NBER WORKING PAPER SERIES

MEDICARE REIMBURSEMENTS AND SHORTAGES OF STERILE INJECTABLE PHARMACEUTICALS

Ali Yurukoglu

Working Paper 17987
http://www.nber.org/papers/w17987

NATIONAL BUREAU OF ECONOMIC RESEARCH
1050 Massachusetts Avenue
Cambridge, MA 02138
April 2012

I thank Ernst Berndt, John Beshears, Tim Bresnahan, Jeremy Bulow, Rob Chess, Liran Einav, Sherry Glied, Joshua Gottlieb, Rick Hornbeck, Michael Link, Steve Mayer, Michael Ostrovsky, Paul Oyer, Mar Reguant, Peter Reiss, Robert Wilson, and Stefanos Zenios for comments. Special thanks to Lanier Benkard and Daniel Kessler who early on suggested theoretical mechanisms that are central to this paper. The views expressed herein are those of the author and do not necessarily reflect the views of the National Bureau of Economic Research.

Medicare Reimbursements and Shortages of Sterile Injectable Pharmaceuticals
Ali Yurukoglu
NBER Working Paper No. 17987
April 2012
JEL No. I11,I18,L51

ABSTRACT

This paper investigates the rise in shortages of sterile injectable pharmaceutical drugs in the United States. I focus on a policy change that occured in 2005 that reduced Medicare reimbursements for sterile injectable drugs. The policy change affected different drugs by different amounts. I empirically look at the change in shortages for drugs after the policy change conditional on the amount that the policy change affected each drug. I find that drugs that were more affected by the policy change, ie with greater "treatment," either because they serve older patient populations or have low fixed costs, have had a greater increase in shortages and a greater decrease in number of manufacturers post-regulation. I interpret these results using a model of capacity choice with supply uncertainty. Total installed capacity is higher and the probability of a shortage is lower when margins are higher. I conclude that Medicare's generous payments before the policy change provided manufacturers with incentives to take actions to avoid shortages either by investing in additional maintenance or capacity, or by inducing more entry into production of the drug. The effect on total welfare of removing those payments is theoretically ambiguous, and would require more detailed data to credibly estimate.

Ali Yurukoglu
Graduate School of Business
Stanford University
Stanford, CA 94305
and NBER
yurukoglu_ali@gsb.stanford.edu

1 Introduction

This paper investigates the economic factors behind the marked recent rise of shortages of sterile injectable pharmaceutical drugs in the United States (Figure 1). Sterile injectable drugs include oncology drugs used in chemotherapy, anesthesia agents, and basic parenteral nutrition products like vitamins and electrolytes. They are mostly administered at a physician's office or in a hospital. Shortages cause doctors and patients to seek alternatives which are unfamiliar. When substitutes are poor, doctors and patients delay or forgo treatment. Delaying or forgoing treatment is expensive and risky. The American Society of Clinical Oncology (ASCO), the American Society of Hematology (ASH), and the American Society of Anesthesiologists (ASA) have all separetely detailed how shortages result in worse patient outcomes, higher medical care costs, and delays in clinical trials for new therapies (American Society of Clinical Oncology (2011), American Society of Hematology (2011), American Society of Anesthesiologists (2010)). Numerous popular press articles have reported on the impact of these shortages on patient outcomes (Hobson (2010), Rabin (2011)). Most of the drugs that have had shortages are off-patent and traditionally have been readily available. Furthermore, shortages for these drugs are not features of other developed countries' health systems. For these reasons, the rise in shortages of these drugs has bewildered patients and health care providers. This paper attributes the recent rise in shortages to a policy change that reduced reimbursements by Medicare to health service providers which adminster these drugs.

The central message of this paper is that manufacturers take actions such as double sourcing ingredients, performing maintenance on manufacturing lines, and building excess capacity that partially determine the likelihood of shortages. The extent to which manufacturers undertake these activities is predicted in theory to depend on the profitability of the drugs. I argue that the reduced Medicare reimbursements that took effect in 2005 would theoretically lower the profitability of the drugs that have experienced increases in shortages. I do not directly observe the profitability of these drugs. However, drugs that theory predicts would be relatively more affected by the policy change have experienced a greater increase in shortages.

Payments by Medicare for drugs administered at a physician's office or in an outpatient setting at a hospital[1] fell following the *Medicare Prescription Drug Improvement and Modernization Act* of

[1] Administration of drugs done in an outpatient setting at hospitals falls under Part B, while inpatient administration

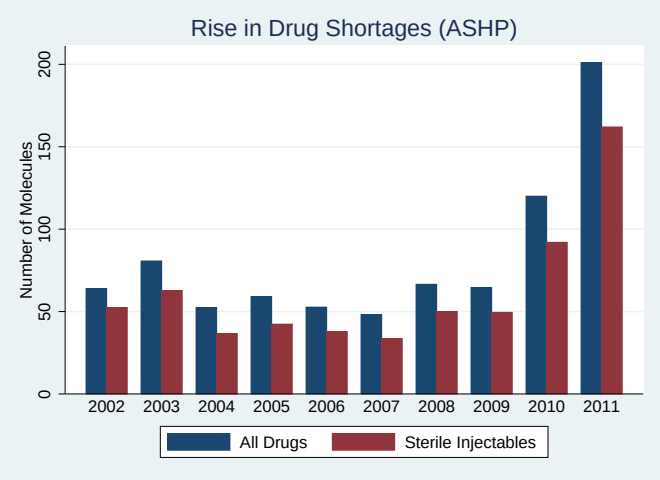

Figure 1: The data for the chart are from the archives of the American Society of Health Pharmacists Drug Shortage web site. For each year, I check the number of months the drug is listed in shortage and divide by the number of months that are available to check (which is determined by how often the Internet Archive visited the site). The height of the bar for each year is equal to the sum of these fractions across molecules.

2003, commonly called the Medicare Modernization Act (MMA). This legislation is well known for creating the prescription drug benefit Medicare Part D. In addition to establishing Medicare Part D, the MMA changed the scheme via which Medicare reimburses for the purchase and administration of drugs in Part B which includes most sterile injectables. Before January 1, 2005, Medicare paid physicians and hospitals for these drugs proportional to their list price under a regime known as "Average Wholesale Price" (AWP) reimbursement. The AWP was not required to correspond to any actual transaction price. Instead, it was a list price from which buyers negotiated discounts. The AWP was substantially higher than the actual transaction price[2]. A study by the Office of Inspector General found that the median percentage difference between AWP and Average Sales Price (ASP) was 50% (Office of Inspector General, 2005). Starting January 1, 2005, Medicare began to reimburse these drugs at 106% of the previous two quarter's ASP. This resulted in decreases on the order of 50% of reimbursements for these drugs to providers. I consider here whether the decrease in payments to providers affected manufacturers incentives to produce, install, and maintain

falls under Part A.

[2]AWP was jokingly referred to as "Ain't What's Paid" (Mullen, 2007).

capacity for these drugs.

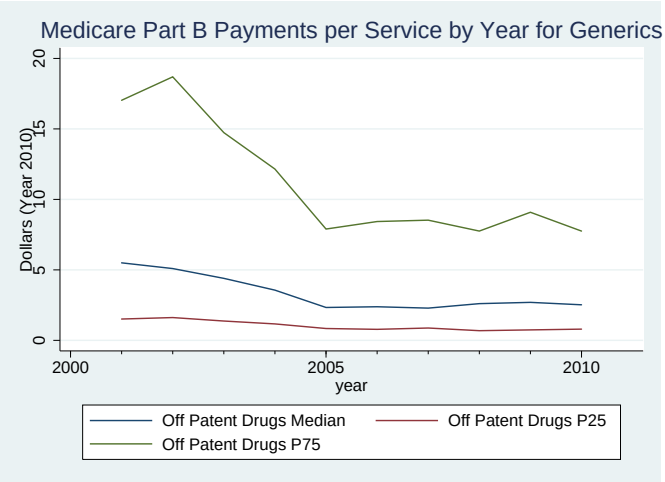

Figure 2: From CMS Part B National Summary File.

Industry experts have pointed to this policy change as a potential culprit for rising shortages (Emmanuel, 2011). In testimony to the U.S. Senate Finance committee in December 2011, industry experts Scott Gottlieb and Rena Conti pointed to decreased reimbursements from Medicare as contributing to drug shortages[3]. There is not, however, consensus on whether the policy change is to blame for the increase in shortages. Private conversations with GPO's and regulatory officials by the author indicate that many feel the policy change is not responsible for the increase in shortages. In the 370 page transcript of the Federal Drug Administrtion's (FDA) "Drug Shortage Workshop" held on September 26, 2011, Medicare payments were not mentioned once (Federal Drug Administration, 2011). President Obama issued an executive order on October 31, 2011 to address the problem of rising shortages. The executive order called for increased reporting by drug manufacturers facing supply issues and increased monitoring by the FDA, but does not mention payments

[3]In testimony to the U.S. Senate Finance Committee, Dr. Patrick Cobb of the Frontier Cancer Center and Blood Institute stated "As far as policy is concerned, I'm not really sure about legally how that would happen. But for us, we think that scrapping the ASP model for reimbursement for generic drugs is really important. The problem for us is that the ASP system for generic drugs has turned generic drugs into commodities. But the problem is that chemotherapy is not really a commodity. Because if you look at pork bellies, if you run out of pork chops, you can reasonably substitute a hamburger. But if you run out of Cytarabines, there are no substitutes for this. So chemotherapy has to be taken out of this commodity-based pricing that's the result of ASP. I think that's really important."

or profitability of producing these drugs. A report by the U.S. Department of Health and Human Services (2011) discusses profitability and strategic behavior by manufacturers, but does not narrow in on Medicare reimbursements. As competing causes, others have suggested that increased scrutiny by the FDA, consolodation amongst manufacturers, grey market distributors, stockpiling by hospitals, and coincident exogenous shocks to the supply chain[4].

More broadly, health care spending has been increasing at a rate which many feel is unsustainable in the long term. However, cutting costs without regard to incentives to innovate and produce can lead to unintended consequences. This paper provides evidence that the reactions of manufacturers to reducing health care expenditures likely reduced capacity and maintenance investments, and resulted in an increase in shortages. Finkelstein (2004) found that increasing market size for vaccines through government policy is associated with increases in new vaccine development and clinical trials. This paper complements studies of the change in provision of services as Medicare reimbursements change such as Clemens and Gottlieb (2012) who find that areas which had higher increases in Medicare reimbursements, after an administrative shift in 1997, experienced larger increases in care provision and health technology adoption.

I begin with a model of manufacturers choosing capacity levels under supply uncertainty. I find that manufacturers will change their investments in capacity due to changes in downstream reimbursement when manufacturers have non-zero market power. Competition sometimes leads to more shortages than a hypothetical social planner would choose. The intuition for this result is that because competition decreases margins, firms are more willing to tolerate stock outs when there is competition. The model implies that moving from generous reimbursement by Medicare to cost reimbursement will lead to lower capacity and more shortages. Furthermore, drugs which serve more Medicare patients will experience a greater increase in shortages. Drugs with lower fixed costs of production will also experience a greater increase in shortages. These two implications serve as the basis of the empirical work.

To empirically test whether the policy change is playing a role in the increase of shortages, I consider a series of regressions. The main dependent variable is the fraction of time in year t that drug i

[4]On this latter suggestion, one of the maintained hypotheses of this paper is that manufacturers can take actions to increase the reliability of the supply chain if they find it profitable.

is under shortage. Nearly all the regressions condition on drug code fixed effects, year fixed effects, and fixed effects for number of years since original approval. The first set of regressions interacts a measure of Medicare Market Share (MMS) with a post-regulation dummy variable. MMS is based on the patient population of the conditions the drugs serve. Medicare predominantly covers elderly patients. Because the policy change would reduce profitability of investing in capacity more for drugs which serve more Medicare patients, we should see a greater increase in shortages for higher MMS drugs. This strategy for identifying the effects of a policy change was employed by Duggan and Morton (2010) in their study of Medicare Part D. The coefficients on the interaction of MMS and a post-regulation dummy variable are statistically indistinguishable from zero after clustering at the drug-route level, but of an economically significant magnitude and positive as expected if the policy change is responsible. Since the MMS variable is measured with error, I use the moments of the age distribution of non-Medicare patients as instrumental variables for MMS. The IV coefficient estimates indicate the interaction of MMS and the post-regulation dummy variable is both economically and statistically significant for off-patent drugs. The coefficient estimates imply that raising the Medicare Market Share of a generic drug by ten percentage points is associated with an increase of shortage frequency of slightly under ten percentage points.

The model also predicts that drugs which have lower fixed costs should have experienced a greater increase in shortages post policy change. This is because those manufacturers theoretically should offer the largest discounts to health care providers, so that the reimbursement rate dropped the most post-policy change. As a measure of fixed costs, I use the average number of manufacturers prior to the policy change (2001 to 2003, excluding 2004 because the legislation was passed by 2004, though not yet implemented). I find that the interaction of the average number of manufacturers prior to the policy change and a post-regulation dummy variable has a economically and statistically significant positive coefficient estimate. Drugs for whom there were many manufacturers prior to the policy change had a greater increase in shortages after the policy change, conditional on the number of manufacturers after the policy change. Since the mechanism of reduced profitability operates through reduced Medicare payments, I next check whether there are more shortages for drugs which had a greater decrease in payments. I find that greater decreases in payments are associated with more shortages using moments of the age distribution of a sample of non-Medicare patients and the average number of manufacturers from 2001 to 2003 interacted

with a post-regulation dummy variable as instrumental variables, though this relationship is not statistically significantly different from zero.

Finally, I discuss potential solutions and why they might not have been implemented yet. I draw an analogy between sterile pharmaceuticals and electricity. Both markets share the features that supply and demand must be equated in fine time intervals and both have considerable uncertainty[5]. Electricity has dealt with these issues by creating extra incentives to produce when there is a danger of a shortage.

2 Institutional Details of the Sterile Injectable Pharmaceutical Industry

Sterile injectable drugs are administered at a physician's office or a hospital. They are administered intravenously or intramuscularly and thus must be kept sterile. A typical generic sterile injectable drug is produced by three to four of the seven big generic manufacturers[6] in the U.S. A typical shortage occurs when a manufacturing line of one of the producers goes down. A line can go down because the manufacturer or the Federal Drug Administration (FDA) identifies a quality issue[7] that could render the drug unsterile and requires that the issue be resolved, or because the manufacturer closes a facility or exits from producing a certain drug. Another reason shortages can occur is because of disruptions further up the supply chain. Manufacturers rely on producers of inputs such as Active Pharmaceutical Ingredients (API) whose supply can be disrupted due to natural disasters or manufacturing breakdowns. Once one manufacturer stops producing, it falls to the other manufacturers to make up the supply difference. However, the other manufacturers may not find it profitable to produce more of the drug, or may not be licensed to produce more of the drug, or may have been hit with the same supply shock as the first non-producing manufacturer.

[5]Sterile pharmaceuticals because of highly controlled manufacturing environments, and electricity because of weather.

[6]APP-Fresenius, Bedford-Ben Venue, Daiichi, Hospira, Sandoz, Teva, and West-Ward. Shortages have been occuring for several of these manufacturers as well as other smaller manufacturers.

[7]Some degradants that have been found are bacterial/mold contamination, particles of foreign matter, glass, metal, or fibers in vials (FDA).

The supply chain for sterile injectable drugs is illustrated in Figure 3. Patients receive the drugs in question at hospitals or physicians' offices. Patients are usually insured by the government through Medicare or Medicaid or by a private insurer. The insurer pays the health service provider at some price per administration of the drug. The health service provider buys the drugs from wholesale distributors. Hospitals often band together to form a group purchasing organization (GPO) which can negotiate volume discounts for buying drugs. The difference between the amount insurers reimburse for a drug and the price at which the health service provider buys the drug is the gross margin for the health service provider. Berndt (2002) provides a more general survey of the economics of pharmaceutical industry, while U.S. Department of Health and Human Services (2011) provides more detail on the sterile injectable portion of the industry.

The industry is highly regulated at all levels. Entry into producing a generic pharmaceutical requires submitting a request for approval to the FDA. To be approved, one must convince the FDA that their manufacturing process is sterile and follows good manufacturing practices. This process is described in Scott Morton (1999). Insurance is regulated by state insurance commissions and for a large number of individuals provided by the federal government via Medicare or by a combination of federal and state government via Medicaid.

2.1 The Policy Change: AWP to ASP

In 1992, Medicare declared that it would reimburse Part B drugs at Average Wholesale Price (AWP). However, "[AWP] does not correspond to any transaction price... AWP has never been defined by statute or regulation. Indiviual AWPs are compiled in compendia like the Red Book and First Databank," (Medicare Payment Advisory Commission, 2003). In response to findings that Medicare's payment were well above acquisition costs for health providers, the reimbursement rate on these drugs was lowered to 95% of AWP in 1998. This lowering did not change that Medicare's payments were above acquisition cost. Medicare Payment Advisory Commission (2003) cite some egregious examples: Vincasar, a chemotherapy drug, had an AWP of $740, while being sold to physicians for $7.50. Berndt (2005) provides a detailed history of AWP. How AWP was chosen by manufacturers, given that it there was no formal basis, is unknown, and likely varied by manufacturer. In theory, there was a strong incentive to raise AWP. In practice, the threat

of regime change by CMS and the upper bound of monopoly prices disciplined the AWP. In the model section, I assume the AWP was set at roughly the monopoly price.

In a well-intentioned effort to reduce Medicare costs, payments were lowered to 85% of AWP in 2004, and to 106% of the Average Sales Price (ASP) in 2005. The ASP is the volume-weighted average prices across all manufacturers of a given drug to all buyers for the previous two quarters. It is therefore updated quarterly. The ASP captures actual transaction prices, including rebates. After the switch to ASP, payments to health providers for these drugs dropped, especially for generic drugs. I argue that these payment drops are associated with greater increases in shortages.

Despite the appeal to economists of the simple story of "payments dropped therefore capacity dropped in response," there are two reasons that cast some doubt on the maintained hypothesis. First, shortages did not start increasing at large rates until 2009, four years after the policy change. Second, the payments that dropped were payments to health providers, not necessarily to the drug manufacturers. That shortages did not begin increasing rapidly until four years after the policy change could be due to simple adjustment frictions. The argument that payments to health providers dropped, but not to manufacturers, does not account for the process by which manufacturers and health providers set prices. The payments made by Medicare to health providers form a large part of the surplus that manufacturers bargain over with health providers. When those payments drop, if manufacturers capture any surplus associated with their production, then the revenues to manufacturers drop as well. Recent empirical research on vertical relationships such as Crawford and Yurukoglu (2012) and Grennan (2012) have found in other markets that the assumption of no market power on one side of a market with large firms on both sides is not supported in their data. This concern would best be addressed with data from manufacturers, but these data are so far kept confidential. There is also case study evidence that doctors responded to payment cuts by increasing the number of patients they treat (Jacobson et al., 2010). This finding may hold more generally, but does not preclude that drug manufacturers respond by decreasing capacity. A separate case study found that when the patent protection of Irinotecan, a medicine used in chemotherapy to treat advanced colorectal cancer, expired and generic manufacturers entered, prices decreased but administration of Irinotecan also decreased (Conti et al. (2012)).

3 Data

This study combines multiple data sources. Shortage information comes from the American Society of Health System Pharmacists (ASHP). Medicare Part B spending on drugs comes from the Center for Medicare Services (CMS). Spending on the same set of drugs for a sample group comes from Thomson-Reuters MedStat database. Finally, the Federal Drug Administration's (FDA) Orange Book provides the approved manufacturers and corresponding approval dates for drugs by year.

The American Society of Health System Pharmacists (ASHP) maintains a website of current drug shortages. I accessed archives of this website on multiple dates per year going back to 2001. I create from this data a variable $shortages_{it}$ which indicates for what fraction of the dates I checked the archive website in year t is drug/route pair i indicated as being in shortage. The main weakness of this data is that it does not capture the varying magnitudes of shortages. The ASHP defines a shortage as "a supply issue that affects how the pharmacy prepares or dispenses a drug product or influences patient care when prescribers must use an alternative agent," (Fox et al., 2009). This broad definition, however, is the best measure of shortages of which I am aware.

Medicare spending and services for the years 2000 to 2010 by Healthcare Common Procedure Coding System (HCPCS) code come from the Center for Medicare Services's (CMS) National Summary File. Providers use HCPCS codes to bill Medicare for procedures. A typical HCPCS code represents one administration of a drug. For example, the spending by Medicare to the hospital or physician's office on a lymphoma patient being treated by chemotherapy agent Doxorubicin once a month for three months would show up as three services of HCPCS code J9000. The same drug ingredient can have multiple HCPCS codes representing different dosages. In the regressions to come, I cluster standard errors at the ingredient level and condition on HCPCS code dummy variables.

Spending by non-Medicare patients is estimated from Thomson-Reuters MedStat. This data set has payments by year at the HCPCS code for a sample of self-insured employers and health systems. I use the years 2001-2009 to estimate the total non-Medicare spending by ingredient. From this measure, I create the variable Medicare Market Share (MMS) of drug i which is what fraction of a drug's revenue comes from Medicare patients. To assess whether the MMS variable I create

is sensible, I check what diseases are served by the lowest MMS drugs and the highest MMS drugs. The highest MMS drugs are those inhalants which treat COPD and immunosuppresants used during organ transplantation. These make sense. The majority of organ transplants are kidney transplants, for which immunosuppresants are covered by Medicare Part B regardless of age. Many of the inhalants use nebulizers, a type of durable medical equipment, for administration. They also therefore fall under Medicare Part B. Other high MMS drugs include Pegaptanib Sodium, which treats age-related macular degeneration, and Triptorelin Pamoate, which treats prostate cancer. The lowest MMS drugs are Somatrem, a human growth horomone for children, Glatiramer Acetate, which treats multiple scelorosis, two drugs which treat hyper-thyroidism, and Urofollitropin, a fertility drug. The constructed MMS is positively correlated with the mean age of recipients of the drug in the MedStat database, as one would require from a credible MMS measure.

I use the Federal Drug Administration's Orange Book for the years 2001-2011 to record how many approved manufacturers of a drug exist in each year, and the number of years since the earliest approval of a manufacturer of the drug. This data allows me to separate drug-year combinations for drugs which have patent protection and those which don't. The Orange Book does not track biological pharmaceuticals which are made by an organic process rather than chemical synthesis. The most famous biological is insulin. These drugs have a more complicated manufacturing process and have been subject to shortages. Most biologicals are still on patent. This paper focuses on inorganic chemical compounds which make up the majority of administered drugs.

4 Theoretical Framework

This section uses a model of entry and capacity choice with supply uncertainty to illustrate the change in production incentives and underlying welfare economics associated with changing reimbursement policies by Medicare. This class of models has been studied by Carlton (1978), Deneckere and Peck (1995), and Dana (2001) amongst others. The following presents results for two regimes: a no regulation regime and an Average Wholesale Price (AWP) regime. The AWP regime features reimbursements for government insured patients at a price that is higher than what would normally be the acquisition price of the drug in some states of the world.

Manufacturers, denoted by i, simultaneously choose capacity levels k_i to produce an identical medicine. After choosing capacities, each manufacturer is hit by a shock ϵ_i which jointly follow a distribution whose CDF is $G(\vec{\epsilon})$. Their new capacity is $k_i\epsilon_i$.

There is a mass of size M of patients which are all willing to pay up to $\bar{p}$ for the medicine. Of those, M_{gov} are insured by Medicare. Absent regulation, if the total capacity in the market after the shocks is less than the market size M, then the market price of the medicine is equal to $\bar{p}$. If the total installed capacity is greater than the market size M, then the price of the good is zero.

$$p(\vec{k}, \vec{\epsilon}, N, M) = \begin{cases} \bar{p}, & \sum_{i=1}^{N} k_i\epsilon_i < M \\ 0, & \sum_{i=1}^{N} k_i\epsilon_i \geq M \end{cases}$$

Under Average Wholesale Price regulation, there is a third party which reimburses hospitals at $\bar{p}$ no matter what the price the hospital purchased the medicine at when they serve Medicare patients. Some fraction γ of that reimbursement rate will go to manufacturers. $\gamma \in [0, 1]$ represents a bargaining power parameter which is assumed to be the same across manufacturers.

$$p_{awp}(\vec{k}, \vec{\epsilon}, N, M, M_{gov}, \gamma) = \begin{cases} \bar{p}, & \sum_{i=1}^{N} k_i\epsilon_i < M \\ \gamma\bar{p}, & \sum_{i=1}^{N} k_i\epsilon_i \geq M \end{cases}$$

The government purchases up to M_{gov} units at $\bar{p}$ no matter what total industry capacity turns out to be.

With no regulation, manufacturer i solves:

$$\max_{k_i \geq 0} E_\epsilon[p(\vec{k}, \vec{\epsilon})k_i\epsilon_i] - c(k_i)$$

where the expectation is over the joint distribution of shocks to capacity. How much each manufacturer sells when total capacity is greater than the market size does not matter because price drops to zero when the industry is not capacity constrained and the marginal cost of production is zero up to the capacity constraint. Under AWP regulation, manufactuer i solves

$$\max_{k_i \geq 0} E_\epsilon[p_{awp}(\vec{k}, \vec{\epsilon})Q_{i,awp}(\vec{k}, \vec{\epsilon})] - c(k_i)$$

where Q_i is the quantity sold by manufacturer i. If total capacity is lower than market size ($\sum_i k_i\epsilon_i < M$), then this is equal to manufacturer i's capacity. If the industry has more capacity than necessary to serve the whole market, the manufacturers split the Medicare market according to what fraction of total capacity they own[8].

Manufacturers must pay an entry cost F to produce and sell the good. The equilibrium number of firms is given by the maximum number of firms such that the variable profits of each firm are greater than F.

I find a symmetric Nash equilibrium to the simultaeneous capacity choice sub-game. If the distribution of ϵ has no mass points, then the symmetric equilibrium capacity per firm when N firms are producing is the solution to following equation under no regulation:

$$E_\epsilon[p(k \otimes \mathbf{e}_N, \vec{\epsilon}, N, :)\epsilon_i] - c'(k) \quad = \quad 0$$

where $\mathbf{e}_N$ is the $1xN$ vector of ones. Under AWP regulation,

$$E_\epsilon[\begin{cases} \bar{p}\epsilon_i, & \sum_{j=1}^N k\epsilon_i < M \\ \gamma\bar{p}M_{gov}\frac{\epsilon_i(\sum_{j=1}^N k\epsilon_j - k)}{(\sum_{j=1}^N k\epsilon_j)^2}, & \sum_{j=1}^N k\epsilon_i \geq M \end{cases}] - c'(k) = 0$$

Analyzing this equilibrium condition analytically proved difficult even with strong distributional and functional form assumptions. I use numerical simulation to show how equilibrium quantities vary with model parameters.

When $\gamma > 0$, equilibrium capacities and average prices are higher under AWP than no regulation. Shortages occur less frequently under AWP than with no regulation (Figure 4). Whether total welfare is higher or lower is ambiguous. When a firm with competition invests in additional capacity, it does not capture the social value of its investment, because competition drives average price below $\bar{p}$. In the other direction, when a firm invests in additional capacity, it imposes an externality on other firms by lowering average price. Furthermore, the government must raise the funds to pay for the AWP regulation, potentially distorting the decisions in some other area of the

[8]Because the price for non-Medicare buyers and marginal costs of production are zero, how they split the quantities there does not affect their profits.

economy. Numerical simulations provide evidence that either effect can dominate, so the effect on total welfare is ambiguous.

The model's predictions for levels are not surprising. The AWP regulation continues to pay manufacturers even when the industry over-produces. This implies higher returns to investing in capacity for manufacturers, thus more total capacity and fewer shortages. The model is useful for empirical analysis because it predicts a differential impact of the AWP regulation depending on features of the drug. In particular, drugs with lower fixed costs and that serve more Medicare patients will experience a greater increase in shortages moving from AWP to acquisition cost based reimbursement.

5 Empirical Analysis

I test whether the change in reimbursement by Medicare for drugs from AWP to ASP is associated with increased shortages. The change in policy occurred simultaneously for all drugs, therefore it is impossible to distinguish the effects of the policy change from a coincident change in the industry. The empirical strategy depends on the policy change affecting different drugs at varying levels as predicted by the model. As a first pass, I estimate the change in shortages as a function of a fifth order polynomial of a time trend and a dummy variable for the policy change (ASP_t is one if the year is greater or equal to 2005) and drug-route effects.

$$Shortage_{it} = \alpha_i + \sum_{j=1}^{5} \delta_j t^j + \beta ASP_t + \epsilon_{it} \quad (1)$$

The results are in Table 2. In the sample of all drugs, the estimate of β is positive and economically significant, but statistically I can not reject that the true β is zero. Focusing on the sample of drugs which were off patent in 2001, the positive estimate of β is both economically and statistically significant. The effect does not exist for drugs which were on patent throughout the sample period, which is consistent with these drugs having high margins. This is suggestive that the post-policy change period had a marked increase in shortages for generics. However, the identification of this effect is partly an artifact of functional form assumptions. I next look more closely at which drugs

had greater increases in shortages.

According to the model, the ASP regulation should increase shortages relatively more for drugs which derive a large fraction of their revenues from Medicare. I next estimate a regression of shortages on drug-route fixed effects, year fixed effects, and an interaction of a post-regulation dummy variable and the Medicare Market Share (MMS_i) of drug i.

$$Shortage_{it} = \alpha_i + \delta_t + \beta ASP_t MMS_i + \epsilon_{it} \quad (2)$$

The results are in Tables 3 and 4. In 3, the estimates are positive and economically significant, but can not reject zero as the true coefficient. The MMS variable is an estimate based on usage of these drugs in the Thomson MedStat database. Under the assumption of classical measurement error, the coefficient on the interaction of post-policy change (ASP) and MMS will be attenuated towards zero. I re-estimate the model using instrumental variables to eliminate the bias due to measurement error. I use the age distribution of patients who receive the drug in the MedStat database as a set of instruments for the interaction of ASP and MMS. Specifically, I use the interaction of the 25th percentile, the median, the mean, and the 75th percentile age for each drug with the ASP dummy variable, and the squares of these interactions. Assuming the unobservable factors (ϵ_{it}) affecting shortages are unexpected supply shocks (plant breaks down) or demand shocks (new treatment approval), then the age distribution of patients receiving the drug should only correlate with shortages through its correlation with MMS. In Table 4, the coefficient estimates change as theory would predict for classical measurement error. The coefficient estimate rises away from zero. It also become statistically significant. Again, the effect is strongest for generic drugs, and does not seem to exist for drugs that are on patent throughout the sample. An increase in MMS of ten percentage points predicts a post-regulation increase in shortage frequency of just under ten percentage points.

Lower fixed costs of production imply more producers of a drug, all else equal. More producers of a drug imply lower average prices in the ASP regime, and a greater increase of shortages when the government moves from AWP to ASP reimbursement. To measure fixed costs, I use the number of manufacturers producing the drug in the years 2001 to 2003. I also condition on the number of manufacturers approved for producing drug i in period t.

$$Shortage_{it} = \alpha_i + \delta_t + \beta_1 ASP_t AvgMan_{i,2001-2003} + \beta_2 Man_{it} + \epsilon_{it} \quad (3)$$

The results are in Table 6. Drugs which had a higher average number of manufacturers producing the drug in 2001 to 2003 are associated with a greater increase in shortages in the post-policy change period, conditional on the number of manufacturers in the present. The results are both economically and statistically significant.

While MMS and fixed costs both predict differential impacts of the policy change, they do not measure the same conceptual object. The two variables have no significant relationship statistically or economically. Including both variables in the regression does not change in any significant manner their coefficient estimates for this reason.

The model predicts that the effect of the Medicare reduction in payments will decrease incentives to install capacity through reduced prices. I estimate whether there has been a greater increase in shortages for drugs with greater decreases in Medicare reimbursement rates that can be attributed to the policy change. The specification is:

$$Shortage_{it} = \alpha_i + \delta_t + \beta_1 Payment\_per\_service_{it} + \beta_2 Man_{it} + \epsilon_{it} \quad (4)$$

Unobservable year-drug specific shocks to demand could affect payments and shortages simultaneously. To isolate the variation in payments due to the policy change, I use the age distribution variables from the previous regressions as instrumental variables for payments. The results in Table 8 are an economically significant estimate of β_1 that is not statistically different from zero.

Some shortages are attributed to a manufacturer of a drug ceasing production and other manufacturers not being able to ramp up production promptly. The next regression uses the number of manufacturers as a dependent variable. The effect of exogenously increasing the number of manufacturers of a drug on shortages is theoretically ambiguous because a smaller number of manufacturers will have higher margins, suggesting higher capacity, but, depending on the correlations of supply shocks across manufacturers, more manufacturers could imply higher total capacity. Nonetheless, I examine whether the policy change has been associated with exit from producing a drug.

$$Man_{it} = \alpha_i + \delta_t + \beta ASP_t MMS_i + \epsilon_{it} \quad (5)$$

The results in Table 7 show that the post-policy change decrease in the number of manufacturers is larger for drugs with higher MMS. This suggests that the profitability of producing these drugs decreased after the Medicare payments dropped, so much so that some manufacturers stopped producing the drug altogether.

5.1 Robustness

5.1.1 Pre-existing Trends

If drugs with higher Medicare market shares were experiencing, for whatever reason, an increase in shortages prior to the policy change, then the estimates above might be capturing this trend, and one would not be justified in interpreting the coefficient estimate as evidence that the policy change has led to an increase in shortages. I assess whether such an effect exists by running the same specifications, but limiting the sample to 2001 to 2004, and considering 2003 and 2004 as a pseudo- "post-policy change" period. The coefficient estimate for the interaction of MMS and the pseudo-post-policy period, on the sample of off-patent drugs, is -0.083 with a standard error 0.114. We can reject that this coefficient is the same as the estimated coefficient on the full sample with high degrees of confidence.

5.1.2 Instrumenting for Interaction Term

The interaction term $MMS * (Year \geq 2005)$ is measured with error, because MMS is measured with error. I use the moments of the age distribution of non-Medicare patients as instrumental variables for this variable. The estimates are equivalent to estimation by two stage least squares. The predicted value of the interaction terms are non-zero and not equal from year to year in the pre-period because of other conditioning variables that vary from year to year. As a robustness check that this variation is not driving the coefficient estimates, I estimate a cross sectional regression of MMS on the moments of the age distribution. I then interact the predicted MMS variable with the

post regulation dummy. The coefficient estimate is larger in magnitude at 1.197. Its standard error is bounded below by 0.327[9]

6 Discussion

6.1 What is Special about Sterile Injectable Generic Pharmaceuticals?

Costly capacity and supply or demand uncertainty are features of many markets. For example, computer component manufacturing, aircraft manufacturing, and agriculture all share these characteristics. There are three additional characteristics that separate generic sterile injectables from these industries. First, supply and demand must match in fine time intervals. Consumption of most goods can be delayed without incurring too much cost. Health problems can get worse over time, so delaying is costly. Second, once there is more than one manufacturer of a drug, margins can drop dramatically because the producers are selling identical products. Third, storing sterile injectable pharmaceuticals is costly. They need to be kept sterile and can be sensitive to light and temperature. One industry which shares these extra characteristics is electricity generation. Electricity supply and demand must be in equilibrium at each instant to avoid power system failures. Electricity produced by different methods is identical for consumption purposes. Storing electricity by battery or with hydro-storage is currently considered prohibitively costly in most cases. The solution in electricity generation has been a mixture of rapid price adjustment and government regulation. Details on how electricity markets deal with shortages are in Cramton and Stoft (2005).

6.2 Options to Reduce Shortages

As mentioned in U.S. Department of Health and Human Services (2011), buyers of pharmaceuticals could sign contracts that impose penalties on manufacturers in cases of shortage[10]. This would increase average prices and increase the incentive to avoid stock outs by manufacturers. Why haven't those contracts been implemented? I conjecture that these types of contracts are one

[9]The standard error estimate does not capture the variance from the pseudo-"first-stage."

[10]The report details that, while there exist "failure to supply" clauses currently, they usually contain language voiding the penalty in case of nationwide shortages.

solution to the problem of shortages that the industry has missed so far for lack of familiarity. Since shortages were not at a level of great concern prior to recent years, there was no need to develop such contracts.

Medicare could increase its payments to reduce shortages. The coefficient estimates here suggest that modest increases could have large effects on shortages. A more radical solution would be for Medicare to conduct a procurement auction for suppliers of the drug with heavy penalties in case of shortages. The FDA could theoretically condition approval to produce on maintaining sufficient levels of capacity, though this imposes a large burden on the regulator.

The model predicts that fewer shortages might not be socially optimal. While more detailed data would be helpful to study the question of total welfare, the model does predict that a monopoly firm will choose the socially optimal level of capacity. Patented drugs have fewer shortages in the data. This is suggestive that the socially optimal level of shortages is lower than what society experiences now for generic drugs, post-policy change.

7 Conclusion

I analyze how a change in Medicare's reimbursement scheme that lowered payments to health providers have likely played a role in the marked increase of shortages of generic sterile injectable pharmaceuticals. I found that drugs which I expect were more affected by the change in policy experienced a greater increase of shortages than drugs which I expect were less affected by the policy change. The drugs I expect were more affected are drugs which treat diseases with older patient populations, because Medicare predominantly covers older patients. Also, drugs for which fixed costs are low were more affected because the policy change required payments by Medicare to depend on discounts made by manufacturers. When fixed costs are low, there are more manufacturers, more competition, and more discounts.

The key weaknesses of this paper are that the measure of shortages is less than ideal, and that I can not directly measure the change in margins going to manufacturers after the policy change. The measure of shortages does not measure how severe the shortages are. The measure I employ is useful, but could be improved upon by looking in greater detail at the individual shortages. I

observe payments by insurance providers to health care providers for administering these drugs. How much of those payments go to the manufacturers from the health care providers is unobserved before the policy change[11]. Further research using data from manufacturers, if made available, would be useful to further test the hypothesis of this paper.

Given that there are different ways to increase the incentives of manufacturers to produce these drugs, further research on the details of these possibilities would be useful. For example, if Medicare were to increase its payments, then it faces the question of how high to increase its payments to ensure a stable supply without needlessly overspending. Theoretically interesting questions arise when considering the design of contracts between manufacturers and health providers with clauses to reduce shortages. If payments are higher in shortage periods, then manufacturers have incentives to create artificial shortages. If health providers are able to multi-source drugs, then manufacturers who maintain more capacity and higher prices might find themselves with low market shares in non-shortage periods.

[11] Because the policy change made Medicare reimbursements a function of the payments from health care providers to manufacturers, I can measure the post-policy change price.

Table 1: Summary Statistics

	N	Mean	St. Dev.	Min	Max
Shortage Freq.	3878	0.113	0.274	0	1
Year	3878	2006.127	3.098	2001	2011
Number of Manufacturers	3878	3.091	2.671	1	25
Always On Patent	3878	0.197	0.398	0	1
Always Off Patent	3878	0.519	0.500	0	1
Medicare Market Share (MMS)	3878	0.181	0.233	0.000	0.984
Number of Manufacturers in 2001	3664	2.970	2.386	1	12
MedStat Age 25th Percentile	3878	36.474	11.965	1.6	57.25
MedStat Mean Age	3878	44.728	8.306	8.629	58.596
MedStat Age 75th Percentile	3878	54.719	6.880	10	62.778
Medicare Payment Per Administration	3111	72.993	514.427	0.012	15520.77
Conditional on Always Off Patent					
Shortage Frequency	2014	0.161	0.313	0	1
Number of Manufacturers	2014	4.073	2.341	1	13
Medicare Market Share (MMS)	2014	0.147	0.199	0.000	0.910
Avg Number of Manufacturers in 2001-2003	2014	4.278	2.337	1.333	12.000
MedStat Age 25th Percentile	2014	35.210	10.968	2.350	52.100
MedStat Mean Age	2014	43.931	7.383	11.904	55.717
MedStat Median Age	2014	46.045	8.519	5.800	57.100
MedStat Age 75th Percentile	2014	54.477	5.885	17.750	61.100
Medicare Payment Per Administration	1717	19.083	65.092	0.012	1269.378
Conditional on Always On Patent					
Shortage Frequency	765	0.006	0.054	0	0.8
Number of Manufacturers	765	1	0	1	1
Medicare Market Share (MMS)	765	0.238	0.265	0.000	0.984
Avg Number of Manufacturers in 2001-2003	590	1	0	1	1
MedStat Age 25th Percentile	765	40.148	10.824	12.000	56.000
MedStat Mean Age	765	47.200	7.402	20.142	58.051
MedStat Median Age	765	49.020	8.206	18.333	60.000
MedStat Age 75th Percentile	765	55.786	5.842	25.000	62.750
Medicare Payment Per Administration	512	271.423	1217.256	0.039	15520.77

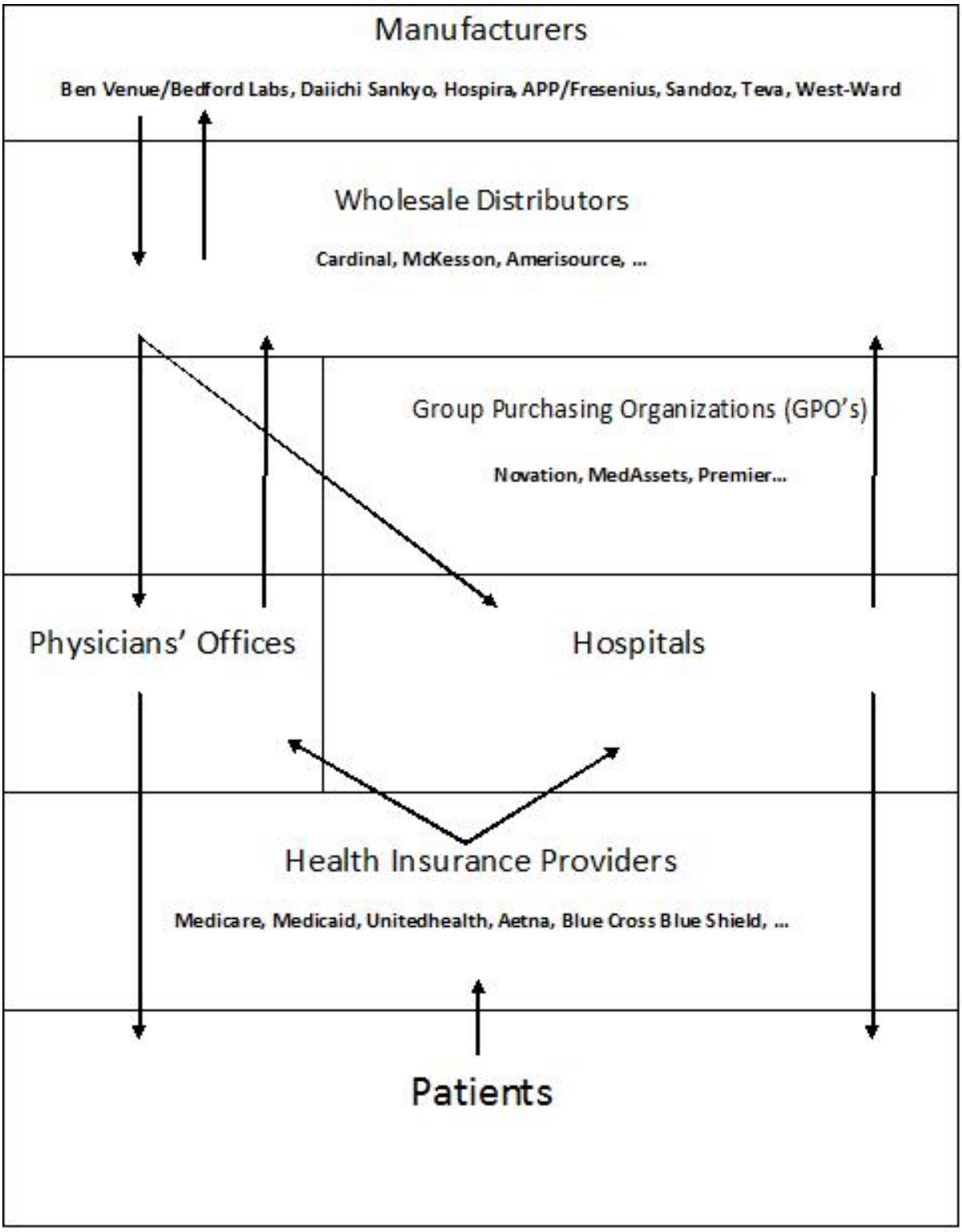

Figure 3: Supply chain of generic pharmaceuticals. Downward arrows are flows of products and services. Upward arrows are payments.

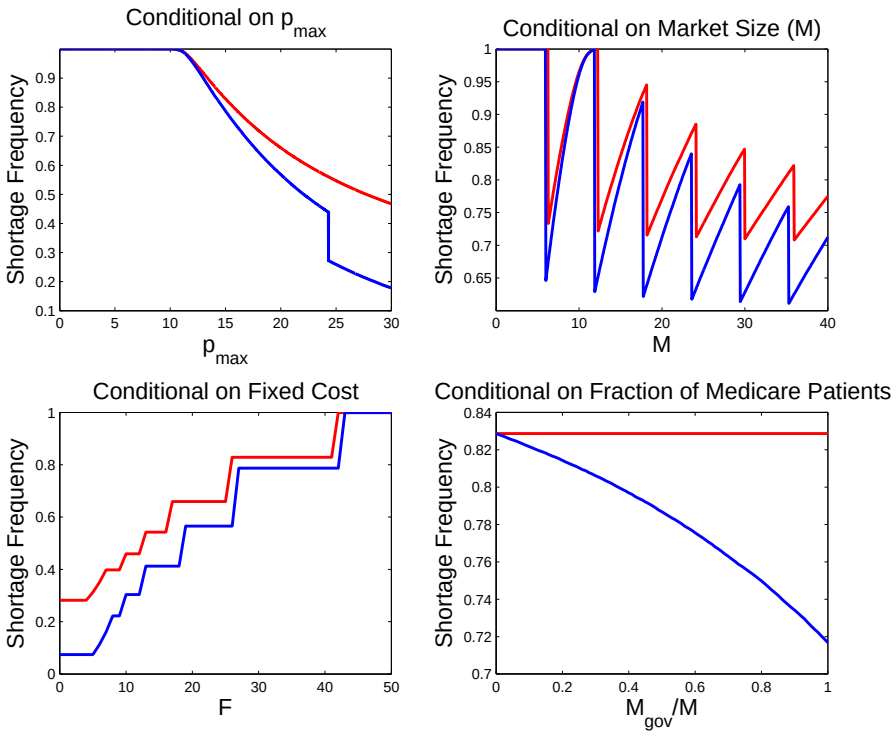

Figure 4: Model's predictions of shortage frequency as functions of model parameters. The red lines are predictions for the unregulated market. The blue lines are predictions under AWP regulation.

Table 2: Shortage Freq. Conditional on Time Trend Polynomial and Post-Regulation Dummy Variable

Dependent Variable:	Shortage Freq.	Shortage Freq.	Shortage Freq.	Shortage Freq.
Year >= 2005 (Post-Regulation)	0.022 (0.024)	0.029 (0.025)	0.128 (0.057) **	0.003 (0.023)
Years Since Earliest Approval Effects	N	Y	Y	Y
HCPCS Code Dummy Variables	Y	Y	Y	Y
Sample:	All	All	Always Off Patent	Always On Patent
$R\hat{2}$	0.334	0.347	0.332	0.179
Number of Observations	3878	3878	2014	765
Number of Drug-Route Clusters	321	321	128	109

Table 3: Shortage Freq. Conditional on Post-Regulation and MMS Interaction

Dependent Variable:	Shortage Freq.	Shortage Freq.	Shortage Freq.	Shortage Freq.
Year $\geq$ 2005 * MMS	0.114 (0.129)	0.141 (0.140)	0.308 (0.254)	0.007 (0.023)
Years Since Earliest Approval Effects	N	Y	Y	Y
HCPCS Code Dummy Variables	Y	Y	Y	Y
Sample:	All	All	Always Off Patent	Always On Patent
$R\hat{2}$	0.337	0.351	0.342	0.182
Number of Observations	3878	3878	2014	765
Number of Drug-Route Clusters	321	321	128	109

Table 4: IV Regression: Shortage Freq. Conditional on Post-Regulation and MMS Interaction

Year $\geq$ 2005 * MMS	0.697 (0.236) ***	0.869 (0.259) ***	0.001 (0.118)
Years Since Earliest Approval Effects	Y	Y	Y
HCPCS Code Dummy Variables	Y	Y	Y
Sample:	All	Always Off Patent	Always On Patent
IV:	Age Distribution	Age Distribution	Age Distribution
Number of Observations	3839	2014	765
Number of Drug-Route Clusters	317	128	109

Table 5: IV Regression: First Stage

Dependent Variable:	Year >= 2005 * MMS	Year >= 2005 * MMS	Year >= 2005 * MMS	MMS
Age25	-0.149 (0.041) ***	-0.177 (0.052) ***	-0.011 (0.062)	-.125 (0.024) ***
Mean Age	0.507 (0.152) ***	0.518 (0.198) **	0.063 (0.332)	0.355 (0.109) ***
Median Age	-0.065 (0.056)	0.018 (0.074)	-0.017 (0.113)	-0.037 (0.037)
Age75	-0.192 (0.089) **	-0.310 (0.104) ***	-0.005 (0.164)	-0.127 (0.056) **
Age25$\hat{2}$	0.002 (0.0006) ***	0.002 (0.0007) ***	-0.00001 (0.0007)	0.002 (0.0003) ***
(Mean Age)$\hat{2}$	-0.006 (0.002) ***	-0.005 (0.002) **	-0.0003 (0.003)	-0.004 (0.001) ***
(Median Age)$\hat{2}$	0.0006 (0.0007)	-0.0003 (0.001)	0.00008 (0.001)	0.0004 (0.0004)
Age75$\hat{2}$	0.002 (0.0001) ***	0.003 (0.001) ***	-0.00009 (0.002)	0.001 (0.0005) **
Years Since Earliest Approval Effects	Y	Y	Y	N
HCPCS Code Dummy Variables	Y	Y	Y	N
Sample:	All	Always Off Patent	Always On Patent	Cross Sectional
F-test P Value (Age*==0)	0.002	0.011	0.918	0
Number of Observations	3839	2014	765	371
Number of Drug-Route Clusters	317	128	109	

Table 6: Shortage Freq. Conditional on Number of Manufacturers in 2001 to 2003 and Number of Manufacturers

Dependent Variable:	Shortage Freq.	Shortage Freq.	Shortage Freq.
Number of Mfctr_t	0.004 (0.008)	0.003 (0.009)	-0.024 (0.025)
Year >= 2005 * Number of Mfctr 2001-2003	0.032 (0.008) ***	0.032 (0.009) ***	0.028 (0.012) **
Years Since Earliest Approval Effects	N	Y	Y
HCPCS Code Dummy Variables	Y	Y	Y
Sample:	All	All	Always Off Patent
Number of Observations	3664	3664	2014
Number of Drug-Route Clusters	292	292	128

Table 7: Number of Manufacturers Conditional on Post-Regulation and MMS Interaction

Dependent Variable:	N	log(N)	N	log(N)	log(N)	log(N)
Year >= 2005 * MMS	-1.835 (0.966) *	-0.587 (0.304) *			-0.491 (0.301)	-1.111 (0.293) ***
Year >= 2005 * Number of Mfctr 2001-2003			-0.251 (0.0533) ***	-0.053 (0.017) ***	-0.045 (0.015) ***	-0.035 (0.016) **
Years Since Earliest Approval Effects	Y	Y	Y	Y	Y	Y
HCPCS Code Dummy Variables	Y	Y	Y	Y	Y	Y
Sample:	Always Off Patent	Always Off Patent	Always Off Patent	Always Off Patent	Always Off Patent	Always Off Patent
IV:	None	None	None	None	None	Age Distribution
Number of Observations	2014	2014	2014	2014	2014	2014
Number of Drug-Route Clusters	128	128	128	128	128	128

Table 8: OLS and IV Estimates of Shortage Freq. Conditional on Medicare Payment per Service

Dependent Variable:	Shortage Freq.	Shortage Freq.	Shortage Freq.	Shortage Freq.	Shortage Freq.	Shortage Freq.	Shortage Freq.	Shortage Freq.
Payment per Service	-0.00001 (9.94e-06)	.	-0.0005 (0.0004)	.	-0.0005 (0.0002) **	.	-0.002 (0.001)	.
log(Payment per Service)	.	-0.047 (0.012) ***	.	-0.058 (0.042)	.	-0.067 (0.019) ***	.	-0.058 (0.070)
Years Since Earliest Approval Effects	Y	Y	Y	Y	Y	Y	Y	Y
HCPCS Code Dummy Variables	Y	Y	Y	Y	Y	Y	Y	Y
Sample:	All	All	All	All	Always Off Patent	Always Off Patent	Always Off Patent	Always Off Patent
IV:	None	None	All	All	None	None	All	All
Number of Observations	3089	3089	3089	2988	1717	1717	1717	1717
Number of Drug-Route Clusters	315	315	315	288	128	128	128	128

References

American Society of Anesthesiologists. 2010. "The Anesthesia Perspective: The Impact of Drug Shortages on Patients and Practitioners." *Presentation to FDA*. September 27, 2010.

American Society of Clinical Oncology. 2011. "Testimony of W. Charles Penley, MD." *Subcommittee on Health of the Committee on Energy and Commerce: Hearing Examining the Increase in Drug Shortages*. September 23, 2011.

American Society of Hematology. 2011. "Prescription Drug Shortages: Examining a Public Health Concern and Potential Solutions." *Testimony to Committee On Health, Education, Labor and Pensions, U.S. Senate*. December 15, 2011.

Berndt, Ernst. 2005. "Report of Independent Expert Prof. Ernest Berndt to Judge Patti B. Saris." *United States District Court of Massachusetts*.

Berndt, Ernst R. 2002. "Pharmaceuticals in U.S. Health Care: Determinants of Quantity and Price." *The Journal of Economic Perspectives*, 16(4): pp. 45–66.

Carlton, Dennis W. 1978. "Market Behavior with Demand Uncertainty and Price Inflexibility." *The American Economic Review*, 68(4): pp. 571–587.

Clemens, Jeffrey, and Joshua Gottlieb. 2012. "Do Physicians' Financial Incentives Affect Medical Treatment and Patient Health?" *Working Paper*.

Conti, Rena M., Meredith B. Rosenthal, Blase N. Polite, Peter B. Bach, and Ya-Chen Tina Shih. 2012. "Infused Chemotherapy Use in the Elderly After Patent Expiration." *Journal of Oncology Practice*, 8(3S).

Cramton, Peter, and Steven Stoft. 2005. "A Capacity Market that Makes Sense." *Electricity Journal 18, 43-54*.

Crawford, Gregory S., and Ali Yurukoglu. 2012. "The Welfare Effects of Bundling in Multichannel Television Markets." *Forthcoming, The American Economic Review*.

Dana, James D., Jr. 2001. "Competition in Price and Availability When Availability is Unobservable." *The RAND Journal of Economics*, 32(3): pp. 497–513.

Deneckere, Raymond, and James Peck. 1995. "Competition Over Price and Service Rate When Demand is Stochastic: A Strategic Analysis." *The RAND Journal of Economics*, 26(1): pp. 148–162.

Duggan, Mark, and Fiona Scott Morton. 2010. "The Effect of Medicare Part D on Pharmaceutical Prices and Utilization." *American Economic Review*, 100(1): 590–607.

Emmanuel, Ezekiel J. 2011. "Shortchanging Cancer Patients." *New York Times Op-Ed*. August 6, 2011.

Federal Drug Administration. 2011. "Transcript of Drug Shortage Workshop." *http://www.fda.gov/downloads/Drugs/NewsEvents/UCM275801.pdf*. September 26, 2011.

Finkelstein, Amy. 2004. "Static and Dynamic Effects of Health Policy: Evidence from the Vaccine Industry." *The Quarterly Journal of Economics*, 119(2): pp. 527–564.

Fox, Erin R., Annette Birt, Ken B. James, Heather Kokko, Sandra Salverson, and Donna L. Soflin. 2009. "ASHP guidelines on managing drug product shortages in hospitals and health systems." *Am J Health-Syst Pharm*. 66:1399-40.

Grennan, Matthew. 2012. "Price Discrimination and Bargaining: Empirical Evidence from Medical Devices." *Forthcoming, The American Economic Review*.

Hobson, Katherine. 2010. "Drug Shortages Accompanied By Lack of Info, "Near Misses," Deaths." *Wall Street Journal Health Blog*. September 23, 2010.

Jacobson, Mireille, Craig C. Earle, Mary Price, and Joseph P. Newhouse. 2010. "How Medicare's Payment Cuts For Cancer Chemotherapy Drugs Changed Patterns Of Treatment." *Health Affairs*, 29(7): 1391–1399.

Medicare Payment Advisory Commission. 2003. "Report to Congress: Variation and Innovation in Medicare." *Chapter 9: Medicare Payments for Outpatient Drugs Under Part B*. June 2003.

Mullen, Patrick. 2007. "The Arrival of Average Sales Price (ASP)." *Biotechnology Healthcare*. June 2007.

Office of Inspector General. 2005. "Medicaid Drug Price Comparison: Average Sales Price to Average Wholesale Price." *OEI-03-05-00200*. June 2005.

Rabin, Roni Caryn. 2011. "Drug Scarcity's Dire Cost, And Some Ways to Cope." *New York Times*. December 13, 2011.

Scott Morton, Fiona M. 1999. "Entry Decisions in the Generic Pharmaceutical Industry." *The RAND Journal of Economics*, 30(3): pp. 421–440.

U.S. Department of Health and Human Services. 2011. "Economic Analysis of the Causes of Drug Shortages." *Assistant Secretary for Planning and Evaluation*. October 2011.