estimate the impact of the pandemic

Figure 5 **(a) Comparison of Multinational Market Share by Revenues between the Treated and Synthetic Control groups. (b) Comparison of Multinational Market Share by Quantity between the Treated and Synthetic Control groups [Color figure can be viewed at wileyonlinelibrary.com]**



shock on the treatment and synthetic control groups in a difference-in-differences framework. As shown in Columns 2 and 6 of Table 6, the results from this analysis remain qualitatively similar to the main results.

5.3.4. Analysis Using the CEM Method. Notwithstanding the benefits of the synthetic control method over matching techniques, we conducted a robustness check by constructing a matched sample using the CEM method, based on a set of observable product–market characteristics (Iacus et al. 2012, Nandkumar and Srikanth 2016, Singh and Agarwal 2011). Such an approach still relies on a "selection on observables" assumption that does not fully eliminate endogeneity concerns related to unobservable factors in the selection of control groups. However, to the extent that unobservable and observable parameters could be correlated, the CEM method allows us to minimize the possibility that the observed results are driven by unobservable differences between the treatment and control groups (Iacus et al. 2012, Nandkumar and Srikanth 2016). Using this method, we constructed a sample that matches product-markets in the pre-treatment period on the *average number of firms* competing in the product-market, the *average number of states* where the vaccines are sold in the product-market, the *average number of SKUs* (i.e., stock-keeping units or products) available in the product-market, and the *average multinational market share* (by revenues) in the product market. Using these criteria, we are able to find comparable matches, termed the CEM sample. Following Singh and Agarwal (2011), we subsequently perform our difference-in-differences estimation on the CEM sample. As shown in Columns 3 and 7 in Table 6, we find that the CEM results are consistent with both the main analysis and synthetic control method results.

5.3.5. Analysis by Excluding AMC-Supported Domestic Firms. To estimate the proportion of the impact that was derived from the products that received AMC support, we conducted additional analysis on a sample that excluded AMC products. While this approach mechanically discounts the effects of competition in the market, as seen in Columns 4 and 8 in Table 6, the effect sizes are qualitatively similar to those found in our main analysis with the difference-in-differences estimators (i.e., the interaction terms) remaining economically and statistically significant.

In addition to the above robustness checks, we also carried out analysis at the state-level as well as a meta-analysis of the effect sizes using the single paper meta-analysis approach suggested by McShane and Böckenholt (2017). Details of these analysis and estimation results are presented in Appendix A.

6. Conclusion

6.1. Summary and Contributions

We examine in this article what is very likely to be a grand challenge for modern societies and vaccine manufacturers in the developing world. Despite technological advancements and decades of medical innovation, pandemics continue to inflict significant welfare costs on nations across the globe. Using the 2009–10 H1N1 pandemic as an exogenous shock and employing a novel dataset that tracks private retail vaccine sales in India, we examine how the pandemic-driven increase in the market size for influenza vaccines shifts the market structure amidst the heterogeneous firm responses of domestic and multinational manufacturers. We find that this reversal of the influenza vaccine market structure in India is driven by the new product introductions of domestic vaccine manufacturers, with effects that persist even after the shock has ended. Finally, we examine the impact of targeted policy instruments, specifically AMCs, in stimulating domestic vaccine manufacturers to introduce new products in India's influenza vaccine market; we do not find empirical evidence in support of any distinctive benefits of AMCs in our study's context.

Our results make some fundamental contributions to the extant literature. At the outset, our study findings contribute to the OM literature on vaccine supply chains—which has primarily examined the production and distribution of seasonal flu vaccines (e.g., Arifoglu et al. 2012, Chick et al. 2008, Cho 2010)—by highlighting the role of pandemic shocks in spurring new product development in the domestic vaccine manufacturing sector. Our findings provide novel evidence regarding the differential responses to pandemic demand shocks across domestic and multinational vaccine manufacturers. We explicate the underlying potential mechanisms through which domestic vaccine manufacturers bring new products to market and capture market share. Our study also addresses an important gap in the OM literature by focusing on the context of emerging economies, where the threat of pandemics is higher because vaccine shortages are likely to be greater. This is in contrast to much of the existing studies on vaccine supply chains, which have focused on the context of developed economies (Kraiselburd and Yadav 2013).

Beyond the OM literature, our findings contribute to prior studies that have focused on the link between demand shocks and new product development in the pharmaceutical industry (Cohen 2010). Existing studies in this area do not report empirical evidence from the developing world, and even in the context of the developed world, research has only emerged in recent years (Acemoglu et al. 2006, Finkelstein 2004). This is surprising, considering pandemics have cross-border

spillover implications. Additionally, primary reliance on the innovation capabilities of the developed world during pandemics does not present an optimal way forward, as the recent Ebola crisis and the ongoing Zika crisis suggest. In documenting variations between domestic and multinational vaccine manufacturers' firm responses to the 2009–10 H1N1 pandemic in India, we contribute answers to the classic question of how market size incentivizes firms to introduce new products. In addition, documentation of the persistence of market share among domestic manufacturers after the 2009–10 H1N1 pandemic suggests the associated development of knowledge and learning benefits in these firms (Banerjee and Seibert 2017, Macher and Boerner 2006).

6.2. Implications for Policy

Findings from our study also have important implications for policy regarding pandemic preparedness in emerging economies. An influenza pandemic presents a threat to global security (Sands et al. 2016), and efforts toward pandemic preparedness have received much recent attention from governments, global agencies, and the popular press. The potential for such a pandemic to arise remains particularly acute, with more adverse consequences for emerging economies. The persistent efforts, therefore, of domestic vaccine manufacturers in responding to the 2009–10 H1N1 pandemic shock in India's vaccine market provides "stability" during national crises and thus presents a sharp contrast to the muted response of multinational vaccine manufacturers, highlighting the significant risk emerging economies face in relying solely on multinational vaccine manufacturers during such events. These findings echo in part Görg and Strobl's (2003) characterization of multinational firms as "footloose" during moments of national crisis in many countries and are consistent with the results of Godart et al.'s (2012) study on the 2008 banking crisis in Ireland, which found that while multinational firms had significantly lower exit rates than comparable domestic firms prior to the crisis, their exit rates increased substantially to the same levels as domestic firms. The footloose behavior of multinational vaccine manufacturers observed in India's vaccine markets in response to the 2009–10 H1N1 pandemic may also be driven by pressures on them to address increasing demand for influenza vaccines in their home countries. Such pressures on multinational vaccine manufacturers are not without historical precedence. For example, during the 1976 H1N1 outbreak in US, vaccine manufacturers based in US were strongly urged by the federal government to address domestic needs first before exporting the vaccine to other countries (Fedson 2003). Similarly, prior to the outbreak of 2009–10 H1N1 pandemic, European governments were actively encouraged to enter into contractual agreements with European vaccine manufacturers to secure the domestic supply of vaccines in the event of a pandemic (Hessel and The European Vaccine Manufacturers Influenza Vaccine Group 2009).

Given these contrasting responses, the role of government efforts in developing the domestic vaccine industry to respond to crisis events in emerging economies cannot be overstated. Toward that end, the lack of empirical evidence regarding the distinctive role of AMCs in stimulating domestic vaccine manufacturers to introduce new products in India's influenza vaccine market raises fundamental questions regarding the conditions under which AMCs may be effective during a crisis scenario and when such policy instruments should be timed. As our findings suggest, the existence of strong, pandemic-induced market demand may be a sufficient incentive for domestic vaccine manufacturers to bring new products to market in and of itself, as the pandemic reduces demand uncertainty on its own. As such, AMCs may be more useful as a part of "preemptive" efforts by governments in emerging economies to simulate a positive demand shock when the demand uncertainty is high prior to the occurrence of an actual pandemic.

6.3. Limitations, Extensions, and Concluding Remarks

Our study is subject to a few limitations that also serve as extensions for future research. The first limitation of the study arises from the fact that our data consider only private market purchases of vaccines (though influenza vaccine consumption is predominantly private in India and not part of the UIP program), and do not take into account the purchases made by the GoI from multinational and domestic vaccine manufacturers. Given that domestic vaccines are typically priced lower than their multinational counterparts, it is plausible that the effects of exogenous demand shocks on *multinational_market_share* may be even more pronounced (with domestic vaccine manufacturers gaining even greater ground) than what is presented in our analysis. Future studies that supplement private market purchase data with public procurement data could provide more accurate estimation of the heterogeneous impact on multinational and domestic vaccine manufacturers brought about by the pandemic shock.

A second limitation of our study relates to the absence of sufficient data to be able to rigorously evaluate the effects of AMC and how it stimulates the vaccine development efforts by domestic vaccine manufacturers. This is a limitation of our natural experiment setting, as only three domestic vaccine manufacturers received AMC support from the GoI.

Nonetheless, this limitation provides an important avenue for more research to understand the boundary conditions of public-private partnerships and their role in stimulating R&D in the context of an emerging economy. As Jourdan and Kivleniece (2017, p. 55) noted, "*. . .the theoretical and phenomenological nature of organizational sponsorship [through public resource allocations] remains elusive and has only recently begun to receive systematic attention*."

Third, we note that while our results are focused on India's experience, the 2009–10 H1N1 pandemic was a global phenomenon, affecting many other emerging economies, such as Brazil, Russia, China, and Indonesia. Therefore, an examination using cross-national data on variations in response to the 2009–10 H1N1 pandemic specifically, and pandemics more generally, merits further investigation. Likening the need for countries to engage in pandemic preparedness efforts in the same way they do for war, Gates (2018) noted, "*Somewhere in the history of these collective efforts is a roadmap to create a comprehensive pandemic preparedness and response system. We must find it and follow it because lives—in numbers too great to comprehend—depend on it*."

Beyond these limitations, it would be interesting to investigate the market entry modes—whether indigenous production or licensing and joint ventures—that were used by domestic vaccine manufacturers to respond to the 2009–2010 H1N1 pandemic. We hope future research will build upon this study and continue to advance knowledge on this important line of inquiry at the intersection of production and operations management, global health, and public policy.

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Appendix A. Additional Robustness Checks

Table A1 Assessment of Parallel Trends in Indian Influenza vs. Non-Influenza Markets

Independent variables	Dependent variable: Multinational_Market_Share_Revenues OLS FE (1)	Dependent variable: Multinational_Market_Share_Quantity OLS FE (2)
period 1 (base category)		
period 2	−0.002	−0.032
	(0.08)	(0.07)
period 3	0.049	0.028
	(0.09)	(0.08)
period 4	0.098	0.073
	(0.07)	(0.07)
period 5	0.149*	0.100
	(0.08)	(0.07)
period 6	0.146*	0.124*
	(0.08)	(0.07)
period 2 × influenza	−0.045	−0.027
	(0.03)	(0.03)
period 3 × influenza	−0.174**	−0.157**
	(0.07)	(0.06)
period 4 × influenza	−0.377***	−0.304***
	(0.07)	(0.06)
period 5 × influenza	−0.421***	−0.366***
	(0.05)	(0.05)
period 6 × influenza	−0.281***	−0.249***
	(0.08)	(0.07)
Constant	0.452***	0.408***
	(0.06)	(0.05)
Observations	1365	1365
R^2	0.101	0.101
Time dummies	Y	Y
Product-market fixed effects	Y	Y
Number of product-markets	20	20

Notes: Robust clustered standard errors at the product-market in parentheses; ***$p < 0.01$, **$p < 0.05$, * $p < 0.1$.

We document here a test of whether the trends in the multinational activity in Indian influenza vaccine markets vs. non-influenza vaccines markets were different prior to the occurrence of the pandemic shock. Each period is defined as one year except for the last period (*period 6* has data for 11 months). The first two time periods (*period 1* and *period 2*) are prior to the occurrence of the pandemic shock whereas the remaining four periods (*period 3*, *period 4*, *period 5* and *period 6*) follow the occurrence of the pandemic shock. The *period 1* serves as the omitted reference category. A statistically significant coefficient of *period 2* × *influenza* would indicate a violation of parallel trends assumption. However, in both Columns 1 and 2, the coefficients of *period 2* × *influenza* reveal no indication of diverging trends for multinational vaccine manufacturers share (either in revenues share or in quantities share) between influenza and non-influenza vaccines in the period prior to the occurrence of pandemic shock. Similar to the specifications in Table 3, all specifications control for competition with total sales each month in each product-market.

Analysis at the State Level: As noted earlier, although we collected data at the state-region level in India, our main analysis is carried out using data aggregated at the national level to test the theoretical predictions proposed in the study at the correct treatment level. Nonetheless, to test the robustness of our results, we carried out supplementary analysis at the product-market-state-time level in addition to the main results from the analysis at the product-market-time level. Columns 1 and 2 in Table A2 below include the results of this test. The two columns employ multi-way clustering (Cameron et al. 2011) to report standard errors conservatively because of repetition of observations at both the product–market level and the state level. The results from analyses at the product–market–state–time level align with our main results at the product-market-time level across the during-pandemic and post-pandemic periods. The difference-in-differences estimators (i.e., the interaction terms) remain economically and statistically significant.

Meta-analysis of Effect Sizes: A meta-analysis is a well-established statistical technique that is increasingly being employed to systematically pool the results from several studies of a common phenomenon (Borenstein et al. 2010, Kontopantelis and Reeves 2010). The pooling of results is carried out using a weighted average approach that yields estimates that are, on average, more accurate than that of any individual study. More recently, McShane and Böckenholt (2017) have pointed out the benefits of using a single paper meta-analysis (SPM) approach that pools results from various studies and approaches (such as different operationalizations or variables) used within a single paper in analysing a phenomenon.

Table A2 State Level Regressions

Independent variables	Dependent variable: Multinational_Market_Share_Revenues OLS FE (1)	Dependent variable: Multinational_Market_Share_Quantity OLS FE (2)
during_shock	0.040	0.023
	(0.05)	(0.04)
after_shock	0.142**	0.147***
	(0.06)	(0.05)
during_shock × influenza	−0.288***	−0.285***
	(0.04)	(0.04)
after_shock × influenza	−0.311***	−0.324***
	(0.03)	(0.03)
Observations	23,810	23,810
R^2	0.574	0.617
Time dummies	Y	Y
Product-market fixed effects	Y	Y
Number of product-markets	20	20

Notes: Columns 1 and 2 employ multi-way clustering (Cameron et al. 2011) and show robust clustered standard errors at the state level in addition to the product-market level. State fixed effects are employed in each column.
Robust clustered standard errors at the product-market in parentheses; ***$p < 0.01$, **$p < 0.05$, *$p < 0.1$.

We apply the SPM approach to get an accurate estimate of the main coefficients of interest, ***during_shock × influenza*** and ***after_shock × influenza***, which measure the change in the multinational market share (by revenues and by quantity) in treated group (i.e., influenza) relative to control group (i.e., non-influenza) in the during-pandemic and in the after-pandemic period relative to the before pandemic period. In a meta-analysis of different studies, it is often recommended to use the random-effects model because the fixed-effects model makes the restrictive assumption of a true effect size across studies (Borenstein et al. 2010). However, because our estimation approaches use the same data and empirical setting, a fixed-effects model with an assumption of a true effect size can be appropriate.[23] We calculate the effect size using the Stata command *metaan* (Kontopantelis and Reeves 2010). It requires the values of effect size and standard error for each study (for a meta-analysis of several studies) or for each estimation approach (for a meta-analysis of several approaches within a single study). We include four estimation approaches in this meta-analysis: estimations with non-influenza vaccines as the control group, estimations with non-influenza non-UIP vaccines as the control group, estimations with sample excluding AMC products, and estimations with state level analyses.[24] Figure S1a–d presents the results from the meta-analysis as forest plots. The point estimates are given by the black dot and 95% confidence intervals are shown by the black horizontal lines. The area of the grey square denotes the weight assigned to the specific estimation approach. Thus, the higher the precision of the estimation approach, the greater is the weight assigned to it. In aggregate, the meta-analytic summary effect size is denoted by the diamond at the bottom of the forest plot and the summary point estimate is shown by the dashed red vertical line.

This meta-analysis results in Figure S1a and b (found online in the Supporting Information section) show that the multinational market share by revenue in influenza vaccine market relative to non-influenza vaccine market declines by 23% (95% CI: −0.28, −0.18) during the pandemic compared to before the pandemic, and by 32% (95% CI: −0.37, −0.28) after the pandemic compared to before the pandemic, respectively. When the market share is measured by quantity, we obtain similar effect sizes as shown in Figure S1c and d (found online in the Supporting Information section). Specifically, the multinational market share by quantity in influenza vaccine market

relative to non-influenza vaccine market declines by 20% (95% CI: −0.26, −0.15) during the pandemic compared to before the pandemic, and by 31% (95% CI: −0.35, −0.27) after the pandemic compared to before the pandemic. Qualitatively similar effect sizes are obtained if random-effects model are used in place of fixed-effects model in the meta-analysis. The multinational market share by revenue in influenza vaccine market relative to non-influenza vaccine market declines by 23% (95% CI: −0.29, −0.16) during the pandemic compared to before the pandemic, and by 32% (95% CI: −0.37, −0.28) after the pandemic compared to before the pandemic, respectively. The multinational market share by quantity in influenza vaccine market relative to non-influenza vaccine market declines by 20% (95% CI: −0.28, −0.12) during the pandemic compared to before the pandemic, and by 31% (95% CI: −0.35, −0.27) after the pandemic compared to before the pandemic.

Notes

[1]Source: http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/case-counts.html

[2]Source: https://www.cdc.gov/zika/geo/united-states.html

[3]Following the careful suggestions of an anonymous referee, we wish to clarify that throughout the text, multinational market share measures the market share for only foreign multinationals in India.

[4]Given that multinational vaccine manufacturers were ahead of their domestic counterparts in developing the H1N1 vaccines, they were approached by the GoI in August 2009 (namely, Novartis from Switzerland, GlaxoSmithKline from the UK, Sanofi-Pasteur from France, and Baxter International from the USA) to conduct phase III clinical trials in India (Lok Sabha 2009).

[5]While general cost trends exist, specific estimates associated with vaccine manufacturing remain closely guarded by manufacturers (Clendinen et al. 2016, Mahoney et al. 2012). Luter et al. (2017, p. 3899) noted that "*Fixed costs (excluding labor), which are often 25–35% of the total production costs, range from tens to hundreds of millions of dollars (depending upon the technology and size of the facility) …*" Similarly, Plotkin et al. (2017, p. 4067) noted that the facilities costs can range from $50 to $700 million and would be on the lower end of this range in emerging economies.

[6]Even if we assume that the fixed costs may be lower in emerging economy markets (due to lower land and building material costs), they have to be distributed across hundreds of millions of doses to ensure competitive pricing. In an emerging economy setting, in which demand for optional vaccines during normal times remains low, the fixed costs are often perceivably higher for domestic vaccine manufacturers.

[7]Plotkin et al. (2017) noted that direct labor costs associated with vaccine manufacturing can be about 25% lower in a country such as India, with manpower efficiency being 120–130% that of Western standards; raw materials for vaccine production (e.g., clean fertilized eggs, chicken feed, filters, sucrose, vials, and syringes) can have prices as low as 15% of those in developed countries.

[8]Specifically, the WHO (2012, p.5), in its global vaccine deployment initiative, reported the following: "*On 15 May 2009, GlaxoSmithKline (GSK) issued a press release announcing that it would pledge 50 million doses of pandemic H1N1 vaccine to WHO once production began… GSK later increased this pledge to 60 million doses… On 18 June 2009, SanofiAventis announced a pledge of 100 million doses of pandemic H1N1 vaccine to support WHO efforts to ensure more-equitable access to vaccines and help strengthen national responses to the pandemic…*"

[9]The Department of Biotechnology, part of the Ministry of Science & Technology of the GoI, approved Panacea Biotec's proposal and awarded financial assistance of 100 million rupees (approximately $1.5 million) as a long-term loan on a concessional rate of interest of 2% per annum. See http://www.panacea-biotec.com/press_releases/PR22032010.pdf for details.

[10]The details of this study are available at https://www.gavi.org/results/evaluations/pneumococcal-amc-outcomes-and-impact-evaluation/.

[11]See the press release by GoI at http://pib.nic.in/newsite/erelcontent.aspx?relid=63879 for details.

[12]As discussed in section 5.3, robustness checks using (i) an alternative control group that excludes UIP vaccines, (ii) the synthetic control method, and (iii) the CEM technique provide consistent results.

[13]As an example, note this physician's column for preventive measures against H1N1 influenza in 2017 where he mentions this prescription behavior: http://economictimes.indiatimes.com/magazines/panache/heres-how-to-fence-yourself-against-swine-flu/articleshow/58102009.cms. We thank an anonymous referee for careful comments here.

[14]Further, analyzing at a level lower than the level of (as if) randomization (i.e., the level of the treatment group variable that is affected by the exogenous shock) can increase the likelihood of Type 1 error (Dunning 2012, Hansen and Bowers 2009). Recommendations for natural experiment–based research design prescribe selecting the level of the unit of analysis consistent with the level of (as if) randomization or the exogenous shock (Dunning 2012, Wing et al. 2018). Because the exogenous shock in our setting is a global pandemic that affects a product-market (influenza) and not a product-market-state, we conduct our main analyses at the product-market-month level. Nonetheless, as additional robustness tests, we replicate our analyses at the product-market-state-month level while employing multi-way clustering of standard errors at the state level in addition to product-market level (Cameron et al. 2011); all the results (shown in Appendix A) remain economically and statistically significant consistent with our main results.

[15]A 6.5 times increase in monthly revenues of influenza vaccine SKUs occurs in the period during and after the pandemic ($\bar{X}_{during\_and\_after\_shock} = 15{,}800$, $SD_{during\_and\_after\_shock} = 13{,}600$, $N = 45$) relative to the period before the pandemic ($\bar{X}_{before\_shock} = 2434$, $SD_{before\_shock} = 2219$, $N = 26$). This increase is statistically significant ($t = 4.97$, $df = 69$, $p < 0.001$).

[16]Our results hold when multinational market share is measured as the ratio of the number of multinational

firms' product types sold to the total product types sold. These results are available upon request.

[17]As perceptively suggested by an anonymous referee, while we do not explicitly discuss competition in a post-pandemic setting, we note here that procurement institutions and product behavior (Bhaskarabhatla et al. 2016) did not undergo significant changes during this period. Even if such differences had a bearing on India's private vaccine markets, they would be controlled for with the monthly time dummies and product–market size trends.

[18]Among domestic vaccine manufacturers, we find that the monthly sales quantity of non-AMC-supported influenza vaccines ($\bar{X}_{non\_AMC} = 6252$, $SD_{non\_AMC} = 8262$, $N = 44$), compared to that of AMC-supported influenza vaccines ($\bar{X}_{AMC} = 2273$, $SD_{AMC} = 4133$, $N = 19$), was significantly higher ($t = 1.99$, $df = 61$, $p < 0.10$).

[19]See http://delhihighcourt.nic.in/dhcqrydisp_o.asp?pn=176058&yr=2012 for an order from the Delhi High Court in the legal dispute between an AMC-recipient domestic vaccine manufacturer and the GoI.

[20]This section builds on perceptive econometric suggestions made by the review team.

[21]We operationalize the indicators for the time periods (i.e., periods 1–6) at the yearly level instead of at the monthly level to minimize introducing too many dummy variables and corresponding interaction terms; with 71 months of data, a monthly level operationalization would introduce 70 dummy variables and corresponding interaction terms. Our unit of analysis remains at the product–market and month level.

[22]The optimization procedure generates the following weights: 0.39 for hepatitis A and hepatitis B vaccines, 0.091 for hemophilus influenza type b vaccines, 0.128 for meningococcal vaccines, and 0.39 for pneumonia vaccines. The remaining non-influenza vaccines get zero weights. The notion of the bulk of the donor pool receiving zero weights is consistent with seminal works employing the synthetic control method. For example, in estimating the impact of California's Tobacco Control Program using this method, Abadie et al. (2010) found that a significant majority of states get zero weights, with only five states getting non-zero weights in the construction of synthetic California.

[23]Nonetheless, we also additionally report the effect size obtained from meta-analysis using the random-effects model in place of the fixed-effects model.

[24]Other estimation approaches used in our study as additional robustness tests, such as synthetic control and coarsened exact matching, are excluded from this meta-analysis because they rely on distinct identifying assumption. In addition, their standard errors are substantively very different: for example, the inclusion of the synthetic control method will result in a 100% weight attached to the estimates from this method (due to its extremely low standard errors), making the meta-analysis redundant.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1: (a) Effect Size of *during_shock* × *influenza* on *Multinational_Market_Share_Revenues*. (b) Effect Size of *after_shock* × *influenza* on *Multinational_Market_Share_Revenues*. (c) Effect Size of *during_shock* × *influenza* on *Multinational_Market_Share_Quantity*. (d) Effect Size of *after_shock* × *influenza* on *Multinational_Market_Share_Quantity*.