Science, Pathogenic Outbreak & Market Structure: Evidence from the 2010 NDM-1 Superbug Discovery & Indian Antibiotics Market[1]

Mayank Aggarwal

(IIM Ahmedabad, India)

Anindya S. Chakrabarti

(IIM Ahmedabad, India)

Chirantan Chatterjee

(IIM Ahmedabad, India &

Hoover Institution, Stanford University)

Very Preliminary Version

Please do not cite or quote without authors' permission

This version [June 3, 2020]

[1] Aggarwal is a doctoral student in business policy at IIM Ahmedabad. Chakrabarti is an Assistant Professor in Economics at IIM Ahmedabad. Chatterjee is an Associate Professor in Economics and Business Policy at IIM Ahmedabad; also a Visiting Fellow at the Hoover Institution, Stanford University. Chatterjee acknowledges the support of the 2018-2019 Campbell and Edward Teller National Fellow program and the 2019-2020 Visiting Fellow program at Hoover Institution, Stanford University and the ICICI Bank Chair in Strategic Management at IIM Ahmedabad for this study. We also acknowledge inputs on the paper from seminar participants at Lancaster University, HEC Lausanne and Mercados, Innovación y Medio Ambiente - Comunidad de Madrid. We especially appreciate comments from Philippe Gorry, Bruce Hollingsworth, Katharina Janke, Gerard Llobet, Catalina Martinez, Ceu Mateus. Emails: phd16mayanka@iima.ac.in; anindyac@iima.ac.in; chirantanc@iima.ac.in Usual disclaimers apply.

Abstract

It is well documented that as market structure changes, science and technology often tend to respond to those changes. However, is there a causal relationship in the opposite direction, where scientific discovery impacts market structure? We answer this question using the natural experiment of the NDM-1 (*New Delhi* Metallo-Beta-Lactamase 1) superbug discovery in India, which was reported in August 2010 in *Lancet Infectious Diseases*. This article demonstrated that the NDM-1 superbug was resistant to the broad spectrum antibiotics, carbapenems, widely recognized as weapons of last resort against infectious bacterial diseases. Using a difference in differences strategy, we find that multinational firms selling antibiotics in India reduced their market shares in sales of carbapenems (our treatment group) compared to narrow-spectrum antibiotics (our control group) immediately after the NDM-1 2010 discovery. We also document a concurrent decline in multinational carbapenem prescriptions by physicians and in channel incentives for drug retailers. Our results are robust to pre-trends, alternative controls and while accounting for regional heterogeneity. They are also consistent with synthetic controls. These findings have implications for the information socialization role of science, its impact on resolving managerial uncertainty within firms and in correcting market failures in healthcare markets and beyond for policy makers.

1.0 Introduction

One of the key issues in the ongoing global SARS-CoV-2 pandemic has been that the source and location of the virus has yet not been precisely identified (though popular press point to its origins in a wet market in Wuhan, China). Neither does the world know yet of how it exactly spread globally, though in separate country contexts, a zoonotic spread (Lee & Hsueh, 2020), travel related mechanisms (Gudbjartsson et al., 2020), bioterrorism (Brivio, Oliveri, & Pravettoni, 2020) or super spreader events (Ebrahim & Memish, 2020) are being examined as likely channels. It is also now clear that the science around identifying the source is laced with uncertainty and lack verifiability given an active world of scientific pre-prints dominating the recent publishing ecosystem around SARS-CoV-2 pandemic.[2] All of these issues could be problematic for future global preparedness[3] and response to pathogenic outbreaks given that pandemics are increasingly likely in future (Adbi, Chatterjee, Drev, & Mishra, 2019; Gates, 2018).

Can peer reviewed scientific publications socialized ex ante aid in solving this lack of information and certainty around sources of pathogenic outbreaks? The Worldwide Outbreak Database from Berlin (Vonberg, Weitzel-Kage, Behnke, & Gastmeier, 2011) seems to suggest that maybe so, though even in this database, searches for newer pathogens like Zika or Ebola yield no evidence that document pathogenic outbreak through peer reviewed publications. In addition, we still don't know for the cases when pathogenic outbreaks are revealed by science (like in SARS), if relevant firm and market responses are immediate or with a lag? Relatedly, our understanding of physician prescribing behavior in bio-pharmaceuticals and vaccines, diagnostics or testing also seems limited once sources of pathogenic outbreaks are identified.

We aim to unpack these issues in our study using the natural experimental context of a superbug discovery in India in August 2010, when a scientific article in *Lancet Infectious Diseases* (Kumarasamy et al., 2010) documented the existence of a strain of NDM-1 (New Delhi metallo-beta-lactamase 1) enzyme in a cross-national panel of patients from UK, Pakistan, and importantly for our empirical setting, from India. The NDM-1 enzyme was already documented in one patient, a Swedish national who returned home from New Delhi in an earlier study (Yong et al., 2009) but till the arrival of cross-national evidence with the Lancet

[2] Read on the role of pre-prints in SARS-CoV-2 pandemic here: https://scholarlykitchen.sspnet.org/2020/05/27/publishers-invest-in-preprints/

[3] https://www.businessinsider.in/tech/bill-gates-thinks-a-coming-disease-could-kill-30-million-people-within-6-months-and-says-we-should-prepare-for-it-like-we-do-for-war/articleshow/63946206.cms

article, there seems to have been less attention paid to NDM-1 in media and society (see Figure 1 for evolution of trends in google searches here relatedly).

NDM-1 is an enzyme that makes bacteria resistant to a broad range of beta-lactam antibiotics of the carbapenem family which are the mainstay for treatment of antibiotic-resistant bacterial infections. Using the Lancet publication of August 2010 as an exogenous credible and verifiable informational shock for the Indian market for antibiotics, we examine, if relative to other classes of antibiotics (narrow spectrum and other broad spectrum antibiotics as our control groups), there were shifts in market structure in carbapenems (our treated group) being sold in the India. Associatedly, we also unpack heterogeneous responses by multinational[4] and domestic firms and are able to demonstrate complementary shifts in channel incentives by firms and movements in physician prescribing behavior.

Our market information comes from aggregate demand for antibiotics provided by the All India Organisation of Chemists and Druggists (AIOCD), an organization that maintains a database Pharmatrac™. To investigate physician prescribing behavior, we turn to monthly IQVIA Prescription Audit data for India. Both the datasets were used for the period April 2007 to October 2013 and has been recently used in some prior work (Dutta 2011; Adbi, Bhaskarabhatla, and Chatterjee 2018; Bhaskarabhatla and Chatterjee 2017), more details in our data section below.

We find that the effects of NDM-1 scientific publication in August 2010 was dramatic and almost immediate in the Indian market for antibiotics. In particular, multinational firms withdrew from the affected carbapenem markets, specifically in new generation carbapenems, and the void they left behind was filled up by increasing market share of domestic firms. In addition, we are also able to demonstrate a decrease in prescriptions by physicians of multinational carbapenems. Finally, after the shock, we are also able to confirm a reduction in channel level push incentives by multinational firms for carbapenems with retailers compared to domestic firms. The results hold accounting for regional heterogeneity within India, in a truncated sample over a shortened time period and with synthetic controls apart from being consistent using alternative controls.

Our findings contribute to some important strands in the literature. In particular, past work, particularly in pharmaceuticals, has shown that a market expansion is likely to move

[4] We use *multinationals* and *multinational corporations* – that is *MNC* – interchangeably in the paper. We assume firms to be multinationals (MNCs) if they had foreign ownership greater than 51%.

science and technological change towards the expanded market (Acemoglu & Linn, 2004; Dubois, De Mouzon, Scott-Morton, & Seabright, 2015; A. Finkelstein, 2004). That there could be a reverse relationship, which is that scientific publications could induce changes in market structures, that too with heterogeneous firm level responses accompanied by shifts in physician prescribing behavior and channel incentives seems to be under investigated (Azoulay, 2002). We also relate to recently emerging but relatively sparse work on technological and product abandonment (Greenwood, Agarwal, Agarwal, & Gopal, 2016; Agarwal, Bayus, & Tripsas, 2005; Burns & Wholey, 1993; Finkelstein & Gilbert, 1985) that document, albeit in developed economies, organizational heterogeneity in antecedents, external information stimuli and influencer preferences in guiding scientific norms and ultimately, technology abandonment.

The heterogeneities in behavior by multinational and domestic firms in our setting aligns also with scholarly conversations around the tradeoffs firms face in deciding between ethics and profits especially when markets receive negative shocks like ours or more broadly in other contexts like product recalls (Cheah, Chan, & Chieng, 2007; Haunschild & Rhee, 2004; Jarrell & Peltzman, 1985; Rhee & Haunschild, 2006). The welfare consequences here are also worth mentioning given regulatory action amidst uncertainty and some recent work has started examining this in the context of medical devices (Grennan & Town, 2020).

A related issue is the role of liability of foreignness and multinational behavior amidst calls for their corporate social responsibility in host countries (Campbell, Eden, & Miller, 2012; Zaheer, 1995; Zaheer & Mosakowski, 1997). This is especially pertinent given the reputational costs multinationals may face by selling dodgy products (carbapenems in our context) in host markets like India once peer reviewed science reveals credibly, information about their quality and health outcome consequences. Finally, our findings on physician prescribing behavior closely relates to studies on clinician heterogeneities in prescribing behavior in healthcare settings, for example in the context of US opioids and also particularly in the context of antibiotic prescribing (Buchmueller, Carey, & Meille, 2019; Lambert et al., 1997; Meeker et al., 2016; Schwartz, Soumerai, & Avorn, 1989 among others).

More broadly, our findings have policy implications given an important global health issue like antibiotics resistance in the developing world and also if one remembers that after the first wave, subsequent waves in the 1918 Spanish Flu influenza actually induced secondary

bacterial infectionscausing pneumonia in a world then without antibiotics.[5] Relatedly, the global health community is already discussing that SARS-CoV-2 may have future waves but this could be complicated with broader global antibiotics resistance as some experts have pointed out.[6]

Our findings also have important policy implications given the *red queen effect* in antibiotics resistance (Baquero, Alvarez-Ortega, & Martinez, 2009; Dieckmann, Marrow, & Law, 1995). The *red queen effect* captures from Lewis Carroll's *Through the Looking Glass* (sequel to *Alice's Adventures in Wonderland*) a situation where- *it takes all the running you can do, to keep in the same place*. In the context of antibiotics, firms globally are running a R&D race to innovate for newer antibiotics at one end, but the more antibiotics are consumed, sometimes indiscriminately prescribed, it causes resistance and destroys incentives for innovation in equilibrium. This horse race between economic and clinical externality is at the heart of designing optimal policy interventions (Eswaran & Gallini, 2019), prompting infectious disease experts like Dr. Anthony Fauci also to comment the following on antibiotics innovation: "*Resistant microbes outstrip new antibiotics. It's an ongoing problem. It's not like we can fix it, and it's over. We have to fight continued resistance with a continual pipeline of new antibiotics and continue with the perpetual challenge*".[7]

Finally, we add to conversations around normative policy prescriptions in the information socialization role of peer reviewed science for identifying pathogenic outbreaks and thereby resolving managerial uncertainty which ultimately guides firm responses and optimal incentives for innovation and entry. To the extent multinationals leave the market for antibiotics in India leaving it for domestic firms, one may need to ponder here creating nuanced interventions to solve this market restructuring with accompanying health outcomes consequences given the shifts in direction of science, inventive activity and industrial R&D, local and global (Chakraborty & Chatterjee, 2017; Gittelman & Kogut, 2003).

The rest of the paper is organized as follows. In the next section, we provide the institutional background and describe the market structure for our study followed by a literature

[5] See for a discussion: https://www.nih.gov/news-events/news-releases/bacterial-pneumonia-caused-most-deaths-1918-influenza-pandemic

[6] See for a discussion: https://www.statnews.com/2020/03/23/antibiotic-resistance-hidden-threat-lurking-behind-covid-19/

[7] See for a discussion: https://www.post-gazette.com/healthypgh/2014/05/25/Medical-marathon-Race-is-on-to-develop-new-antibiotics-Medical-marathon-U-S-Centers-for-Disease-Control-and-Prevention-employ-shotgun-approach-to-bring-antibiotic-resistance-under-control/stories/201405250015

review. We then describe our data and the empirical estimation strategy along with the results. Finally, we conclude with managerial and policy recommendations.

2. Institutional Background

2.1 Antibiotic Consumption & Resistance

High levels of antibiotic consumption and related rise in antibiotic resistance is a globally well-recognized problem. Between 2000 and 2015, global antibiotic consumption increased by 65% (Klein et al., 2018). Alsan et al. (2015) point out relatedly that antibiotic consumption and resistance is rising substantially particularly in Low and Middle Income Countries because of out-of-pocket healthcare expenditures that accompany economic and population growth coupled with the high burden of infectious diseases.

India is an important contributor to this global rise in antibiotic resistance, with some calling it as a source of dangerous bacterial mutation coming from excess consumption and the evolution of the NDM-1 enzyme.[8] NDM-1 has now spread to more than 70 countries and the latest report of its outbreak has emerged from as far away as a remote Norwegian archipelago or Tuscany in Italy.[9] Antibiotic resistance kills more than 700 thousand people each year with projected deaths of more than 10 million a year by 2050 (O'neill, 2014). While the dangers have been recognized since the 1960s, due to the complex nature of the market and the race to garner market share, it has proven difficult to reduce the use of the antibiotics. The Indian market has in fact seen an aggressive expansion, a 103% increase from 2000 to 2015 (3.2 to 6.5 billion defined daily doses as per (Klein et al., 2018)).

2.2 The Supply Side of Antibiotics & Firms in Indian Pharmaceutical Industry

From the supply side, Indian pharmaceutical market is marked by over-dependence on antibiotics as the source of revenue. In 2006, most of the best selling drugs in India were antibiotics (Duggan, Garthwaite, & Goyal, 2016) and some of the highest selling brands in India includes products from both multinationals and domestic firms like GlaxoSmithKline Pharmaceuticals' Augmentin and Alkem Laboratories' Clavam (both having active ingredient

[8] See: https://www.downtoearth.org.in/blog/health/india-the-antibiotic-capital-of-the-world-63097

[9] See: https://www.wsj.com/articles/superbug-from-india-spread-far-and-fast-study-finds-11548633600 and http://outbreaknewstoday.com/italy-superbug-ndm-1-outbreak-reported-in-tuscany-24484/

amoxicillin and clavulanic acid), and Aristo Pharmaceuticals' Monocef (active ingredient being ceftriaxone, a cephalosporin).[10]

Antibiotics account for around 8% of total pharmaceutical sales in developed countries and in countries such as India, their share is higher at around 20% (Chaudhuri, Goldberg, & Jia, 2006). Before the NDM-1 publication, it would be safe to guess that neither the demand and the supply side were paying enough attention in India to the brewing problem of drug-resistance. Post the event, due recognition started towards rationalizing usage of drugs (Pulcini et al., 2012). Eventually, the Indian government instructed pharmacists to set up registers to maintain detailed record of drug sales in 2014 and also implemented other comunnity surveillance techniques to monitor irrational antibiotic prescribing behavior.[11]

More broadly, the Indian pharmaceutical industry is highly fragmented with official estimates pointing to greater than 5000 multinational, big domestic firms and small domestic firms (listed and unlisted) operating in the market (Adbi, Bhaskarabhatla, & Chatterjee, 2018; Adbi, Chatterjee, & Mishra, 2019). Traditionally dominated by generic manufacturers, recent decades have seen a rise in dominance by multinational firms (Kapczynski, 2009). Key events that have marked industry evolution in this sector have been the 1991 liberalization of the Indian economy that led to a rise of Indian generic medicines exports to other developing economies (Hafner & Popp, 2011) and the Trade Related Intellectual Property Rights agreement as per provisions of the World Trade Organization when India implemented a stronger patent protecting environment domestically in 2005 (Chatterjee, Kubo, & Pingali, 2015; Scherer, 2004) after signing the Act in late 1994. Also, since the late 1990s, the US Hatch Waxman Act has opened a developed market opportunity to Indian generic firms (Branstetter, Chatterjee, & Higgins, 2016; Chatterjee, 2009; Chaudhuri, 2005)

A final discussion is merited on the role of physicians as influencers in the Indian antibiotic ecosystem. From the firm perspective, the market is often seen as a zero sum game. If one firm reduces production, others will capture the market. For an innovative and rapidly evolving product like antibiotics, the competition would be intense with most of world's largest drug manufacturers being competitors. In the Indian context, competition between physicians also play a role, who are pressurized by patients for a quick remedy. This pressure forces them to use the ultimate weapon they possess or risk losing the patient to other physicians (Kotwani,

[10] See: https://www.livemint.com/news/india/dcgi-moves-to-curb-sales-of-antibiotics-without-prescriptions-11577380637918.html

[11] http://origin.searo.who.int/india/topics/antimicrobial_resistance/amr_containment.pdf

Wattal, Katewa, Joshi, & Holloway, 2010). Another reason for physicians to quickly prescribe strong dosage of antibiotics is due to the concern for patients[12] where they end up deciding that it is better to err on the side of caution and cure the patient as soon as possible, i.e. type-I error is more acceptable, psychologically and socially. Proposed solutions to this problem is curtailment of use of advanced antibiotics and favouring older antibiotics for consumption (O'neill, 2014), but policy makers are also grappling with determinants and conditions under which firms can be incentivized to abandon newer antibiotics for older ones.

3. Literature Review

3.1 Evolution of Antibiotics: Science, Technological Choice & Path Dependence

In this section, we briefly review the interaction between scientific breakthroughs, technological change and corporate innovation in the development of modern antibiotics, where all three factors were deeply intertwined with each other (see e.g. Aminov, 2010; Davies & Davies, 2010; Ventola, 2015). We also observe that with the development of each new antibiotic, there is an associated rise of antibiotic resistant bacteria.

Penicillin was discovered in 1928 by Alexander Fleming. By 1940, scientists found existence of Penicillin resistant bacterial strains, even before Penicillin became a therapeutic. The fear of over-use and growth of antibiotic-resistance was in fact recognized around the same time, as early as 1945 by Alexander Fleming himself (Spellberg & Gilbert, 2014).[13] Streptomycin, a successful drug for tuberculosis was introduced in 1944 and very soon streptomycin-resistant bacteria grew. 1940s were the period of Sulpha drugs along with Cephalosporins and Cholorampheniсols. 1950s saw the development of most of the antibiotics that were used in the later periods till date (Tetracyclines, Macrolides/lincosamides/streptogramins, Glycopeptides, Rifamycins, Nitroimidazoles for example). After 1950s, most of the developments took place in terms of bio-chemical engineering and genetic studies for almost five decades along with sporadic discovery of Quinolones and Trimethoprim in the 60s and after a long gap, Oxazolidinones and Lipopeptides around 2000 (for a complete discussion see Conly & Johnston, 2005; Davies & Davies, 2010). Meanwhile industry-scale production of antibiotics took place and there was

[12] Informal discussions with multiple physicians indicate this channel.

[13] https://www.nytimes.com/1945/06/26/archives/penicillins-finder-assays-its-future-sir-alexander-fleming-says.html

enough demand worldwide to be met by ever-increasing supply and shifting market structures globally (Klepper & Simons, 1996; Sampat & others, 2015).

The triumph of global pharmaceutical industry from those days over infectious diseases was captured by Nobel-laureate M. Burnet's quip- "*the virtual elimination of the infectious diseases as a significant factor in social life"* (Burnet, Burnet, & White, 1972). A large set of global pharmaceutical firms including Novartis, AstraZeneca, Sanofi, Allergen, Merck, Roche, GlaxoSmithKline and Pfizer were active in antibiotics development and manufacturing program. But slowly the supply of new antibiotics dried up, but bacteria kept on evolving, which eventually led to a scenario where scientists realized- "*there is no 'endgame'*" (Spellberg & Gilbert, 2014). Development of new antibiotics by pharmaceutical firms are also getting scarcer. As per the World Health Organization's list of antibiotics in pipeline, only three of them[14] can potentially target NDM-1 bacteria which for the last ten years has shown resistance towards Carbapenems, the broad-spectrum antibiotic also known as the 'last line of defence' for bacterial infections and also our focal treated group in the empirical analysis.[15] With the advent of this new generation of antibiotic resistant pathogens, most of the large manufacturers have left the carbapenem R&D efforts globally with only Merck, Roche, GlaxoSmithKline and Pfizer having active research programs.[16] Thus scientific advancement, growth of markets, onset of resistance, all in conjunction have influenced firm decisions to enter and exit the market in a very nonlinear way globally and historically.

3.2 Technology Abandonment

One key issue of interest in this study is the heterogeneous firm reaction to the publication of the NDM-1 paper in *The Lancet*, especially between multinationals and domestic firms. Essentially, this relates to the bigger question of technology choice and associatedly, the technology and product abandonment & extinction (Bayus & Agarwal, 2007; Klepper & Simons, 1997). Traditionally, prior influential work in technological change has demonstrated that new technologies are usually welfare enhancing (Trajtenberg, 1989, Petrin 2002 among others) which may lead to better productivity, aiding also in solving existing problems, thereby increasing consumer welfare (Agarwal, Moeen, & Shah, 2017). But given the peculiar characteristics of the antibiotics market, the downside of technological advancement is that

[14] https://www.who.int/news-room/detail/17-01-2020-lack-of-new-antibiotics-threatens-global-efforts-to-contain-drug-resistant-infections

[15] https://www.theguardian.com/business/2020/jan/17/big-pharma-failing-to-invest-in-new-antibiotics-says-who

[16] https://www.nature.com/articles/nbt.4193 Editorial- Wanted: a reward for antibiotic development (Published: 06 July 2018)

with rapid evolution in the pathogens, new technology gets obsolete. The solutions to these problems lie in more rational use and ultimately abandoning overuse of such technologies and products.[17]

The literature on technological change and industry evolution has focussed on how new technologies emerge due to competition (Murmann & Frenken, 2006), appearance of dominant design (Utterback & Suárez, 1993) and technology diffusion (Rogers, 2003) among others. At the firm level, shift from product to process innovation and emergence of dominant firms have been studied (Klepper & Simons, 2005). Firms make non-trivial technological choices (Kapoor & Furr, 2015) which in turn is associated with entry-exit decisions (Agarwal et al., 2017). The effects of pre-existing capabilities of firms and the consequent differential survival propensities have also been studied (Furr & Kapoor, 2018). Diffusion patterns herein have been documented with probably the most well-known among them being the S-curve (Bass, 1969; Rogers, 2003; Talukdar, Sudhir, & Ainslie, 2002). The role of the ecosystem of firms in facilitating the adoption of innovation is also well recognized (Adner & Feiler, 2019; Adner & Kapoor, 2016). It is also well established here that frictions arise due to information flows (Abrahamson & Rosenkopf, 1997), social dynamics (Borgatti & Cross, 2003) and stickiness of practices (David, 1985) among others and an important role here is also played by complementary assets (Teece, 1986).

But prior work on technological change, diffusion and industry evolution seems to have less understanding of how technologies and product markets get abandoned. A related question that remains less investigated is why firms reduce their commitment to existing technologies. Reducing market commitment to existing technologies is tough for firms because this entails foregoing sunk cost and investment they have already made in the technology (S. N. Finkelstein & Gilbert, 1985) and also conceding space to their competitors (Younkin, 2016). These factors act as a severe impediment to abandonment. Also, in case the existing technology captured a market with no other replacement technology, firms may leave consumer demand to cede the market to competitors. These factors explain why firm may not be willing to reduce their commitment to technologies, which might also create negative externality for the society.

Some recent studies make important advances in this literature. Greenwood et al. (2016) study abandonment and replacement of coronary stents of sequential generations, that are used for treatment of stable coronary arterial diseases. They analyse the phenomena of technological

[17] https://cddep.org/wp-content/uploads/2017/06/swa_edits_9.16.pdf

abandonment from an organizational point of view, relating it to salience of norms and heterogeneity in economic trade-offs. They show that economic incentives matter, so does availability of new generation technology. Our study provides complementary understanding to the findings of Greenwood et al. (2016) showing how scientific advancements in catching problems early and credibly with product markets (in our case with pathogenic outbreaks) could create disincentives for heterogeneous firms causing changes in market structure. In addition, the presence of the red queen effect in antibiotics compared to its absence in markets like coronary stents is an important nuance distinguishing our findings.

3.3 Liabilities of Foreignness: Science and Ethics

In the context of antibiotics market in India, an important dimension of supply-side heterogeneity arises from whether firms operating are multinationals or domestic drug manufacturers. They differ not only in scope of business and product portfolios, but also differ significantly in innovativeness. Differential responses to uncertainty and scientific information might arise with multinationals due to *foreignness* of their activity within and outside India leading to higher opportunity cost of losing business in case of a downturn and the corresponding ethical responsibilities compounded with a lack of knowledge of the local market. While local firms are able to extract influence rents due to institutional familiarity (Ahuja & Yayavaram, 2011), multinationals can be expected to not have institutional backing, potentially leading to a need for higher responsiveness to the scientific evidence to avoid possible sanction by customers and regulators (Kostova, Roth, & Dacin, 2008). To maintain their market positions therefore, multinationals need to signal reputation continuously in order to differentiate themselves from local firms and show themselves as being more responsible (Crilly, Ni, & Jiang, 2016). Thus ethical considerations along with concerns about losing profits and market share in other non-antibiotics markets within India and in all other product markets outside India might elicit a differential response in the average multinational firm compared to the domestic manufacturer. This is also coupled with the realization in our particular case that there is no final product as the target is ever-evolving in the focal market of interest.[18]

From a signalling perspective, engagement with scientific community indicates quality of firms (Cockburn, Henderson, & Stern, 1999). On a complementary note, science has a fundamentally public nature and a normative hold over social consciousness (Weingart, 1998).

[18] https://www.nature.com/articles/nbt.4193 Editorial- Wanted: a reward for antibiotic development (Published: 06 July 2018)

Science influences demand and supply of products (Azoulay, 2002), specifically in the presence of mediator professionals who follow science for guidance in their practice (Timmermans & Angell, 2001). Firms can also rely on scientific evidence to stop reputation loss associated with technologies with potential status risk (Marris & Fairless, 2007). Finally, from an international business perspective, scientific evidence in favour or against product markets, might lead to potentially global repercussions for firms drawing higher attention towards multinational firms due to possible impact on their home market (Taussig, 2017) and other advanced markets they are active in. The net result is that multinationals would be potentially much more receptive to scientific evidence than local firms. They might be expected to pay more attention to their channel incentives if a focal product market receives a negative shock and might be less sticky with influencers after the occurrence of a negative shock coming from information disclosure through science.

Overall, our study attends to the above strands in the literature using the setting of antibiotics market in India. We use our focal exogenous scientific shock from the publication of a pathogenic outbreak rendering certain markets less viable over others, to examine if there are shifts in market structures with fall in shares of multinational firms relative to domestic firms. Associatedly, we also examine channel incentives and influencer behaviour.

4. Data

For this study, we use two main sources of data. For drug sales data at the molecule-region-time level, we use the Pharmatrac database maintained by the All India Organisation of Chemists and Druggists (AIOCD). This data is collected from more than 500,000 retailers representing about 60% of drug sales in India capturing sales at the stock-keeping unit (SKU) – region - month level with information about the price at which drug is supplied to the retailer, maximum retail price and quantity sold. This dataset has become the standard source of sales data to study Indian pharmaceutical market in recent times given the geographical heterogeneity it provides and multiple previous studies have exploited it (see Adbi, Bhaskarabhatla, & Chatterjee, 2018; Adbi, Chatterjee, Drev, & Mishra, 2019; Bhaskarabhatla, Chatterjee, Anurag, & Pennings, 2016). For the present analysis, we concentrated on the time from April 2007 to October 2013 with monthly data consisting of a total of five carbapenems and sixteen narrow-spectrum molecules sold by more than 100 firms all over India in the market for antibiotics in India.

In our baseline specification, the treatment group consists of the carbapenems (ATC[19]code J01DH with suffix 03, 04, 02 and 51) and the control group consists of the narrow-spectrum antibiotics. For selection of the narrow spectrum antibiotics, we follow the medical literature. In particular, following Kristensen, Johnsen, & Thomsen, (2019), our control group of narrow spectrum antibiotics consist β-lactamase sensitive penicillins (J01 CE with suffix 01, 02), β-lactamase resistant penicillins (J01CF with suffix 01, 02), first-generation cephalosporins (J01DB with suffix 01, 04, 05), and macrolides (J01FA with suffix 01). All molecule names along with ATC classifications are given in table 1 in the Appendix.

Two points are in order about the choice of the treatment group and the control group. First, for robustness we have also tested all other broad-spectrum antibiotics (i.e. other than carbapenems) as an alternate control group. All results hold qualitatively and quantitatively. Second, our choice of narrow spectrum antibiotics to be the optimal choice of control group is due to the peculiar nature of the product. Note that broad spectrum antibiotics are not substitute of each other, since once resistance appears in the bacteria, one has to resort to narrow spectrum antibiotics. Some medical intervention studies have tried replacing carbapenem with narrow-spectrum antibiotics (e.g. Sadyrbaeva-Dolgova et al., 2019) to control antibiotic resistance, hinting at the comparability in terms of these drugs' use and efficacy. All of these justify our baseline choice of narrow spectrum as an ideal control group which we off course test for robustness with synthetic controls and other broad spectrum antibiotics as a control group.

We complement the analysis on the sales data with an econometric analysis of the physicians' prescribing behaviour. For that purpose, we have utilized a unique dataset created by IQVIA that collects roughly around 1 million physicians' prescriptions at a monthly frequency with a regional spread within India. This dataset has been used in earlier studies (Adbi et al., 2019; Bhaskarabhatla & Chatterjee, 2017; Dutta, 2011; Farooqui, Mehta, & Selvaraj, 2019).

We treat the publication of the article by Kumarasamy et al. (2010) titled "The emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study", published in the *The Lancet Infectious Diseases*, in August 2010 as the exogenous unanticipated shock in the form of scientific evidence bringing in question the efficacy of the prevailing dominant mode of medical treatment (carbapenems as the last resort antibiotic). This publication led to intense debates in scientific research

[19] ATC is Anatomical Therapeutic Code, a standard code used in the pharmaceutical economics literature specified by the World Health Organization, for details see: https://www.whocc.no/atc_ddd_index/

community, drug manufacturers and the policy-world about superbugs and more broadly about antibiotic resistance. In Figure 1, we present cumulative Google searches about two keywords viz. 'superbug' and 'NDM-1' within India. The pattern of a sudden upward jump in the search volume right around the time of the publication of the NDM-1 paper in *The Lancet Infectious Diseases* is evident. This whole episode also led to questioning of the irrational use of carbapenems in India and how important are anthropogenic factors (Davies & Davies, 2010) in causing the bacteria develop resistance to the same. In Figure 2, we have plotted the world map with the fraction of randomly tested bacteria that tested positive for carbapenem resistance, across the world. As is evident, India has the highest density of carbapenem-resistant bacteria in the world.

5.0 Empirical Analysis & Identification Strategy

5.1 Multinational Shares in the Carbapenems Market

To understand the causal effect of the NDM-1 publication on multinationals, we estimate the impact in terms of their market shares in the treated carbapenem market vis-à-vis our control narrow-spectrum market with the following econometric specification:

$$\boldsymbol{mncshare_{mt} = \beta_0 + \beta_1\, carbapenem_m + \beta_2 NDMdummy_t + \beta_3 carbapanem_m \times NDMdummy_t + \beta_4 X_{mt} + molecule_m + time_t + \epsilon_{mt}} \text{ --- Eq (1)}$$

where the estimation is done nationally in India our data at the molecule (*m*) and monthly time unit (*t*) level. The left hand side represents the sales share of the multinationals. We have two dummies in Equation (1). One for the molecules belonging to the treatment group carbapenems ($carbapenem_m$), and the second, a time-varying dummy that differentiates between the pre and post periods of publication of the NDM-1 paper in the Lancet ($NDMdummy_t$). In order to account for time-specific variations in our data we also control for time specific fixed effects. Molecule specific idiosyncrasies are accounted for by incorporating molecule-level fixed effects. $X_{\_mt}$ represent controls for molecule-time varying effects, like variation in market sizes and associated firm incentives to enter and exit. We have hence controlled for molecule sales in millions of Indian currency (rupees) in a particular month. Standard errors are clustered at the molecule level.

Parameter β_3 provides the estimate for the impact of NDM-1 publication on market share of multinationals in the carbapenem market relative to narrow spectrum antibiotics, which is a bounded variable between 0 and 1. We use both OLS and fractional logit method for estimation

(Papke & Wooldridge, 2008). As a robustness check, we examine the impact in terms of share in monetary sales as well.

To capture inter-firm heterogeneity, we estimate the firm sales in DDD (Defined Daily Dosage) by changing our unit of observation to the firm-molecule-month level, using the following triple differences specification:

$$\boldsymbol{logfirmmoleculesales_{fmt} = \alpha_0 + \beta_1 carbapenem_m + \beta_2 NDMdummy_t + \beta_3 MNC_f + \beta_4 carbapanem_m \times NDMdummy_t + \beta_5 MNC_f \times carbapenem_m + \beta_6 MNC_f \times NDMdummy_t + \beta_7 carbapanem_m \times NDMdummy_t \times MNC_f + \beta_8 X_{fmt} + molecule_m + firm_f + time_t + molecule_m \times calendermonth_t + molecule_m \times firm_f + \epsilon_{mft}} \textbf{ -- Eq (2)}$$

where $firmmoleculesales_{fmt}$ corresponds to the sales of a particular firm f in molecule m in period *t*. The interpretations of the dummies remain identical to those in model 1, except that *MNC* represents whether a firm is multinational or not. The parameter β_7 provides the estimate of change of multinational sales in carbapenem post-publication of NDM-1 paper. In this model, we controlled for the prices of the molecules that are picked up in the vector X_{fmt} . To account for potential endogeneity between price and quantity, we utilized the richness of the dataset here, which breaks down the final cost paid by customer into retailer margin and price. Retailer margin influences the profit of the manufacturer and their marketing expense (Lal & Narasimhan, 1996; Sudhir, 2001) and hence acts as a cost shifter (Ellison, Cockburn, Griliches, & Hausman, 1997; Nevo, 2001)[20], it influences the price but not sales satisfying the exclusion criteria; building on this, we use it as an instrumental variable for prices. First stage F-statistic was 520 which is substantially more than recommended value of 10 (Staiger & Stock, 1994) in our instrumental variable estimations. Detailed variable description and how they are constructed are given in Table 1.

We also control for unobserved heterogeneity at the month, molecule and firm level with respective fixed effects. We account for any seasonal changes in molecule sales (due to weather pattern or diseases peaking in certain months driving molecule sales) with a control for seasonality using $molecule_m \times time_t$ fixed effects where *time* is at the month level. To account for molecule-firm level idiosyncrasies (such as time-invariant heterogeneity in

[20] The demand of a particular product is directly related to the price paid by consumer. The final price consists of two factors, price at which the drug is procured by the retailer and retailer margin which includes the retailer profit along with marketing, distributional and other expenses borne by the retailer. This variable represents a cost shifter for the firm, as the consumer will be unaware of the mark-up but the firm needs to incorporate this margin in their profit maximising exercise as this represents a cost for them to distribute and sell their product.

historical capabilities of some firms in producing some molecules over others), we also controlled for molecule-firm paired fixed effects. The errors are clustered at the molecule-firm level.

5.2 *Difference in Differences on Physician's Prescription Behaviour*

Next, we employ a regression specification similar to Equation (1) to study the impact of the publication of the NDM-1 paper on not just sales but concomitant physician prescription behaviour in our data. We sourced this information on the number of the prescriptions written by physicians for carbapenem vs. narrow-spectrum antibiotics from the IQVIA Prescription Audit Database for India (from April 2007 to Oct 2013) as highlighted earlier.

We note that physicians are a major stakeholder in this phenomenon (Guan et al. 2019; Ahmadi et al. 2017;Basu et al. 2008;;). Physicians directly influence patients by treating them during illness and by training and selection into the profession, they would be more knowledgeable than the patients about the nature of the treatment. Therefore, it is only natural that they would readily recognize the problem of over-prescription of antibiotics and the consequent growth of antibiotic resistant strains. Second, drug manufacturing firms regularly send sales personnel to practicing physicians to apprise them of recent developments and products in the drug market. Thus there is a clear channel of information flow from the drug manufacturing firms to the physicians. Therefore, it is expected that the physicians prescribing antibiotics would react to the Lancet publication.

In the IQVIA prescription data, we test whether the share of prescriptions for multinationals went down using the following specification almost identical to Eq (1) above:

$$\boldsymbol{prescriptionshare_{mt} = \beta_0 + \beta_1\, carbapenem_m + \beta_2 NDMdummy_t + \beta_3 carbapanem_m \times NDMdummy_t + molecule_m + time_t + \epsilon_{mt}} \textbf{ – Eq (3)}$$

Similar to earlier specifications, we controlled here also for molecule and time fixed effects. Our interest is in the variable β_3 which captures the impact of the treatment on the prescription share for multinationals in the post-treatment period. To account for presence of excess zeroes and bounded nature of variable (from 0 to 1) we use fractional probit model (Papke & Wooldridge, 2008). Next, we consider an analogous of the quantity model described in Eq (2) above. But this time it is estimated on the IQVIA prescription data:

$$\boldsymbol{logfirmmoleculeprescriptions_{fmt} = \alpha_0 + \beta_1 carbapenem_m + \beta_2 NDMdummy_t + \beta_3 MNC_f + \beta_4 carbapanem_m \times NDMdummy_t + \beta_5 MNC_f \times carbapenem_m +}$$

$$\beta_6 MNC_f \times NDMdummy_t + \beta_7 carbapanem_m \times NDMdummy_t \times MNC_f + molecule_m + firm_f + time_t + molecule_m \times time_t + molecule_m \times firm_f + \epsilon_{mft} \text{ ----Eq (4)}$$

Similar to Equation 2, we control for the firm, molecule, time, seasonal variation using molecule and time paired fixed effects and firm-molecule pair fixed effects and our coefficient of interest here is β_7.

6.0 Findings

6.1 Descriptive Analysis

Before getting into the econometric analysis, we examine the overall market trend during the period 2007 to 2013. Figure 3 presents sales in defined daily dosages (DDD)[21] over this period. We note that that even after the publication of the NDM-1 paper in August 2010, overall, the market for carbapenems expanded in India[22]. However, in Figure 4, we observe that multinational market share both in terms of quantity sold (from 71.5 percentin April 2007 to 68.7 percentin August 2009 to 29.5 percentin October 2013) and monetary sales (from 74.4 percentin April 2007 to 71.2 percentin August 2009 to 33.8 percent in October 2013) went down post the publication of NDM-1 paper. But in the market for narrow spectrum antibiotics, multinationals maintained their presence with a relatively stable market share of around 10 to 20 percent, both in quantity and in monetary sales.

In Table 2, we provide descriptive statistics. We see that in terms of narrow spectrum, slightly fewer number of firms were operating in the market after the shock, while the size of the market expanded substantially in terms of monetary sales suggesting an increase in market power here. The changes in the level of competition (measured through Hirschman-Herfindahl index computed over sales in DDD) were minor. In contrast, in the carbapenem market, we see that while multinational share decreases and monetary sales value shrinks, the number of firms remain quite stable along with a very similar level of competition. The overall take way is that

[21] While computing the *defined daily dosage* (DDD) in the paper, we followed the recommendation of the World Health Organisation (WHO). For example, as per WHO, defined daily dosage of Doripenem is 1500 mg per day for a person weighing 70 kg. So for *Q* mg of Doripenem, the units of defined daily dosage would be *Q*/1500. In case of intravenous injections for antibiotics as well as oral administration, we convert the mg content of the antibiotics into DDD count following the above method so that the medicines are exactly comparable in terms of DDD.

[22] Sales of carbapenems in our data in April 2007 were 57.3 million defined daily dosesand around $7.4 million USD whereas in October 2013 the combined sales were 113.5 million defined daily doses and around $ 9.5million USD

while multinationals were leaving the market, domestic firms started entering and capturing market shares. A complementary analysis in terms of prescribing behaviour of physicians, indicates a very similar scenario. Next we take forward these non-parametric findings with our formal econometric analysis.

6.2 Impact of the Lancet Publication on the Antibiotics' Market

Model 1 in Table 3 reports OLS regression results with multinational market share as a dependent variable while estimating Equation 1. Model 2 reports results from estimating Equation 1 using fractional logit specifications. Model 3 and 4 report corresponding results based on monetary market share using OLS and fractional logit specification. One of the reasons we use both absolute sales (Q) and monetary market share (shares in terms of price times Q) in alternative specifications as dependent variables was to check if there was any price confounder in our baseline results being estimated in Equation (1). We find strong support across all the models that the market-share of multinationals went down in carbapenems in the post-treatment period. Interpreting model 1, we can say that NDM-1 article led to on an average reduction of 13.9% in market share of MNC in carbapenem molecules. This implies that in terms of daily doses sold, multinationals combined were selling 4688018 lesser daily doses in the market for carbapenems after the NDM-1 was published compared to domestic firms combined selling 28484991 daily doses more over the entire post treatment period per month. In model 5, we present the results of the same regression specification on the share of multinationals as prescribed by physicians. The effect is even stronger. We will discuss physician behaviour in more details in the following section. Next, we present the results from Equation (2) in column 1 of Table 4 with the dependent variable being firm level sales measured in DDD. In a triple difference setting, we observe that the quantity-estimation model exhibits sharp drop in quantity sold by multinationals after controlling for instrumented prices, in the post-treatment period. Overall, we see a drop in terms of shares and sales for multinationals in carbapenems post the NDM-1 publication.

6.3 Impact on Physician Prescribing Behaviour

In Table 3, Model 5 we present the results on physician prescribing behaviour. We find that the multinationals' share of prescriptions went down in the post-treatment period. The results for the quantity-model estimation from the prescription data are presented in Table 4, Model 3. The triple difference setting has been specified using controls for firm, molecule and

time-level fixed effects along with firm-molecule and month-molecule level fixed effects to control for various levels of unobserved heterogeneity as discussed earlier.

Given the finding that the total number of prescriptions for carbapenems went down in the post-treatment period for multinational firms compared to domestic firms, we examined the mechanisms more deeply to understand that decrease. It is potentially possible in two ways. First, it is probable that fewer physicians were prescribing carbapenems after the shock. Second, on an average, the physicians might have been prescribing lesser prescriptions after the shock. While the dataset does not allow us to track individual physician's prescriptions, we can extract average number of prescriptions per physician prescribing carbapenems for a particular firm. Using a specification similar to Equation (3), we estimate Model 4 in Table 4 and report the corresponding results. We see that the average number of prescriptions for carbapenems per physicians for a multinational also went down significantly compared to domestic firm. This finding indicates that the behaviour change occurred through the intensive margin.

To summarize the results so far, we have established two major points. First, in the post-treatment period, multinationals were significantly reducing their market presence in terms of quantity as well as monetary share, accompanied by a general decline in the aggregate quantity produced and sales by multinationals. Second, physicians exhibited a complementary response, potentially contributing to reduction in presence of multinationals in the carbapenem market. They prescribed fewer carbapenems produced by multinationals along with an overall reduction in carbapenem prescriptions. These effects lined up also at the individual level (for a representative physician in the database). Next, we unpack the mechanisms behind these shifts in the market-level behaviour along with examining the robustness of the findings.

6.4 Heterogeneous Effects: Old versus New Generation Carbapenems

In all our investigations thus far, we have considered carbapenems as one homogeneous group of molecules that belong to the same class. But there are differences within carbapenems in terms of generational factors and vintage of the active ingredient. Broadly, we can divide carbapenems into two groups, old versus new following prior work (Chahine, Ferrill, & Poulakos, 2010; Papp-Wallace, Endimiani, Taracila, & Bonomo, 2011; Shah & Isaacs, 2003). This division is important from the perspective of drug manufacturing firms' point of view, especially if they are also innovators. Note that the old generation molecules in general would be more stable simply because they have stayed in the market for a longer time and have been

proven to be more efficacious potentially with lesser side effects. In the context of antibiotics, there is an additional feature that we need to consider. Firms knew that bacteria were becoming resistant to their drugs. In that case, the new generation molecules would likely have two disadvantages. First, if the bacteria indeed became resistant to them then there is no more incentives left at the margin to run the technological races to beat the bacteria. This is evidenced by the fact that within antibiotics, innovation has been sparse in recent times and new molecules are few and far between (Spellberg & Gilbert, 2014).[23] Second, given the endless race between the evolution of bacteria and antibiotics like Dr. Anthony Fauci mentioned (quoted earlier), firms find it more and more difficult to carry on, thus negatively impacting investment in new molecules and innovation.[24]

Combining these ideas, we can hypothesize that in this context of technology abandonment, multinationals would react more aggressively in the production of new generation of molecules. In order to test our hypothesis, we divided our treatment group into two sub-groups consisting of newer carbapenems (*Ertapenem* and *Doripenem*) and older carbapenems (combination of *Imipenem* and *Cilastatin*, combination of *Meropenem* and *Sulbactam*, and only *Meropenem*)[25] and examine which sub-group within carbapenems saw higher reduction of market shares for multinationals.

We estimate Equation (1) within this sub-group of carbapenems both using sales data (from AIOCD) and prescription data (from IQVIA). All results have been presented in Table 5. We have employed fractional logit models for estimation with time dummies, controlling for total market size. Models (1) and (2) describe the results for multinationals' sales share in newer carbapenems in quantity and monetary terms. Models (3) and (4) show the same for older carbapenems. Models (5) and (6) show the results for prescription regressions for newer and older carbapenems. All results support the hypothesis that multinationals reacted more sharply in newer carbapenems and actively reduced corresponding sales. The results from models (5) and (6) show that physicians while they reduced prescriptions for both, they were more conservative in prescribing newer carbapenems and here the reduction was very substantial compared to older carbapenems.

[23] https://www.theguardian.com/business/2020/jan/17/big-pharma-failing-to-invest-in-new-antibiotics-says-who
[24] https://www.nature.com/articles/nbt.4193 Editorial- Wanted: a reward for antibiotic development (Published: 06 July 2018)
[25] See table 1 in Appendix for the set of molecules along with the ATC classification. Ertapenem and Doripenem were introduced after 2000 whereas Imipenem and Meropenem were patented in the 1970s and 80s and marketed long before 2000. Table 2 in Appendix list the introduction dates of carbapenem in US. Imipenem and Meropenem were introduced before 2000 and Ertapenem and Doripenem were introduced after 2000

6.5 Tracing the Mechanism Through Firm-level Reduction in Bonus Quantity

So far, our analysis focuses on firm and physician choices. It is also conceivable that the supply side would react to the NDM-1 shock more than the demand side since potentially, there is some information barrier between consumers and producers of drugs. We can go one step further to bolster this point. As an additional mechanism of the average multinational firm's revealed preferences, we can analyse the level of bonus quantities that firms give to stockists and retail pharmacists as a direct way to incentivize the sellers. This has been highlighted earlier to be a pervasive phenomenon in Indian pharmaceutical markets (Bhaskarabhatla, Chatterjee, & Karreman, 2016). We examine this using Equation (2) on bonus quantities at the molecule-firm-month level in a triple difference set up. Bonus quantity represents the extra quantity provided to retailers by a focal firm to boost up sales of a particular molecule of the firm (for example, a firm may give a retailer one extra strip of medicine for free for every 100 strips of medicines they are able to sell within a fixed time period, and hence incentivise retailer to promote sales of the medicine). To estimate the effects on bonus quantities, we use inverse hyperbolic sine transform (Bahar, Choudhury, & Rapoport, 2020; Bellemare & Wichman, 2020) which is well-defined for zeros. The results are presented in Model 2 of Table 4. We find that in the post-treatment period, the multinationals were also provisioning relatively lesser amount of bonus quantities to local retailers in carbapenems compared to domestic firms. This finding in conjunction with the fact that domestic firms sold larger volumes of antibiotics in the absence of foreign competition, also establishes that it is not the case that consumer turned away from the market. The demand side remained relatively stable. The multinationals deliberately seem to have pulled out of the market, as is evidenced by reduced incentives provisioned by them after the publication of the NDM-1 paper in *Lancet Infectious Diseases* rendering carbapenems, more so, newer variants of carbapenems less viable for them.

6.6 Robustness of Results with respect to Regional Heterogeneity

Next, we examine if our results hold if we accounted for regional heterogeneity in the Indian context. Previous studies like Adbi, Chatterjee, & Mishra, 2019 and Dandona et al., 2017) examine the spatial heterogeneity leading to differential within market responses in India given a 'nation within nation identity'. To account for regional heterogeneity, we controlled for inter-regional heterogeneity in Eq (1) and re-estimated the specifications, results are presented in Table 7. We find that the baseline result holds both qualitatively and

quantitatively; multinational shares on an average decline in the treated carbapenem markets in the post-treatment period, even after controlling for inter-regional heterogeneity.

6.7 Robustness with Alternate Control Group, Pre-trends & Synthetic Control

So far all our analyses above have used narrow spectrum antibiotics as the control group. As a robustness check, we re-estimated the specifications against an alternate control group comprising broad spectrum antibiotics other than carbapenems. The reason for considering this alternate control group is as follows. The NDM-1 paper explicitly mentioned carbapenem in its abstract itself: "*Gram-negative Enterobacteriaceae with resistance to carbapenem conferred by New Delhi metallo-beta-lactamase 1 (NDM-1) are potentially a major global health problem*." (quoted from Kumarasamy et al. 2010)). Therefore, there is a possibility that the physicians might consider carbapenems as a separate entity within the group of broad-spectrum antibiotics or firm-physician conversations may evolve in this direction during sales visits.

We have estimated Eq (1) using rest of the broad spectrum antibiotics as the control group and present the results in Table 6. We see that the effects are muted but still there are traces of differential responses between the treatment and the control group of molecules. Multinational average market shares in terms of quantity sold show significant reduction (but of lesser magnitude than the corresponding coefficients in Table 1) with both OLS and fractional logit estimation. For monetary sales, the coefficients are negative but not significant.

We also present our investigations on pre-trends in the data and examine the robustness of our results while employing synthetic controls. Following Angrist & Pischke (2008), we checked for the existence of pre-trend in the sales data using the following derivative of Eq (1):

$$\boldsymbol{mncshare_{mt} = \alpha_0 + \beta_1\, carbapanem_m + \beta_2 year_{2008} + \beta_3 year_{2009} + \beta_4 year_{2010} + \beta_5 year_{2011} + \beta_6 year_{2012} + \beta_7 year_{2013} + \beta_8 carbapanem_m \times year_{2008} + \beta_9 carbapanem_m \times year_{2009} + \beta_{10} carbapanem_m \times year_{2010} + \beta_{11} carbapanem_m \times year_{2011} + \beta_{12} carbapanem_m \times year_{2012} + \beta_{13} carbapanem_m \times year_{2013} + \beta_{14} \times X_{\{mt\}} + molecule_m + time_t + \epsilon_{mt}} \text{ --- } \boldsymbol{Eq\ (6)}$$

Insignificant coefficients in the pre-trend periods (i.e. for β_8, β_9, β_{10}) would signify the absence of pre-trends between our treatment and control markets in our estimated results. We have plotted the coefficients β_9 to β_{13} for both sales and monetary sales in Figure 5. We find that indeed the coefficients in the pre-treatment period are very close to zero and practically

insignificant. In the post-treatment period, the coefficients are significantly negative. Therefore, our results stand robust to the possibility of existence of pre-trends. We also performed a subsample test with 36 month of data from April 2009 to March 2012 to test for confounding due to pre trend or post shock.[26] Our results are qualitatively similar with somewhat weaker significance (Appendix table 3). Finally, we used the synthetic control method (Abadie, Diamond, & Hainmueller, 2010; Abadie & Gardeazabal, 2003) to control for unobserved heterogeneity, and also establish robustness of our main findings with respect to the choice of the control group. The synthetic control method is a matching technique, which creates an artificial control group to match the characteristic of treated group in the pre-treatment period, based on observed covariates and outcome variable. This data-driven approach makes the synthetic control method more objective way to create a counterfactual world in the absence of the treatment, as opposed to subjective choices to create counterfactuals. These advantages of the synthetic control method had led to wide-spread use of the method in recent studies (Adbi, Chatterjee, Drev, & Mishra, 2019; Green, Heywood, & Navarro, 2014; Peng, Meyerhoefer, & Chou, 2018) as a means for robustness test for differences in difference estimation.

For our analysis, the outcome of interest is the mean market share of multinationals in carbapenems pre and post-publication of NDM-1 paper. Using the synthetic control method, we assign weights to narrow-spectrum molecules to create an artificial matched sample to match the carbapenem molecules on an average. The results are plotted in Figure 6. The results for synthetic controls are qualitatively and quantitatively in line with our difference in difference estimates. The counterfactual results show a stable, horizontal path of sales share of the multinationals in the absence of treatment, whereas the real observed path of sales share for the multinationals shows a clear downward decline with a sizeable gap between them in the post-treatment period.

7.0 Conclusion & Discussion

In this paper, we study the relationship between science and market structure and associatedly examine product and technology abandonment. In August 2010, an academic paper got peer reviewed and published in *The Lancet Infectious Diseases* which presented evidence for antibiotic-resistant superbugs in India. This paper stirred intense scholarly and

[26] Due to introduction of Doripenem by multinationals in June 2009, there is an upward bump in Figure 3. We try to address this issue by focussing on a sample with a smaller time period, and find our results to be broadly consistent.

policy debates for primarily two reasons. First, the authors named the superbug by *New Delhi* where they found the bacteria. This led to speculations about regional discrimination (like we are witnessing now with the *Wuhan Coronavirus* (Yang et al. 2020; Corman et al. 2020) although some of the authors were Indians themselves, as well as a fear about adverse impact of this discovery on medical tourism in India (Saliba et al, 2016). Second, this study showed that the superbug became resistant to the antibiotics of last resort, carbapenems.

We study how multinationals and domestic pharmaceutical firms in India reacted to this news of discovery of superbugs and super-resistance (Davies & Davies, 2010). Given the *red queen* race between germs and medicines, we see that the average multinational firm reacted very differently than the average domestic firm. In particular, the multinationals withdrew from the market for carbapenems and the domestic firms started filling in the void that was created. Part of the differences in firm behaviour in exiting the markets could be attributed to corporate ethics, perhaps also to safeguard the multinationals from reputational damages in other products and peer markets within and beyond India, however we cannot test for that explicitly with our data. That said, we can also establish that within India, physician behaviour changed substantially in terms of prescription patterns, moving away from the multinational carbepenems being prescribed.

Our results are robust with respect to alternate control groups and remain unchanged accounting for inter-regional heterogeneity. The results are not affected by pre-trends, and are consistent even while employing synthetic controls. Our exploration into the underlying mechanisms show that multinationals were more aggressively pulling back from new generation of carbapenems vis-à-vis the older generation. Also, a complementary analysis shows that they were actively providing lesser push incentives to retailers by cutting down on bonus quantities for retailers stocking and selling the drugs.

Overall, our study contributes to the understudied area of product and technology abandonment (Greenwood et al., 2016). Also, in line with previous research we find that scientific evidence can influence technological abandonment (S. N. Finkelstein & Gilbert, 1985), but there are firm-level heterogeneities herein. However this is not a given since even in the presence of scientific evidence of ineffectiveness of products, firms may not abandon technology (David, 1985), hence the debate continues with our findings. Additionally, we find that some firms may actually expand their market share in a problematic product and technology market at the expense of other firms. This mechanism works at both intensive and

extensive margins and has long run welfare implications coming from health outcomes of patients which future work should revisit.

Our findings also supplement the analysis of entry-exit decisions by bringing in the importance of liability of foreignness (Zaheer & Mosakowski, 1997) as an important determinant of firm behaviour. Recognition of differential costs borne by different firms associated with their technological choices is important and these costs shape firm attitude towards particular markets and for innovative firms, also shaping their attitude towards science and technological development in general (Arora, Belenzon, & Patacconi, 2018; Gittelman & Kogut, 2003; Li, Azoulay, & Sampat, 2017).

Our work does have limitations. Our focal exogenous treatment of the scientific shock was cross-national and it would be worth investigating in international pharmaceutical demand and prescription data if there were spill overs of the *NDM1* shock in impacting the global market structure for carbapenems in relation to other antibiotics. A related question would be to estimate the impact of the shock on upstream science and innovation in both public and private antibiotics R&D. The fact that the declining share of multinationals were replaced with increasing shares of domestic firm products warrants a careful future investigation of patient outcomes from medical claims data. This is especially important to understand the welfare consequences of the NDM1 shock given recently emerging concerns in India about quality of medicines. Finally, while we don't explicitly test for it, it might be worthwhile to estimate the speed of exit between heterogeneous firms as a function of the NDM1 shock in a future study.

This paper also informs policy-makers in the world of high dispersion in success for different inventions and innovations (Scherer & Harhoff, 2000) given the impact of scientific advances on industry structure and profitability of innovations. Broadly speaking, our paper provides empirical evidence on impact of scientific advances on market structure. Coupled with the empirical evidence on effect of market size on scientific innovations (Acemoglu, 1998, 2002), we provide nuanced understanding of the intertwined nature of endogenous growth process of science and markets.

References (Incomplete)

Abadie, A., Diamond, A., & Hainmueller, J. (2010). Synthetic control methods for comparative case studies: Estimating the effect of California's tobacco control program. *Journal of the American Statistical Association*, *105*(490), 493–505.

Abadie, A., & Gardeazabal, J. (2003). The economic costs of conflict: A case study of the Basque Country. *American Economic Review*, *93*(1), 113–132.

Abrahamson, E., & Rosenkopf, L. (1997). Social network effects on the extent of innovation diffusion: A computer simulation. *Organization Science*, *8*(3), 289–309.

Acemoglu, D. (1998). Why do new technologies complement skills? Directed technical change and wage inequality. *The Quarterly Journal of Economics*, *113*(4), 1055–1089.

Acemoglu, D. (2002). Directed technical change. *The Review of Economic Studies*, *69*(4), 781–809.

Acemoglu, D., & Linn, J. (2004). Market size in innovation: theory and evidence from the pharmaceutical industry. *The Quarterly Journal of Economics*, *119*(3), 1049–1090.

Adbi, A., Bhaskarabhatla, A., & Chatterjee, C. (2018). Stakeholder Orientation and Market Impact: Evidence from India. *Journal of Business Ethics*, 1–18.

Adbi, A., Chatterjee, C., Drev, M., & Mishra, A. (2019). When the Big One Came: A Natural Experiment on Demand Shock and Market Structure in India's Influenza Vaccine Markets. *Production and Operations Management*, *28*(4), 810–832.

Adbi, A., Chatterjee, C., & Mishra, A. (2019). Nations within a Nation: Pandemic, Regional Heterogeneity, and MNC Share of Vaccine Uptake. In *Academy of Management Proceedings* (Vol. 2019, p. 12668).

Adner, R., & Feiler, D. (2019). Interdependence, Perception, and Investment Choices: An Experimental Approach to Decision Making in Innovation Ecosystems. *Organization Science*.

Adner, R., & Kapoor, R. (2016). Innovation ecosystems and the pace of substitution: Re-examining technology S-curves. *Strategic Management Journal*, *37*(4), 625–648.

Agarwal, R., Bayus, B. L., & Tripsas, M. (2005). Abandoning innovation in emerging industries. *Voice*, *8*(4), 356–370.

Agarwal, R., Moeen, M., & Shah, S. K. (2017). Athena's birth: Triggers, actors, and actions preceding industry inception. *Strategic Entrepreneurship Journal*, *11*(3), 287–305.

Ahmadi, F., & Zarei, E. (2017). Prescribing patterns of rural family physicians: a study in Kermanshah Province, Iran. BMC Public Health, 17(1), 908.

Ahuja, G., & Yayavaram, S. (2011). Perspective—Explaining influence rents: The case for an institutions-based view of strategy. *Organization Science*, *22*(6), 1631–1652.

Alsan, M., Schoemaker, L., Eggleston, K., Kammili, N., Kolli, P., & Bhattacharya, J. (2015). Out-of-pocket health expenditures and antimicrobial resistance in low-income and middle-income countries: an economic analysis. *The Lancet Infectious Diseases*, *15*(10), 1203–1210.

Aminov, R. I. (2010). A brief history of the antibiotic era: lessons learned and challenges for the future. *Frontiers in Microbiology*, *1*, 134.

Angrist, J. D., & Pischke, J.-S. (2008). *Mostly harmless econometrics: An empiricist's companion*. Princeton university press.

Arora, A., Belenzon, S., & Patacconi, A. (2018). The decline of science in corporate R&D.

Strategic Management Journal, *39*(1), 3–32.

Azoulay, P. (2002). Do pharmaceutical sales respond to scientific evidence? *Journal of Economics & Management Strategy*, *11*(4), 551–594.

Bahar, D., Choudhury, P., & Rapoport, H. (2020). Migrant inventors and the technological advantage of nations. *Research Policy*, 103947.

Baquero, F., Alvarez-Ortega, C., & Martinez, J. L. (2009). Ecology and evolution of antibiotic resistance. *Environmental Microbiology Reports*, *1*(6), 469–476.

Bass, F. M. (1969). A new product growth for model consumer durables. *Management Science*, *15*(5), 215–227.

Basu, S., Chatterjee, M., & Chandra, P. K. (2008). Antibiotic misuse in children by the primary care physicians-an Indian experience. Nigerian Journal of Clinical Practice, 11(1), 53-58.

Bayus, B. L., & Agarwal, R. (2007). The role of pre-entry experience, entry timing, and product technology strategies in explaining firm survival. *Management Science*, *53*(12), 1887–1902.

Bellemare, M. F., & Wichman, C. J. (2020). Elasticities and the inverse hyperbolic sine transformation. *Oxford Bulletin of Economics and Statistics*, *82*(1), 50–61.

Bhaskarabhatla, A., & Chatterjee, C. (2017). The role of physicians in prescribing irrational fixed-dose combination medicines in India. *Social Science & Medicine*, *174*, 179–187.

Bhaskarabhatla, A., Chatterjee, C., Anurag, P., & Pennings, E. (2016). Mitigating regulatory impact: the case of partial price controls on metformin in India. *Health Policy and Planning*, *32*(2), 194–204.

Bhaskarabhatla, A., Chatterjee, C., & Karreman, B. (2016). Hit where it hurts: cartel policing using targeted sales and supply embargoes. *The Journal of Law and Economics*, *59*(4), 805–846.

Borgatti, S. P., & Cross, R. (2003). A relational view of information seeking and learning in social networks. *Management Science*, *49*(4), 432–445.

Branstetter, L., Chatterjee, C., & Higgins, M. J. (2016). Regulation and welfare: evidence from paragraph IV generic entry in the pharmaceutical industry. *The RAND Journal of Economics*, *47*(4), 857–890.

Brivio, E., Oliveri, S., & Pravettoni, G. (2020). Empowering Communication in Emergency Contexts: Reflections From the Italian Coronavirus Outbreak. In *Mayo Clinic Proceedings* (Vol. 95, pp. 849–851).

Buchmueller, T. C., Carey, C. M., & Meille, G. (2019). *How Well Do Doctors Know Their Patients? Evidence from a Mandatory Access Prescription Drug Monitoring Program*.

Burnet, M., Burnet, F. M., & White, D. O. (1972). *Natural history of infectious disease*. CUP Archive.

Burns, L. R., & Wholey, D. R. (1993). Adoption and abandonment of matrix management programs: Effects of organizational characteristics and interorganizational networks. *Academy of Management Journal*, *36*(1), 106–138.

Campbell, J. T., Eden, L., & Miller, S. R. (2012). Multinationals and corporate social

responsibility in host countries: Does distance matter? *Journal of International Business Studies*, *43*(1), 84–106.

Chahine, E. B., Ferrill, M. J., & Poulakos, M. N. (2010). Doripenem: a new carbapenem antibiotic. *American Journal of Health-System Pharmacy*, *67*(23), 2015–2024.

Chakraborty, P., & Chatterjee, C. (2017). Does environmental regulation indirectly induce upstream innovation? New evidence from India. *Research Policy*, *46*(5), 939–955.

Chatterjee, C. (2009). *New Suppliers & New Markets: Essays on the Global Pharmaceutical Industry*. Carnegie Mellon.

Chatterjee, C., Kubo, K., & Pingali, V. (2015). The consumer welfare implications of governmental policies and firm strategy in markets for medicines. *Journal of Health Economics*, *44*, 255–273.

Chaudhuri, Shubham, Goldberg, P. K., & Gia, P. (2006). Estimating the effects of global patent protection in pharmaceuticals: a case study of quinolones in India. *American Economic Review*, *96*(5), 1477–1514.

Chaudhuri, Sudip. (2005). *The WTO and India's pharmaceuticals industry: Patent protection, TRIPS, and developing countries*. Oxford University Press, USA.

Cheah, E. T., Chan, W. L., & Chieng, C. L. L. (2007). The corporate social responsibility of pharmaceutical product recalls: An empirical examination of US and UK markets. *Journal of Business Ethics*, *76*(4), 427–449.

Cockburn, I., Henderson, R., & Stern, S. (1999). *The diffusion of science-driven drug discovery: organizational change in pharmaceutical research*.

Conly, J. M., & Johnston, B. L. (2005). Where are all the new antibiotics? The new antibiotic paradox. *Canadian Journal of Infectious Diseases and Medical Microbiology*, *16*(3), 159–160.

Corman, V., Bleicker, T., Brünink, S., Drosten, C., & Zambon, M. (2020). Diagnostic detection of Wuhan coronavirus 2019 by real-time RT-PCR. Geneva: World Health Organization, January, 13.

Crilly, D., Ni, N., & Jiang, Y. (2016). Do-no-harm versus do-good social responsibility: Attributional thinking and the liability of foreignness. *Strategic Management Journal*, *37*(7), 1316–1329.

Dandona, L., Dandona, R., Kumar, G. A., Shukla, D. K., Paul, V. K., Balakrishnan, K., … others. (2017). Nations within a nation: variations in epidemiological transition across the states of India, 1990--2016 in the Global Burden of Disease Study. *The Lancet*, *390*(10111), 2437–2460.

David, P. A. (1985). Clio and the Economics of QWERTY. *The American Economic Review*, *75*(2), 332–337.

Davies, J., & Davies, D. (2010). Origins and evolution of antibiotic resistance. *Microbiol. Mol. Biol. Rev.*, *74*(3), 417–433.

Dieckmann, U., Marrow, P., & Law, R. (1995). Evolutionary cycling in predator-prey interactions: population dynamics and the Red Queen. *Journal of Theoretical Biology*, *176*(1), 91–102.

Dubois, P., De Mouzon, O., Scott-Morton, F., & Seabright, P. (2015). Market size and pharmaceutical innovation. *The RAND Journal of Economics*, *46*(4), 844–871.

Duggan, M., Garthwaite, C., & Goyal, A. (2016). The market impacts of pharmaceutical product patents in developing countries: Evidence from India. *American Economic Review*, *106*(1), 99–135.

Dutta, A. (2011). From free entry to patent protection: Welfare implications for the Indian pharmaceutical industry. *The Review of Economics and Statistics*, *93*(1), 160–178.

Ebrahim, S. H., & Memish, Z. A. (2020). COVID-19: preparing for superspreader potential among Umrah pilgrims to Saudi Arabia. *Lancet (London, England)*, *395*(10227), e48.

Ellison, S. F., Cockburn, I., Griliches, Z., & Hausman, J. (1997). Characteristics of demand for pharmaceutical products: an examination of four cephalosporins. *The RAND Journal of Economics*, 426–446.

Eswaran, M., & Gallini, N. (2019). can competition and Patent Policies Avert the Antibiotic crisis? *Canadian Public Policy*, *45*(1), 74–92.

Farooqui, H. H., Mehta, A., & Selvaraj, S. (2019). Systemic antibiotic prescription rates and patterns in private sector in India: Evidence from medical audit data. *International Journal of Infectious Diseases*, *79*, 41–42.

Finkelstein, A. (2004). Static and dynamic effects of health policy: Evidence from the vaccine industry. *The Quarterly Journal of Economics*, *119*(2), 527–564.

Finkelstein, S. N., & Gilbert, D. L. (1985). Scientific evidence and the abandonment of medical technology: A study of eight drugs. *Research Policy*, *14*(4), 225–233.

Furr, N., & Kapoor, R. (2018). Capabilities, technologies, and firm exit during industry shakeout: Evidence from the global solar photovoltaic industry. *Strategic Management Journal*, *39*(1), 33–61.

Gates, B. (2018). The next epidemic is coming. Here's how we can make sure we're ready. Shattuck Lecture Boston, MA.

Gittelman, M., & Kogut, B. (2003). Does good science lead to valuable knowledge? Biotechnology firms and the evolutionary logic of citation patterns. *Management Science*, *49*(4), 366–382.

Green, C. P., Heywood, J. S., & Navarro, M. (2014). Did liberalising bar hours decrease traffic accidents? *Journal of Health Economics*, *35*, 189–198.

Greenwood, B. N., Agarwal, R., Agarwal, R., & Gopal, A. (2016). The when and why of abandonment: The role of organizational differences in medical technology life cycles. *Management Science*, *63*(9), 2948–2966.

Grennan, M., & Town, R. J. (2020). Regulating innovation with uncertain quality: information, risk, and access in medical devices. *American Economic Review*, *110*(1), 120–161.

Guan, X., Tian, Y., Song, J., Zhu, D., & Shi, L. (2019). Effect of physicians' knowledge on antibiotics rational use in China's county hospitals. Social Science & Medicine, 224, 149-155.

Gudbjartsson, D. F., Helgason, A., Jonsson, H., Magnusson, O. T., Melsted, P., Norddahl, G. L., … others. (2020). Spread of SARS-CoV-2 in the Icelandic population. *New England*

Journal of Medicine.

Hafner, T., & Popp, D. (2011). *China and India as suppliers of affordable medicines to developing countries*.

Haunschild, P. R., & Rhee, M. (2004). The role of volition in organizational learning: The case of automotive product recalls. *Management Science*, *50*(11), 1545–1560.

Jarrell, G., & Peltzman, S. (1985). The impact of product recalls on the wealth of sellers. *Journal of Political Economy*, *93*(3), 512–536.

Kapczynski, A. (2009). Harmonization and its discontents: a case study of TRIPS implementation in India's pharmaceutical sector. *Calif. L. Rev.*, *97*, 1571.

Kapoor, R., & Furr, N. R. (2015). Complementarities and competition: Unpacking the drivers of entrants' technology choices in the solar photovoltaic industry. *Strategic Management Journal*, *36*(3), 416–436.

Klein, E. Y., Van Boeckel, T. P., Martinez, E. M., Pant, S., Gandra, S., Levin, S. A., … Laxminarayan, R. (2018). Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proceedings of the National Academy of Sciences*, *115*(15), E3463--E3470.

Klepper, S., & Simons, K. L. (1996). Innovation and industry shakeouts. *Business and Economic History*, 81–89.

Klepper, S., & Simons, K. L. (1997). Technological extinctions of industrial firms: an inquiry into their nature and causes. *Industrial and Corporate Change*, *6*(2), 379–460.

Klepper, S., & Simons, K. L. (2005). Industry shakeouts and technological change. *International Journal of Industrial Organization*, *23*(1–2), 23–43.

Kostova, T., Roth, K., & Dacin, M. T. (2008). Institutional theory in the study of multinational corporations: A critique and new directions. *Academy of Management Review*, *33*(4), 994–1006.

Kotwani, A., Wattal, C., Katewa, S., Joshi, P. C., & Holloway, K. (2010). Factors influencing primary care physicians to prescribe antibiotics in Delhi India. *Family Practice*, *27*(6), 684–690.

Kristensen, P. K., Johnsen, S. P., & Thomsen, R. W. (2019). Decreasing trends, and geographical variation in outpatient antibiotic use: a population-based study in Central Denmark. *BMC Infectious Diseases*, *19*(1), 337.

Kumarasamy, K. K., Toleman, M. A., Walsh, T. R., Bagaria, J., Butt, F., Balakrishnan, R., … others. (2010). Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *The Lancet Infectious Diseases*, *10*(9), 597–602.

Lal, R., & Narasimhan, C. (1996). The inverse relationship between manufacturer and retailer margins: A theory. *Marketing Science*, *15*(2), 132–151.

Lambert, B. L., Salmon, J. W., Stubbings, J., Gilomen-Study, G., Valuck, R. J., & Kezlarian, K. (1997). Factors associated with antibiotic prescribing in a managed care setting: an exploratory investigation. *Social Science & Medicine*, *45*(12), 1767–1779.

Lee, P.-I., & Hsueh, P.-R. (2020). Emerging threats from zoonotic coronaviruses-from SARS

and MERS to 2019-nCoV. *Journal of Microbiology, Immunology and Infection*.

Li, D., Azoulay, P., & Sampat, B. N. (2017). The applied value of public investments in biomedical research. *Science*, *356*(6333), 78–81.

Marris, E., & Fairless, D. (2007). Wind farms' deadly reputation hard to shift. *Nature*, *447*(7141), 126.

Meeker, D., Linder, J. A., Fox, C. R., Friedberg, M. W., Persell, S. D., Goldstein, N. J., … Doctor, J. N. (2016). Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: a randomized clinical trial. *Jama*, *315*(6), 562–570.

Murmann, J. P., & Frenken, K. (2006). Toward a systematic framework for research on dominant designs, technological innovations, and industrial change. *Research Policy*, *35*(7), 925–952.

Nevo, A. (2001). Measuring market power in the ready-to-eat cereal industry. *Econometrica*, *69*(2), 307–342.

O'neill, J. I. M. (2014). Antimicrobial resistance: tackling a crisis for the health and wealth of nations. *Rev. Antimicrob. Resist*, *20*, 1–16.

Papke, L. E., & Wooldridge, J. M. (2008). Panel data methods for fractional response variables with an application to test pass rates. *Journal of Econometrics*, *145*(1–2), 121–133.

Papp-Wallace, K. M., Endimiani, A., Taracila, M. A., & Bonomo, R. A. (2011). Carbapenems: past, present, and future. *Antimicrobial Agents and Chemotherapy*, *55*(11), 4943–4960.

Peng, L., Meyerhoefer, C., & Chou, S.-Y. (2018). The health implications of unconventional natural gas development in Pennsylvania. *Health Economics*, *27*(6), 956–983.

Petrin, A. (2002). Quantifying the benefits of new products: The case of the minivan. Journal of Political Economy, 110(4), 705-729.

Pulcini, C., Bush, K., Craig, W. A., Frimodt-Møller, N., Grayson, M. L., Mouton, J. W., … for Antibiotic Policies, E. S. G. (2012). Forgotten antibiotics: an inventory in Europe, the United States, Canada, and Australia. *Clinical Infectious Diseases*, *54*(2), 268–274.

Rhee, M., & Haunschild, P. R. (2006). The liability of good reputation: A study of product recalls in the US automobile industry. *Organization Science*, *17*(1), 101–117.

Rogers, E. M. (2003). *Diffusion of innovations*. *Free Press of Glencoe*. Simon and Schuster. https://doi.org/citeulike-article-id:126680

Sadyrbaeva-Dolgova, S., Aznarte-Padial, P., Pasquau-Liaño, J., Expósito-Ruiz, M., Calleja-Hernández, M. Á., & Hidalgo-Tenorio, C. (2019). Clinical Outcomes of Carbapenem De-escalation regardless of microbiological results: a propensity score analysis. *International Journal of Infectious Diseases*.

Sampat, B. N., & others. (2015). *Intellectual property rights and pharmaceuticals: the case of antibiotics* (Vol. 26). WIPO.

Scherer, F. M. (2004). A note on global welfare in pharmaceutical patenting. *World Economy*, *27*(7), 1127–1142.

Scherer, F. M., & Harhoff, D. (2000). Technology policy for a world of skew-distributed

outcomes. *Research Policy*, *29*(4–5), 559–566.

Schwartz, R. K., Soumerai, S. B., & Avorn, J. (1989). Physician motivations for nonscientific drug prescribing. *Social Science & Medicine*, *28*(6), 577–582.

Shah, P. M., & Isaacs, R. D. (2003). Ertapenem, the first of a new group of carbapenems. *Journal of Antimicrobial Chemotherapy*, *52*(4), 538–542.

Spellberg, B., & Gilbert, D. N. (2014). The future of antibiotics and resistance: a tribute to a career of leadership by John Bartlett. *Clinical Infectious Diseases*, *59*(suppl_2), S71--S75.

Staiger, D., & Stock, J. H. (1994). *Instrumental variables regression with weak instruments*.

Sudhir, K. (2001). Structural analysis of manufacturer pricing in the presence of a strategic retailer. *Marketing Science*, *20*(3), 244–264.

Talukdar, D., Sudhir, K., & Ainslie, A. (2002). Investigating new product diffusion across products and countries. *Marketing Science*, *21*(1), 97–114.

Taussig, M. (2017). Foreignness as both a global asset and a local liability: How host country idiosyncrasies and business activities matter. *Journal of International Business Studies*, *48*(4), 498–522.

Teece, D. J. (1986). Profiting from technological innovation: Implications for integration, collaboration, licensing and public policy. *Research Policy*, *15*(6), 285–305.

Timmermans, S., & Angell, A. (2001). Evidence-based medicine, clinical uncertainty, and learning to doctor. *Journal of Health and Social Behavior*, 342–359.

Trajtenberg, M. (1989). The welfare analysis of product innovations, with an application to computed tomography scanners. *Journal of Political Economy*, *97*(2), 444–479.

Utterback, J. M., & Suárez, F. F. (1993). Innovation, competition, and industry structure. *Research Policy*, *22*(1), 1–21.

Ventola, C. L. (2015). The antibiotic resistance crisis: part 1: causes and threats. *Pharmacy and Therapeutics*, *40*(4), 277.

Vonberg, R.-P., Weitzel-Kage, D., Behnke, M., & Gastmeier, P. (2011). Worldwide Outbreak Database: the largest collection of nosocomial outbreaks. *Infection*, *39*(1), 29–34.

Weingart, P. (1998). Science and the media. *Research Policy*, *27*(8), 869–879.

Yang, J., Zheng, Y., Gou, X., Pu, K., Chen, Z., Guo, Q., ... & Zhou, Y. (2020). Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. International Journal of Infectious Diseases.

Yong, D., Toleman, M. A., Giske, C. G., Cho, H. S., Sundman, K., Lee, K., & Walsh, T. R. (2009). Characterization of a new metallo-$β$-lactamase gene, blaNDM-1, and a novel erythromycin esterase gene carried on a unique genetic structure in Klebsiella pneumoniae sequence type 14 from India. *Antimicrobial Agents and Chemotherapy*, *53*(12), 5046–5054.

Younkin, P. (2016). Complicating abandonment: how a multi-stage theory of abandonment clarifies the evolution of an adopted practice. *Organization Studies*, *37*(7), 1017–1053.

Zaheer, S. (1995). Overcoming the liability of foreignness. *Academy of Management Journal*, *38*(2), 341–363.

Zaheer, S., & Mosakowski, E. (1997). The dynamics of the liability of foreignness: A global study of survival in financial services. *Strategic Management Journal*, *18*(6), 439–463.

Figure 1. Patterns in Google search: Cumulative frequency of Google searches within India for NDM-1 and superbug from April 2007 to October 2013. The sudden surge around August 2010 (NDM-1 paper's publication) illustrates increased public awareness about NDM-1 and the associated risk of superbugs. Vertical bar denotes the treatment i.e. publication of NDM-1 article in *The Lancet* in August 2010.

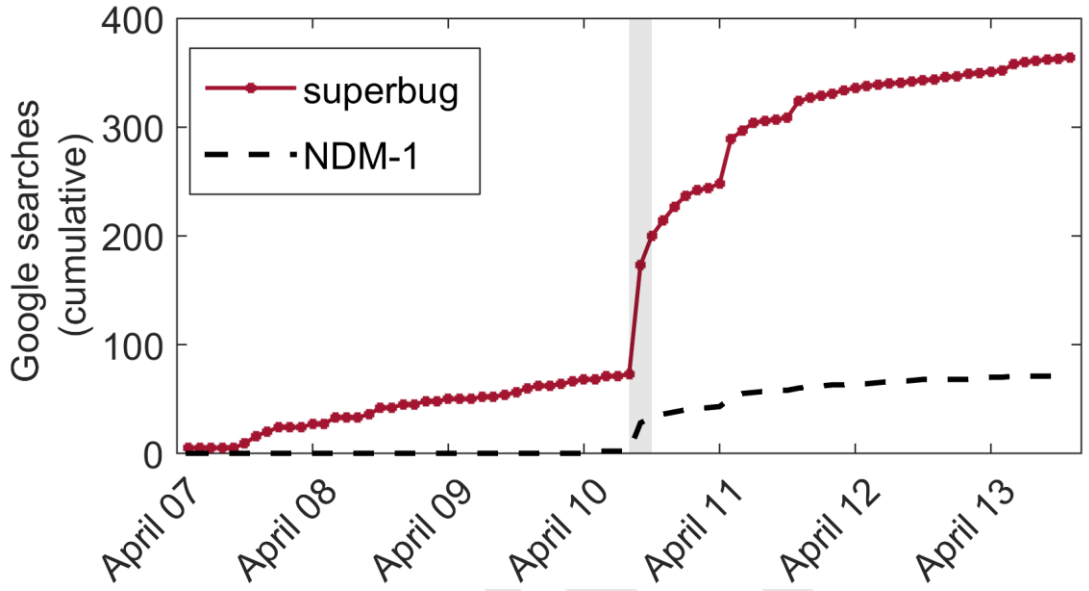

Figure 2. Resistance to Carbapenems across countries all over the world: India evidently has the highest resistance. Resistance has been measured by randomly testing bacteria with respect to treatment in carbapenems and noting the frequency of resistant bacteria. Used with permission from- The Center for Disease, Dynamics Economics & Policy. ResistanceMap: Antibiotic resistance. 2019. https://resistancemap.cddep.org/AntibioticResistance.php. Date accessed: Dec 30, 2019

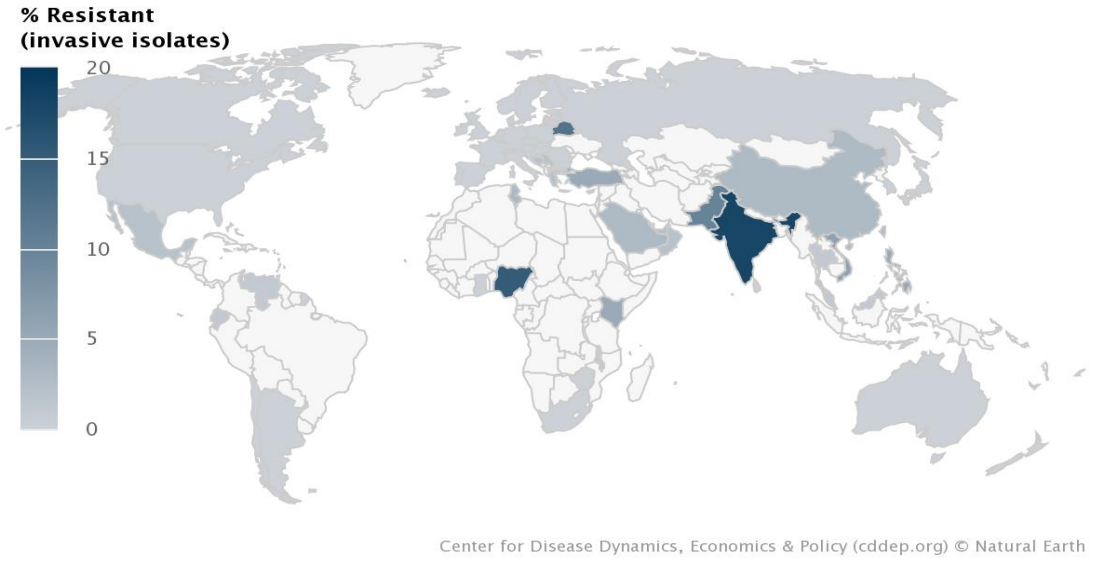

Figure 3. Total sales of Carbapenems in India from April 2007 to October 2013, in terms of log of Defined Daily Dosages (DDD): The total sales time series shows an increasing trend in the post-treatment period. Vertical bar denotes the treatment i.e. publication of NDM-1 article in *The Lancet* in August 2010.

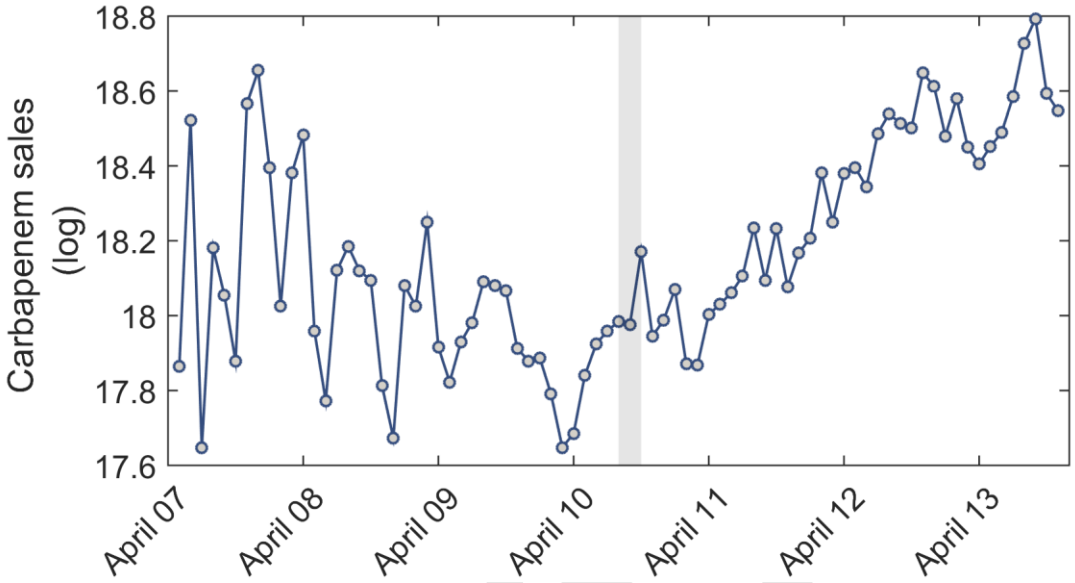

Figure 4. Multinational share in sales and monetary terms during pre- and post-treatment periods (separated by the vertical line) in the carbapenems and narrow-spectrum antibiotics market. Multinational market shares show a steep decline both in terms of quantity (left panel) and monetary sales(right panel) in the post-treatment period while the corresponding share in the market for narrow spectrum antibiotics remain stable. The x-axis denotes the number of months (data spans from April 2007 to October 2013 i.e. over 79 months).

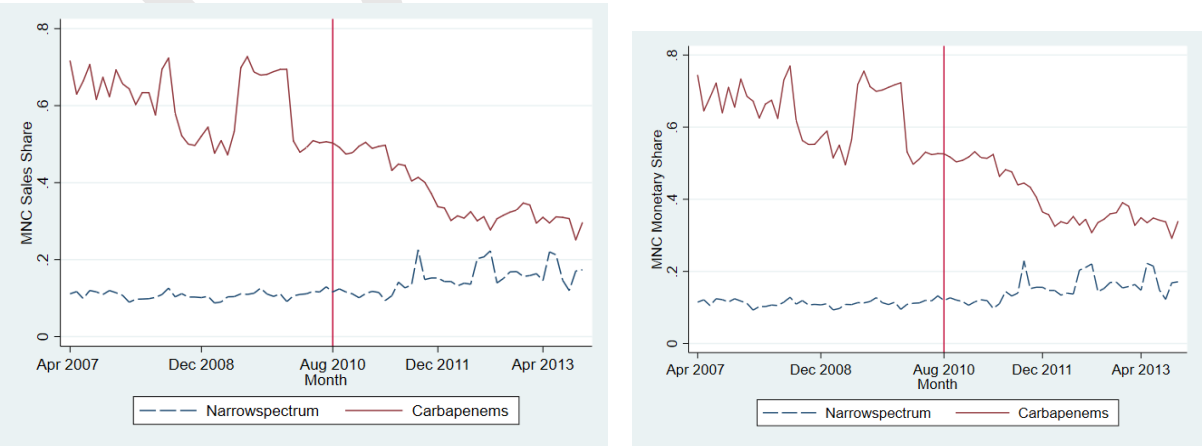

Figure 5. Coefficient estimates from Eqn. 6 of year-carbapenem interaction dummies: In the pre-treatment period, the coefficients are statistically zero and in the post-treatment period, they are negative. We conclude absence of pre trend in multinational sales (left panel) and monetary shares (right panel).

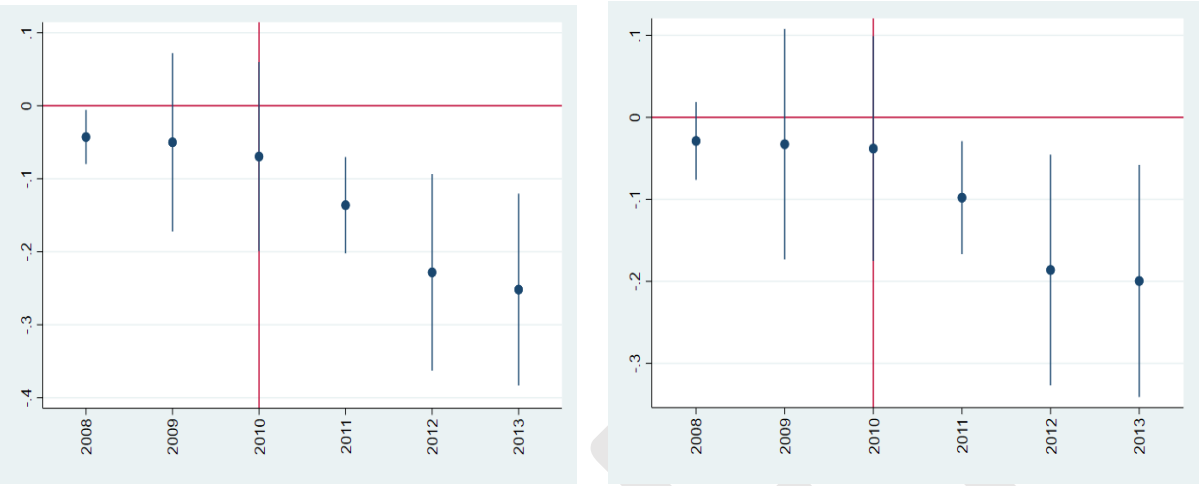

Figure 6. Synthetic control results for multinational sales share (left panel) and monetary share (right panel). In both cases, the simulated series (synthetic control) is substantially above the realized sales path, indicating a substantial decay in sales in the multinational share in the post-treatment period (treatment period is indicated by the vertical line) compared to the counterfactual of no treatment.

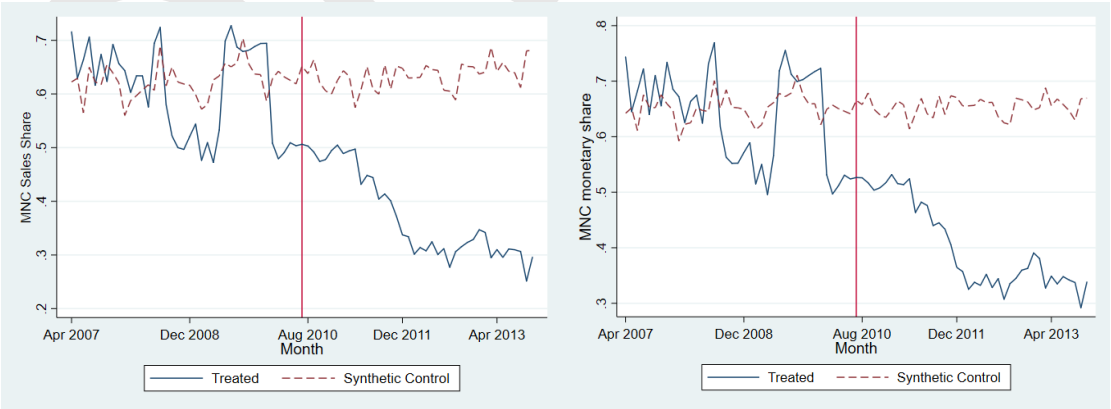

Table 1. Variable description

Dependent variables	**Description**
MNC Sales Share	Aggregated market share of multinational firms in a particular molecule in particular month in terms of sales in Defined Daily Dosage
MNC Monetary Share	Aggregated market share of multinational firms in a particular molecule in particular month in terms of sales revenue
Sales	Sales in DDD of a particular molecule as per AIOCD data. In the regression models, we use log(totalsales) in all cases
MNC Prescription Share	Aggregated market share of multinational firms in a particular molecule in particular month in terms of prescriptions written
Prescriptions	For a particular molecule how many prescriptions were written as per IQVIA Rx Data. In the regression models, we use log(prescriptions) in all cases
Prescription per Physician	For a particular molecule how many prescriptions per physician were written as per IQVIA Rx Data. In the regression models, we use log(rxperphysician) in all cases
Independent variables	**Description**
NDMdummy	0 for months before August 2010 and 1 after August 2010 (*NDM-1 article appeared online in August 2010*)
Carbapenem	Molecules belonging to the carbapenem(ATC code J01DH) have a value of 1, otherwise 0
NDMdummy × Carbapenem	Interaction term between variables NDMdummy and Carbapenem. It takes the value one for carbapenem fromAugust 2010.
MNC	Whether a firm had majority foreign ownership as on August 2010
MNC × NDMdummy × Carbapenem	Interaction term between variables, multinational, NDMdummy and Carbapenem. It takes the value one for carbapenem molecules sold by multinationals from August 2010.
Control variables	**Description**
Total monetary sales	Total revenue of a particular molecule in a particular month aggregated over all the firms(in million)
pricepermg	Average maximum retail price per DDD of molecule. In the regression models, we use log (pricepermg) in all cases.
time	Dummy variable for each month *t* where *t* ranges from 1 (April 2007) to 79 (October 2013)
molecule	Dummy variable for each molecule *m*
Firm	Dummy variable for each firm
molecule × firm	Interaction between molecule dummies and firm dummies
molecule × Calendar month	Interaction of calendar month with molecule to account for seasonality
molecule (prescription)	Dummy variables for each molecule *m* (prescription)
geography (prescription)	Dummy variables for each firm as per IQVIA medical audit database
molecule × firm (prescription)	Interactions between molecule and firm (both for prescriptions)

Table 2. Summary statistics of the narrow spectrum and carbapenem antibiotics, pre- and post-publication of the NDM-1 article. During the post-treatment period, market share of multinationals decreased drastically in sales, monetary sales and prescriptions compared to narrow spectrum antibiotics.

	(1)			(2)		
	Narrowspectrum pre-treatment			Narrowspectrum post-treatment		
	mean	sd	Count	mean	Sd	count
MNC Sales Share	0.1076	0.2487	591	0.1471	0.2865	461
MNC Monetary Share	0.1119	0.2646	591	0.1498	0.3016	461
HHI(sales)	0.6843	0.2986	591	0.7030	0.3172	461
Number of firms	11.5296	19.9636	591	9.0868	13.0937	461
Total monetary sales	26400000	55000000	591	34800000	63700000	461

	(3)			(4)		
	Carbapenem pre-treatment			Carbapenem post-treatment		
	mean	sd	Count	mean	Sd	count
MNC Sales Share	0.5992	0.3447	100	0.3636	0.3263	179
MNC Monetary Share	0.6280	0.3317	100	0.3948	0.3304	179
HHI(sales)	0.4496	0.3273	100	0.4777	0.3527	179
Number of firms	15.3100	11.3464	100	14.2011	12.9165	179
Total monetary sales	148000000	102000000	100	106000000	109000000	179

	(5)			(6)		
	Narrowspectrum pre-treatment (prescription)			Narrowspectrum post-treatment (prescription)		
	mean	sd	count	mean	sd	count
MNC Prescription Share	0.0260	0.1324	353	0.0673	0.2483	258
Number of firms	10.9518	19.0459	353	8.5271	11.6566	258
HHI(Prescriptions)	0.5956	0.2974	353	0.5718	0.2968	258
Total prescriptions	438897	900373	353	431824	682620	258

	(7)			(8)		
	Carbapenem pre-treatment (prescription)			Carbapenem post-treatment (prescription)		
	mean	sd	count	mean	Sd	count
MNC Prescription Share	0.2628	0.4069	56	0.1544	0.3401	41
Number of firms	2.3929	1.3028	56	1.4390	0.7433	41
HHI(Prescriptions)	0.5794	0.2641	56	0.4485	0.2808	41
Total prescriptions	687.3036	615.1142	56	528.1951	519.7750	41

Table 3. Multinational Shares in Sales, Revenues and Prescriptions Fall in Carbapenems After NDM-1 Discovery. Multinationals' market shares in terms of quantity (models 1 and 2) and monetary sales (models 3 and 4) decreased significantly in the post-treatment period compared to the pre-treatment period, in both OLS and fractional logit estimation. Quantitatively and qualitatively similar effects are seen in physicians' prescribing pattern as well (model 5). Time horizon is April 2007- October 2013.

	(1) MNC sales share (OLS)	(2) MNC sales share (fractional logit)	(3) MNC monetary share (OLS)	(4) MNC monetary share (fractional logit)	(5) MNC prescription share (fractional logit)
NDMdummy	0.0000	-0.9513+	0.0000	-1.1234*	13.9115***
	(.)	(0.4892)	(.)	(0.4776)	(3.7413)
Carbapenems	0.0000	17.6956***	0.0000	16.5874***	15.3599***
	(.)	(1.1317)	(.)	(1.1625)	(3.0769)
NDMdummy × Carbapenem	-0.1391**	-1.0965**	-0.1142*	-0.9771*	-11.2205***
	(0.0463)	(0.3777)	(0.0530)	(0.4262)	(2.7591)
Total monetary sales	0.0006***	0.0073**	0.0007**	0.0087**	
	(0.0001)	(0.0025)	(0.0002)	(0.0031)	
_cons	0.1805***	-19.7591***	0.1846***	-18.0640***	-20.1359***
	(0.0044)	(1.0575)	(0.0085)	(1.0508)	(4.1425)
Time dummies	Yes	Yes	Yes	Yes	Yes
Molecule dummies	Yes	Yes	Yes	Yes	Yes
R^2	0.9627		0.9663		
log_pseudolikelihood		-244.7227		-231.1682	-28.6252
N	1331	1331	1331	1331	708

Note: Robust clustered standard errors at the molecule-firm level in parentheses; + p<.1, * p<.05, ** p<.01, *** p<.001. Time horizon is April 2007- October 2013.

Table 4. Declining Multinational Sales, Bonus Quantity, Prescriptions & Prescriptions per Physician in Carbepenems After NDM-1 Discovery. A significantly negative coefficient for the triple interaction term indicate that in the post-treatment period sales of carbapenems decreased for multinational firms in absolute value (model 1). Price has been instrumented by retailer margin. Model 2 shows multinational firms offered lesser bonus quantity to retailers decreased compared to local firms, in the post-treatment period. Model 3 shows that number of prescriptions of carbapenem produced by multinationals decreased in the post-treatment period. Similarly, average number of prescriptions per physician (model 4) also decreased for carbapenems produced by multinational s in the post-treatment period. Time horizon is April 2007- October 2013.

	(1) log(sales)	(2) Invsine (Bonus)	(3) log(Prescriptions)	(4) log(Prescription per Physician)
Logpricepermg	-0.3228*			
	(0.1452)			
MNC × NDMdummy	0.8045*	1.2301	0.0455	0.2301
	(0.3380)	(0.8980)	(0.2761)	(0.2107)
NDMdummy × Carbapenem	0.7105***	0.8314	0.9073***	-0.3711
	(0.1835)	(0.5208)	(0.2335)	(0.2744)
MNC × NDMdummy × Carbapenem	-1.0394**	-4.0140**	-1.4791**	-1.2693***
	(0.3908)	(1.4190)	(0.5657)	(0.3288)
Time dummies	Yes	Yes	Yes	Yes
Molecule dummies	Yes	Yes	Yes	Yes
firm dummies	Yes	Yes	Yes	Yes
molecule × Calendermonth dummies	Yes	Yes	Yes	Yes
Molecule × firm dummies	Yes	Yes	Yes	Yes
R^2	0.0234	0.0139	0.8671	0.5113
First_stage_F	520.2466			
N	15047	15050	6232	6232

Note: Robust clustered standard errors at the molecule-firm level in parentheses; + p<.1, * p<.05, ** p<.01, *** p<.001. Time horizon is April 2007- October 2013.

Table 5. Multinational Shares in Sales, Monetary sales and Prescriptions Fall more in Newer Carbapenems than in Older Carbapenems After NDM-1 Discovery. Multinationals' market shares in terms of quantity and monetary sales decreased significantly post the publication of NDM-1 article more in newer carbapenems (models 1 and 2) compared to older carbapenems (models 3 and 4). The same feature is seen more aggressively in prescription patterns (models 5 and 6). Time horizon is April 2007- October 2013. All models have been estimated via fractional logit specification.

	(1) MNC sales share (newer carbapenems)	(2) MNC monetary share (newer carbapenem)	(3) MNC sales share (older carbapenems)	(4) MNC monetary share (older carbapenems)	(5) MNC prescription share (newer carbapenems)	(6) MNC prescription share (older carbapenems)
NDMdummy	-0.2923	-0.3870	-0.3072	-0.3694*	5.3237*	8.6276***
	(0.3114)	(0.2925)	(0.2063)	(0.1726)	(2.1951)	(1.9773)
Carbapenems	0.4832+	0.5243*	4.1933***	4.3066***	38.6076***	8.8052***
	(0.2602)	(0.2660)	(0.2076)	(0.2136)	(2.6931)	(1.5391)
NDMdummy × Carbapenem	-5.3337***	-5.2912***	-0.4342***	-0.3149*	-33.6671***	-3.8469*
	(0.1818)	(0.1817)	(0.1273)	(0.1278)	(2.1821)	(1.5132)
Total monetary sales	0.0015	0.0013	0.0026***	0.0030***		
	(0.0018)	(0.0016)	(0.0005)	(0.0004)		
_cons	-6.0260***	-5.9827***	-5.5332***	-5.4678***	-14.9012***	-15.6022***
	(0.2608)	(0.2413)	(0.2230)	(0.2140)	(2.0534)	(2.4035)
Time dummies	Yes	Yes	Yes	Yes	Yes	Yes
Molecule dummies	Yes	Yes	Yes	Yes	Yes	Yes
log_pseudolikelihood	-156.2909	-139.9347	-218.4946	-204.6932	-15.0983	-24.9096
N	1150	1150	1233	1233	629	690

Note: Robust clustered standard errors at the molecule-firm level in parentheses; + p<.1, * p<.05, ** p<.01, *** p<.001. Time horizon is April 2007- October 2013.

Table 6. Robustness Of Baseline Results with Alternate Control Group of Other Broad Spectrum Antibiotics. Instead of narrow spectrum antibiotics, we consider broad spectrum antibiotics other than carbapenem itself, to constitute the control group. Since this is a within group comparison, the effects are expected to be muted. We see that multinationals' sales share in carbapenem has decreased significantly (models 1 and 2), the results for monetary sales share are negative but insignificant (models 3 and 4). Time horizon is April 2007- October 2013.

	(1) MNC Sales Share (OLS)	(2) MNC Sales Share (fractional logit)	(3) MNC Monetary Share (OLS)	(4) MNC Monetary Share (fractional logit)
NDMdummy	0.0000	-0.3928	0.0000	-0.3532
	(.)	(0.2427)	(.)	(0.2357)
Carbapenems	0.0000	-1.0567***	0.0000	-1.0789***
	(.)	(0.2583)	(.)	(0.2840)
NDMdummy × Carbapenem	-0.1146*	-0.4040+	-0.0933	-0.3309
	(0.0533)	(0.2235)	(0.0606)	(0.2491)
Total monetary sales	0.0000	0.0003	0.0000	0.0004
	(0.0001)	(0.0006)	(0.0001)	(0.0006)
_cons	0.1777***	-0.3955*	0.1918***	-0.2364
	(0.0069)	(0.1537)	(0.0075)	(0.1490)
Time dummies	Yes	Yes	Yes	Yes
Molecule dummies	Yes	Yes	Yes	Yes
log_pseudolikelihood		-1299.1400		-1343.9232
N	6057	6057	6057	6057

Note: Robust clustered standard errors at the molecule-firm level in parentheses; + p<.1, * p<.05, ** p<.01, *** p<.001. Time horizon is April 2007- October 2013.

Table 7. Robustness Of Baseline Results Accounting For Regional Heterogeneity. Even after accounting for regional heterogeneity within India, multinationals' market share in carbapenems is seen to be significantly reduced in the post-treatment period in both OLS and fractional logit estimation with respect to quantity (models 1 and 2) as well as monetary sales(models 3 and 4). Time horizon is April 2007- October 2013.

	(1) MNC Sales Share (OLS)	(2) MNC Sales Share (fractional logit)	(3) MNC Monetary Share (OLS)	(4) MNC Monetary Share (fractional logit)
NDMdummy	0.0000	-0.3520	0.0000	-0.4218
	(.)	(0.2835)	(.)	(0.2654)
Carbapenems	0.0000	5.0099***	0.0000	5.2330***
	(.)	(0.3344)	(.)	(0.3460)
NDMdummy × Carbapenem	-0.1490*	-0.6601**	-0.1209+	-0.5347*
	(0.0574)	(0.2032)	(0.0644)	(0.2168)
Total monetary sales	0.0056**	0.0451***	0.0056**	0.0495***
	(0.0016)	(0.0116)	(0.0019)	(0.0122)
_cons	0.2375***	-5.8949***	0.2417***	-6.0715***
	(0.0113)	(0.3658)	(0.0130)	(0.3504)
Time dummies	Yes	Yes	Yes	Yes
Molecule dummies	Yes	Yes	Yes	Yes
Region dummies	Yes	Yes	Yes	Yes
log_pseudolikelihood		-5363.9257		-5149.6120
N	22540	22540	22540	22540

Note: Robust clustered standard errors at the molecule-firm level in parentheses; + p<.1, * p<.05, ** p<.01, *** p<.001 Time horizon is April 2007- October 2013.

Appendix -1

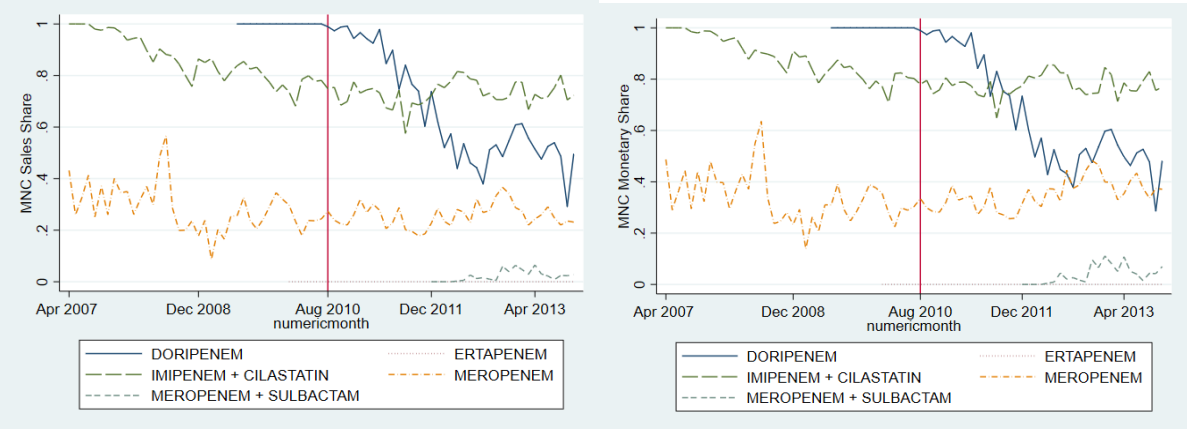

Figure 1:- Individual molecule wise multinationals' share. With the introduction of Doripenem in early 2009 multinationals' average share went up but with post the NDM-1 shock multinational firms reduced there share in newer carbapenem. In early 2010 Lupin introduced Ertapenem (newer carbapenem). This explains the sharp drop in average share. NDM-1 episode may also explain multinationals' reluctance to enter this market.

Table 1. Molecule classification based on ATC-code

Molecule	ATC_code	Classification
AMBROXOL + CEFADROXIL	J01DB05	narrow-spectrum
CEFADROXIL + CLAVULANIC ACID	J01DB05	narrow-spectrum
CEFADROXIL + LACTOBACILLUS ACIDOPHILUS	J01DB05	narrow-spectrum
CEFADROXIL + PROBENECID	J01DB05	narrow-spectrum
CEFADROXIL COMBINATIONS	J01DB05	narrow-spectrum
CEFADROXIL	J01DB05	narow-spectrum
CEFALEXIN + BROMHEXINE	J01DB01	narrow-spectrum
CEFALEXIN + CARBOCISTEINE	J01DB01	narrow-spectrum
CEFALEXIN + PROBENECID	J01DB01	narrow-spectrum
CEFALEXIN	J01DB01	narrow-spectrum
CEFAZOLIN	J01DB04	narrow-spectrum
CLOXACILLIN	J01CF02	narrow-spectrum
DICLOXACILLIN	J01CF01	narrow-spectrum
DORIPENEM	J01DH04	carbapenem
ERTAPENEM	J01DH03	carbapenem
ERYTHROMYCIN	J01FA01	narrow-spectrum
IMIPENEM + CILASTATIN	J01DH51	carbapenem
MEROPENEM + SULBACTAM	J01DH02	carbapenem
MEROPENEM	J01DH02	carbapenem
PENICILLIN G	J01CE01	narrow-spectrum
PENICILLIN V	J01CE02	narrow-spectrum

Table 2: Molecule introduction as per USFDA orange book

Molecule	Introduction date
IMIPENEM + CILASTATIN	Nov 26, 1985
MEROPENEM	Jun 21, 1996
ERTAPENEM	Nov 21, 2001
DORIPENEM	Oct 12, 2007

Table 3:- Robustness of Baseline Results in Truncated Sample This table provides the findings from a truncated sample with a 18 months pre and 18 months post truncated sample. Results are consistent with our baseline findings in Table 3, where there continues to be decrease in multinationals' market share both in quantity terms and monetary sales terms.. Robust clustered standard errors at the molecule level in parentheses. Time horizon is April 2009 to March 2012 i.e. 3 years in total for this sample.

	(1) MNC sales share(OLS)	(2) MNC sales share(fractional logit)	(3) MNC monetary share (OLS)	(4) MNC monetary share (fractional logit)	(5) MNC prescription share (fractional logit)
NDMdummy	0.0000	-0.0386	0.0000	-0.0379	4.9661+
	(.)	(0.1357)	(.)	(0.1402)	(2.8378)
Carbapenems	0.0000	0.5642	0.0000	0.5392	16.5015***
	(.)	(0.4417)	(.)	(0.4725)	(3.6731)
NDMdummy × Carbapenem	-0.0728*	-0.3573+	-0.0615	-0.3125	-12.0688***
	(0.0325)	(0.2139)	(0.0365)	(0.2290)	(2.9431)
Total monetary sales	0.0008+	0.0051	0.0009+	0.0056	
	(0.0005)	(0.0032)	(0.0005)	(0.0036)	
_cons	0.1739***	-5.9007***	0.1783***	-5.8593***	-22.9086***
	(0.0166)	(0.1866)	(0.0169)	(0.1896)	(5.2423)
Time dummies	Yes	Yes	Yes	Yes	Yes
molecule dummies	Yes	Yes	Yes	Yes	Yes
R^2	0.9847		0.9863		
log_pseudolikelihood		-105.7349		-99.2409	-16.0833
N	601	602	601	602	447

Note: Robust clustered standard errors at the molecule-firm level in parentheses; + p<.1, * p<.05, ** p<.01, *** p<.001 Time horizon is April 2009 to March 2012.

Table 4: Robustness with respect to inter-regional heterogeneity. Even after accounting for regional heterogeneity within India, multinationals' market share in carbapenems is seen to be significantly reduced in the post-treatment period in both OLS and fractional logit estimation with respect to quantity (models 1-6) as well as monetary sales (models 7-12). Time horizon is April 2007- October 2013.

	(1) MNC sales share(OLS)	(2) MNC sales share(OLS)	(3) MNC sales share(OLS)	(4) MNC sales share(fractional logit)	(5) MNC sales share(fractional logit)	(6) MNC sales share(fractional logit)	(7) MNC monetary share (OLS)	(8) MNC monetary share (OLS)	(9) MNC monetary share (OLS)	(10) MNC monetary share (fractional logit)	(11) MNC monetary share (fractional logit)	(12) MNC monetary share (fractional logit)
NDMdummy	0.0000	0.0000	0.0000	-0.2423	-0.2698	-0.5988*	0.0000	0.0000	0.0000	-0.2973	-0.3332	-0.9559***
	(.)	(.)	(.)	(0.2606)	(0.2983)	(0.2486)	(.)	(.)	(.)	(0.2450)	(0.2834)	(0.2352)
Carbapenems	0.0000	0.0000	0.0000	5.0376***	0.6827	0.5116	0.0000	0.0000	0.0000	4.8518***	0.5215	0.4141
	(.)	(.)	(.)	(0.3758)	(0.5880)	(0.4384)	(.)	(.)	(.)	(0.3923)	(0.6078)	(0.4532)
NDMdummy × Carbapenem	-0.1490*	-0.1406*	-0.1393*	-0.5633*	-0.5856*	-0.5825*	-0.1209+	-0.1122+	-0.1112+	-0.4278+	-0.4325	-0.4227
	(0.0574)	(0.0558)	(0.0575)	(0.2300)	(0.2584)	(0.2475)	(0.0644)	(0.0626)	(0.0644)	(0.2483)	(0.2792)	(0.2695)
Total monetary sales	0.0056**	0.0035	0.0037+				0.0056**	0.0037	0.0039			
	(0.0016)	(0.0021)	(0.0020)				(0.0019)	(0.0024)	(0.0023)			
Time dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Molecule dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Region dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mmolecule-region dummies	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Region-time dummies	No	No	Yes	No	No	Yes	No	No	Yes	No	No	Yes
R^2	0.7791	0.8650	0.8751				0.7936	0.8699	0.8795			
log_pseudolikelihood				-5464.0340	-4783.4514	-4608.8825				-5260.6776	-4611.7075	-4429.5070
N	22540	22528	22528	22540	22540	22540	22540	22528	22528	22540	22540	22540

Note: Robust clustered standard errors at the molecule-firm level in parentheses; + p<.1, * p<.05, ** p<.01, *** p<.001 Time horizon is April 2007- October 2013.