Do Higher Health Insurance Reimbursements Encourage Antibiotic Innovation?: Evidence from Medicare's 2007 DRG Restructuring

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Abstract

I estimate the impact of the 2007 restructuring of Medicare's Diagnostic-Related Groups (DRGs) in the US on the innovation of antibiotic drug patents. This restructuring had a first-stage effect on average hospital charges per stay (price of stay) reimbursed to hospitals with an average increase of $8,584 per annum for treating the most-severe patient across base-DRGs corresponding to bacterial infectious syndromes for 4 years following the policy change. Hypothesizing passthrough of hospital charges to pharmaceutical usage, I assess whether this first-stage effect in turn caused antibiotic drug innovation by comparing patent trends. But I do not find evidence for these second-stage effects on patent outcomes. To measure drug patent innovation, I attribute US drug patents to DRGs by mapping them to Medical Subject Headings (MeSH) terms in SureChEMBL, a publicly available patents database containing biomedical annotations. This work is salient in light of recent efforts by policymakers to develop novel 'pull incentive' mechanisms to hasten antibiotic innovation to ameliorate the burden of bacterial antimicrobial resistance.

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1 Introduction

Bacterial Antimicrobial Resistance (AMR) has been recognized as a global public health problem with 1.27 million worldwide deaths in 2019 attributed to it (Murray et al. 2022). To combat the "threat" (CDC 2019) of AMR which is forecasted to worsen (Naghavi et al. 2024), policy recommendations have treated antibiotic drug innovation as an integral component (Hoffman and Outterson 2015; McDonnell et al. 2023). Several policy incentives are currently being explored to 'pull' and/or 'push' antibiotic drug innovation further (McDonnell et al. 2023; Renwick, Brogan, and Mossialos 2016) with attempts being made to estimate the appropriate size of such incentives (Towse and Bonnifield 2022; Outterson 2021). In this regard, changes to how the public health insurance market reimburses novel antibiotics have been proposed as part of a broader "Lego-regulatory pull strategy" (Renwick, Brogan, and Mossialos 2016). In light of this, in this work, I examine how an existing US policy that made changes to how specific diagnoses were reimbursed by public health insurance impacted antibiotic drug innovation.

In the public health insurance market in the US, the Centers for Medicare and Medicaid Services (CMS) reimburses hospitals for treating patients in an inpatient setting (i.e) patients admitted to a hospital, based on a Prospective Payment System (PPS) formalized as Medicare Part A (Mayes 2007). As part of this system, the CMS prospectively sets the rate of reimbursement annually for a list of Diagnostic-Related Groups (DRGs) which are classified based on a set of International Classification of Diseases (ICD) codes. In 2007, the CMS changed the DRG classification system by revising the list of ICD codes considered as valid secondary diagnoses that constitute a Complication or Comorbidity (CC). This led to many base DRGs to get split into at most 3 different severity-adjusted tiers - a version of the same DRG with Major CC (MCC), another with only CC, and another without any CC. I construe this 2007 splitting of base DRGs as a plausibly exogenous shock to patenting outcomes. I study how this shock affected the direction of innovation across different base DRGs attributable to antibiotics.

I do not find a statistically significant effect of the 2007 DRG policy on patent outcomes within antibiotic DRGs (see Figure 8). This lack of an effect is despite there being a first stage effect. The 2007 policy change caused an average increase in the average hospital charges per stay (price of stay) by $8,584 per annum paid to hospitals for treating the most-

severe patient across antibiotic base DRGs in 4 years following the 2007 policy change (see Figure 7). But this change didn't translate to an effect in the second stage possibly due to there not being an effect on the aggregate hospital charges (see Figure 9). I explore robustness of my results to alternative specifications of the patent outcome variable (see Table 8).

My work makes two salient contributions. Firstly, it contributes to the literature studying the impact of health insurance on innovation by focusing on innovation outcomes in a specific drug class (i.e.) antibiotics. Previous work has established the importance of demand-side factors such as market size (Acemoglu and Linn 2004) in affecting the rate of innovation. But evidence on the impact of health insurance on innovation remains mixed. Early work by Acemoglu et al. (2006) couldn't detect any significant impact from the introduction of Medicare on drug innovation, since the "first-stage effect" on market size was missing. More recent works have measured the impact of health insurance on innovation via different mechanisms such as formulary exclusions by Pharmacy Benefit Managers (Agha, Kim, and Li 2022), the introduction of Medicare Part D (Blume-Kohout and Sood 2013) and changes in it (Bennette et al. 2019), cost-sharing and entry deregulations (Grossmann 2013), and coverage provided to routine care of clinical trial participants (Chun and Park 2013) with many of them detecting an impact on innovation while others do not (Byrski, Gaessler, and Higgins 2021; Chun and Park 2013). In this line of work, the paper by Azoulay, Heggeness, and Kao (2025) is particularly relevant to my work here. They also study the impact of Medicare Part A on innovation but focus on the impact of the adjustments component of Medicare Part A reimbursements provided to academic medical centers, while I focus on the DRG weighting component of Medicare Part A. While there is a voluminous literature studying the impact of Medicare on patient outcomes as opposed to innovation outcomes, it is worth highlighting the work of Cook and Averett (2020) since they also study the impact of the 2007 DRG restructuring policy in Medicare Part A as I do here. But their work focuses on patient-level diagnosis upcoding while I study DRG-level patent innovation. Overall, existing works do not focus on the impact of changes to Medicare Part A on antibiotic drug innovation specifically, as I do here. This is valuable for policymakers working to combat Antimicrobial Resistance.

The second contribution of this work is in overcoming the attribution challenge of relating patents to DRGs to measure innovation at the level of base DRGs, my unit of analysis

in this study. To do this, I use SureChEMBL (Papadatos et al. 2016), a publicly-available cheminformatics database of global chemical patents annotated with the molecules specified in each patent. This database allows me to map the International Chemical Identifier (InChi) keys of patent molecules to MeSH concepts from the Unified Medical Language System (UMLS) (Bodenreider 2004). The UMLS in turn maps MeSH concepts to the International Classification of Diseases (ICD-10) codes. Since the CMS uses ICD-10 codes to define CMS-DRGs, I can use the MeSH concepts as a bridge between patents and particular DRGs. While my use of SureChEMBL to overcome the innovation-to-DRG attribution challenge is novel, the use of cheminformatics data and patent molecules to understand drug innovation is not new. Specifically, the work by Krieger, Li, and Papanikolaou (2022) exploited the biochemistry of structure-activity relationships to use similarity in the structure of drug molecules as a measure of drug novelty, and hence studied the impact of Medicare Part D on novelty in drug innovation. I, instead, use patent molecules merely as a bridge between DRGs and patents, and study the impact of Medicare Part A.

In the next section (section 2), I begin by describing the need for studying the inpatient Medicare system aimed at a specific subpopulation (those over 65 years of age) in the context of antibiotics. Then, I describe the policy under study - the 2007 DRG restructuring policy. In section 3, I describe the datasets used which is followed by a discussion of the empirical strategy in section 4. In section 5, I present the results. Section 6 concludes.

2 Background

2.1 The inpatient setting, Medicare, and antibiotics

I propose to study the policy changes to inpatient reimbursements via Medicare in the context of antibiotic resistance. This is an important endeavor for two reasons. Firstly, note that 33.6% of antibiotic expenditures in 2009 (i.e. during the period under study) was from the inpatient setting (K. J. Suda et al. 2013). This inpatient usage trend has largely persisted into 2013 as well (K. Suda et al. 2015). While outpatients (who buy antibiotics from a retail pharmacy) still constitute the majority of antibiotic spending, it has been recognized that a study of inpatients is also relevant for combating antibiotic resistance (Davey, Brown, and Hartman 2002). Secondly, Medicare reimburses an important share

of inpatient hospital charges in the US. As shown in Figure 1, Medicare is an important payer of inpatient hospital charges providing reimbursements to a subpopulation (eligible US residents older than 65 enrolled in Part A) that incurs a higher average charge per stay, and which also accounts for a plurality of discharges during the time period under study (2003-2011). Note that in Figure 1 'Medicare' is inclusive of both Fee-For-Service (FFS), and managed care (Part C/Medicare Advantage) patients. The Nationwide Inpatient Sample (NIS) dataset used in making Figure 1 does not enable me to distinguish Medicare beneficiaries along these lines. But it suffices to understand that studying the inpatient population covered by Medicare is a worthy endeavor in the context of antibiotics.

2.2 Diagnostic Related Groups (DRGs), and the 2007 restructuring policy

The CMS administers reimbursements to hospitals as part of the Medicare Part A program by setting standardized national rates prospectively each Fiscal Year (FY). This institutional arrangement is termed the Inpatient Prospective Payment System (IPPS). To reckon the reimbursement amount for each discharge, the CMS has to further multiply the standardized national rate by the weights of several factors. An explanation of the factors involved in the weighting mechanism of Medicare Part A payments is described in appendix section 7.1 along with an illustration of a hypothetical patient. One of the factors involved is the weightage given to services in a specific DRG which is the subject of my study here. This weight is the ratio of the average cost of the products/services offered to the respective patient in that DRG relative to the average cost of all products/services a hospital could offer a given patient across all DRGs. To define this weight the CMS requires a lineup of well-defined products/services to be standardized. This standardization is achieved by a DRG classification system. Such a classification system bundles all the intermediate products/services - such as drugs, lab tests, beds, meals etc. - a hospital would provide to an average patient for delivering some final product - such as midwifery or a heart transplant - into a DRG, and thus identifies each DRG as a specific product offered by a hospital. In this study, I attempt to understand the impact of a policy that overhauled this DRG classification system in calendar year 2007 (i.e.) for fiscal year 2008. Figure 2 illustrates this overhaul in a particular base DRG which corresponds to cardiac arrhythmia

& conduction disorders.

Before describing the policy of interest, it is worth clarifying the taxonomy of the DRG classification system as components of Figure 2. The purple circle in Figure 2 is a *base DRG* defined as a taxonomical level in the DRG classification system that is created as a set of International Classification of Diseases (ICD) codes for conditions of, and/or procedures offered to, a patient. The yellow shapes in Figure 2 show that the base DRG can comprise one or more tiers each with a set of Comorbidites or Complications (CC), and each tier is called a *DRG*. These DRGs are differentiated within a base DRG by a list of ICD codes mentioned in the patient's chart as a secondary diagnoses. For instance, if a patient suffering from cardiac arrhythmia & conduction disorders (base DRG) also has Hyperkalemia (ICD 10 code E87.5) as a secondary diagnosis in his charts, he would be considered under the highest tier (DRG), and reimbursed according to the weight set prospectively by the CMS for that DRG. The decisions about within which DRG a patient belongs is typically made by a piece of computer software called GROUPER which takes all the ICD codes in the patient's charts, along with the patient's demographics to make a decision based on CMS' classification system. Medical coders are trained professionals who interact with both the medical workers and the GROUPER software to ensure the latter gets the right inputs from the former.

With the taxonomy clear, the 2007 DRG restructuring can be understood as a major overhaul of the list of secondary diagnoses considered as CC. Specifically, the ICD list of CC were further subdivided as Major CC and CC. This in turn meant that the tiers within the base DRGs, and their corresponding DRG weights changed. Specifically in Figure 2 the changes to the CC list meant that the cardiac arrhythmia & conduction disorders DRG went from having 2 DRGs in FY 2007 to 3 DRGs in FY 2008 with the range of weights expanding by 0.13 from 0.31 in FY 2007 to 0.44 in FY 2008. While Figure 2 illustrates a split from 2 to 3 DRGs, some other base DRGs underwent a consolidation of DRGs as well moving to fewer DRGs than before. The full list of changes to the DRGs across all base DRG in FY 2007 is summarized in Figure **??**. For instance, Figure **??** clarifies that Figure 2 is but one example among 63 base DRGs that underwent a split of 2 DRGs to 3 DRGs while 14 base DRGs consolidated the 3 DRGs they had in FY 2007 down to 2 DRGs in FY 2008. It also summarizes that the average expansion in weights was generally higher when the base DRGs split into more DRGs. In this study, I exploit this variation in

the expansion of weights in those base DRGs corresponding to antibiotics as a plausibly exogenous shock to patenting activities attributable to the base DRGs.

It is worth mentioning in this section that the policy change described here supposedly only applies to the payment process for FFS Medicare Part A beneficiaries only. In the case of managed care (Medicare Part C) beneficiaries whose hospital stays may also be eligible for reimbursement, it is unclear whether the 2007 DRG restructuring would be salient. It is known that the intermediate insurers of Part C also use a DRG classification system. But it is unclear whether they structure their insurance plans in a way that pegs them to the FFS Part A system or not. For instance, it is possible that intermediate insurers of Part C use the same DRG classification system as Part A with the same or different weightage process. It is also possible that they might use an entirely different DRG classification system. So, it is unclear whether Part C's private insurers would change their DRG weights independent of CMS. I reiterate that the data from the NIS used here can't disambiguate FFS and managed care patients which means that while it will carry the signals of the 2007 DRG restructuring policy's impact on hospital charges, it may also have the noise from any simultaneous changes made by the managed care insurers as well.

3 Data

The variability in the policy, the hospital charges, and the patent outcomes across base DRGs are protrayed respectively in Figure 3, Figure 4, and Figure 5. Each of the data sources used is described in this section.

3.1 Finding antibiotic DRGs and their weights

Data on the DRG weights for each FY between 2004-2011, my study period, comes from the final rule on rates for the IPPS published in the Federal Register by the CMS.[1] For instance, the rates established for FY 2008 were provided in 72 Fed. Reg. 47130 (Aug. 22, 2007). The crosswalk from the DRG system in FY 2007 to FY 2008 is available from the CMS' website.[2] This crosswalk lets me identify the base DRGs in FY 2008, the unit

[1]To understand why this period is being studied please refer to Table 7.2 in appendix section 7.2 which shows how the relevant legislative events delimit the study period.

[2]It is available in the following URL: https://www.cms.gov/medicare/medicare-fee-for-service-payment/acuteinpatientpps/acute-inpatient-files-for-download-items/cms1247844

of analysis in this study, and the corresponding tiers in it in the pre-policy change DRG regime and the post-policu change regime.[3]

While the CMS provides the data on DRG weights and crosswalks, identifying those base DRGs which are relevant to infectious syndromes where antibiotics would be used requires additional data. This additional data comes from the work of Murray et al. (2022) (See Table S3 in the supplementary materials provided online by the authors). In this work which is treated as the primary reference for details on AMR burden, the authors disambiguate their burden estimates by infectious syndrome identified using a set of ICD codes. I use the same set of codes and flag base DRGs corresponding to those codes as antibiotic DRGs. Note that mapping of base DRGs to ICD codes is available from the DRG definitions manual.[4] This flagging resulted in picking 67 base DRGs out of the 332 as antibiotic DRGs. The list of the 67 Base DRGs and the severity levels in each of them is listed in Table **??**. Figure 3 portrays the trend of weights during my study period of the most severe patient's DRG across all these 67 base DRGs.

3.2 Nationwide Inpatient Sample (NIS) data

Data on hospital charges comes from the Nationwide Inpatient Sample (NIS) between 2004 and 2011 calendar years. The NIS is an administrative dataset that contains data from a nationally representative 20% sample of hospitals from across most of the states in the US. This data is provided by the respective governmental organizations of each state. It contains data at an individual discharge-level on all the ICD codes assigned to the respective inpatient for that discharge, the corresponding pre and post-FY 2008 DRG, the charges incurred by the hospital in treating that patient, the expected payer for the insured patients, among other attributes. A summary of this data is in 1 which describes that Medicare is an important payer of inpatient hospital charges providing reimbursements to a subpopulation that incurs a higher average charge per stay, and which also accounts for a plurality of discharges during the time period under study. Variability of hospital charges

[3] In the pre-policy period the classification system was called "CMS-DRG" and in the post period it was called "MS-DRG" (Medicare Severity-adjusted DRG).

[4] An important caveat here is that the earliest publicly available DRG definitions manual is from 2015. I confirmed this fact in an email conversation with a CMS staffer who mentioned that any DRG definitions manual earlier than 2015 "was only available for purchase but it was through a third party who is no longer selling." While I use this manual from outside my study period in this proposal, this limitation can be overcome with the Nationwide Inpatient Sample (NIS) data acquired with tolerable monetary costs, as described in the next section since it contains the DRG for each patient separately along with all their ICD codes.

across base DRGs is portrayed in Figure 4.

As was mentioned in the 2, while the NIS codes 'Medicare' as the insurer and differentiates them from a private payer, it doesn't differentiate between FFS (Part A), and managed care (Part C) payers. So the noise from simultaneous changes made by the intermediary insurers in managed care will act as a limitation in interpreting the results from this study.[5]

3.3 Attributing patents to antibiotic DRGs using SureChEMBL (Papadatos et al. 2016)

The data for attributing patents to antibiotic DRGs comes from two sources - the medical vocabularies available from the SureChEMBL (Papadatos et al. 2016) and Unified Medical Language System (UMLS) (Bodenreider 2004). SureChEMBL is a publicly-available cheminformatics database of global chemical patents annotated with the Medical Subject Headings (MeSH) codes specified in each patent. The Unified Medical Language System (UMLS) (Bodenreider 2004) maps MeSH codes to ICD codes. Since the CMS uses ICD codes to define DRGs (as described in section 2), I can use the MeSH codes in SureChEMBL as a bridge between patents and DRGs.

When attributing patents to DRGs, I ensure to check that both the ICD codes corresponding to the primary diagnoses of the base DRGs, and the secondary diagnoses of the severity DRGs within that base DRG are both mentioned in the patent. Further since SureChEMBL describes in which section of the patent the MeSH code was mentioned such as claims or abstract or title, I check robustness to alternative attribution mechanisms as well (see section 5.3). In addition, I account for multiple attributions as well. One patent can get attributed to multiple DRGs if it cites MeSH codes relevant to multiple indications. In this case, I reweight the count of patents belonging to the DRG by "fractionalizing"[6] it as $1/n$ if the patent belongs to n base DRGs. So, if a patent belongs to 2 base DRGs, then it counts as 0.5 (1/2) in each base DRG.

The attribution is summarized in Figure 5 which shows variability in patent outcomes across base DRGs. Note that SureChEMBL only annotates successfully granted patents

[5]Overcoming this limitation will require overcoming significant monetary barriers to acquire MedPAR claims data. These costs are 10x the costs of acquiring NIS data.

[6]I borrow this term from Azoulay et al. (2019) who fractionalize the number of patents beloning to an NIH grant in their work.

and not unsuccessful patent applications. But, as shown in Figure 5, I index the granted patents based on their application year so that I can include patents granted until 2024 as long as it was applied for within the short time horizon I study. Finally, i take advantage of the fact that SureChEMBL annotates the chemical compounds referenced in each granted patent. I join these molecular structures with those mentioned in AntibioticDB (Farrell et al. 2018) which contains a manually curated list of compounds known to have antibiotic action across different phases of the drug approval process. This lets me test the robustness of my results to different operationalization of patent counts (see section 5.3).

4 Empirical strategy

The identification strategy relies on the plausible exogeneity of any changes to the DRGs weights created by the 2007 DRG restructuring policy to the patent ecosystem. Specifically, I expect to see parallel trends in patent innovation across the antibiotic base DRGs absent the DRG restructuring policy.

I estimate the effect of the changes to the DRG weights of the most severe patient in a base DRG on patent innovation in 4 years following the 2007 DRG restructuring policy, only among those base DRGs that correspond to infectious syndromes relevant to antibiotics. Denoting antibiotic-relevant base DRG as g and calendar years as t, the main Difference in Differences (DiD) regression specification can be written as:

$$y_{gt} = \alpha_g + \alpha_t + \left[\sum_{\substack{t=2004 \\ t \neq 2007}}^{2011} \beta_t \times I_t \times MaxWt_{gt} \right] + \epsilon_{gt} \tag{1}$$

α_g, α_t are the base-DRG, and year specific fixed effects, respectively. Here y_{gt} is the fractionalized[7] count of granted patent counts in patent application year t attributable to the severe DRGs in base DRG g, β_t is the coefficient of interest, and I_t is a year indicator-dummy for each of the years in my study period (2004-11) with 2007 being the reference year. $MaxWt_{gt}$ is the weight of the most severe DRG within base DRG g. So, I estimate the effect of the 2007 policy change upto 4 years (between 2008 and 2011) after the change.

[7] See section 3.3 for a description of how fractionalization of patent counts was done.

To understand the mechanisms that drive the effect here, I also propose a two-stage DiD estimation process.

$$y_{gt} = \alpha_g + \alpha_t + \left[\sum_{\substack{t=2004 \\ t \neq 2007}}^{2011} \beta_t \times I_t \times z_{gt} \right] + \epsilon_{gt}$$
$$z_{gt} = \alpha_g + \alpha_t + \left[\sum_{\substack{t=2004 \\ t \neq 2007}}^{2011} \beta_t \times I_t \times MaxWt_{gt} \right] + \epsilon_{gt} \quad (2)$$

z_{gt} here is the Average hospital charges per stay. This specification reflects my hypothesis that an increase in the weight in a DRG affects patent innovation via a pass-through of hospital charges to the pharmaceutical firm. In other words, since an increase in DRG weights means that the hospital can charge more per stay, this gives the hospital bandwidth to pay more for drugs which in turn can provide additional revenue for the pharmaceutical firm which might now consider innovation for drugs in the respective DRG to be profitable.

5 Results

5.1 Reduced form estimation: Effect of policy on patent outcomes

I first present results from a reduced form estimation to check whether the 2007 DRG restructuring policy impacted patenting outcomes. The results of this estimation is shown in the event study plot in Figure 6. It is clear that I don't observe a statistically significant effect. The exact magnitudes of the standard errors, clustered at the DRG level is shown in Table 4. While the main takeaway from Figure 6 is the absence of an effect, one can also notice that there is parallel trends in the pre-treatment period. This adds to the plausibility of the parallel trends assumption described in section 4.

5.2 Two stage estimation: Effect of policy via hospital charges

My hypothesis in expecting a reduced form result to show up was that the 2007 policy change would have an effect on hospital charges which in turn would pass through as revenue to the pharmaceutical firm. So, my hypothesized mechanism may not be addressed

if the effect on hospital charges was also absent. Figure 7 shows this to not be the case. Indeed, the 2007 policy change had a first-stage effect in the hypothesized direction on average hospital charges per stay paid to hospitals for treating the most severe patient (i.e) the price of treating the patient in the highest DRG within each base DRG. Specifically, as shown in Table 5 a unit increase in the DRG weights due to the 2007 policy change for the most severe patient led to an average increase across base DRGs of $8,584 in the average hospital charges paid per stay (price of stay) for such patients. So, there was indeed a price increase created by this policy change, and my hypothesis is being addressed by this policy change. Then, why is the reduced form result absent? There can be several reasons, and I address some of them below.

Firstly, absence of the reduced form effect could be chalked up to the fact that the average price increase was not large enough in those DRGs where there was a patenting effect. In the lingo of design-based causal inference, the compliance rate was low in the first stage. To address this issue, I performed a two-stage estimation wherein the effect of hospital charges on patenting was studied by first instrumenting hospital charges by the 2007 policy change. The results of this analysis is shown in Figure 8. There is still no effect and the corresponding magnitudes of standard errors shown in 6. So, a lack of compliance rate can't be an explanation for the missing reduced form effect.

Secondly, one might argue that an average annual increase of $8,584 (Figure 7) in the average hospital charges paid per stay is simply not large enough to encourage innovation in the antibiotic base DRGs being considered here. Figure 9 shows the plausibility of this second argument. While the Figure 7 shows an increase in the *average* hospital charges per stay (price), Figure 9 shows an absence of an effect in the *aggregate* hospital charges hence bostering this argument. But, assuming my passthrough hypothesis is true, this argument also means a larger increase in the price would be sufficient to pull the required innovation. Then what is the right size of the price increase? My analysis tells me that a $8,584 anuual increase is not enough. It is difficult to empirically estimate the required size of this price increase due to a lack of credible estimates on the costs of innovation in these base DRGs.[8] This difficulty makes this argument harder to digest, especially since I am counting patents which costs a lot less to make than the final products (FDA-approved

[8]Outterson (2021) relies on cost estimates from Sertkaya et al. (2014) and sizes pull incentives at $4.2 billion to bring a new antibiotic to market but this estimate is not disambiguated by disease/indication let alone at a DRG-level as required for my analysis here.

drugs), assuming patenting happens prior to the clinial trial stage of drug development.[9]

Finally, one might argue that the reduced form effect is missing since hospitals don't passthrough a lot of their charges to pharmaceutical firms. This argument is a much stronger counter to my counter than the second argument. Estimating the passthrough rate of hospital charges to inpatient drug usage requires data that disambigutes hospital charges by cost centers (such as bed, lab tests, drugs etc.). While the Healthcare Cost Report Information System (HCRIS) of the CMS collects this information, this data is only available at a hospital-level but not at a DRG-level which is required for my analysis here.[10] So, I am unable to address this argument sufficiently in this work.

5.3 Robustness to alternate operationalizations of patent outcomes

I present results from measuring patent outcomes differently. Table 8 shows these results with all the plots being the second stage effect of the 2007 policy change via increased average hospital charges per stay. As the table shows, counting patents via a different attribution mechanism, or only patents having drug compounds, or only patents having antibiotic compounds doesn't change the absence of the effect.

6 Conclusion

In this work, I estimated the impact of the 2007 restructuring of Medicare's Diagnostic-Related Groups in the US on the innovation of antibiotic drug patents. I didn't find a statistically significant effect. This lack of an effect is despite there being a first stage effect. The 2007 policy change caused an average increase in the average hospital charges per stay (price of stay) by $8,584 per annum paid to hospitals for treating the most-severe patient across antibiotic base DRGs in 4 years following the 2007 policy change. These results should be interpreted in light of several shortcomings in the methodology I employed. Some of these can be fixed in future drafts of this paper but some of them can't be fixed. By obtaining patient-level data of the Nationwide Inpatient Sample I aim to redefine the policy variable (encouragement) as a counterfactual increase in DRG weights instead

[9] There are good reasons to believe this would be true. Patenting must happen within a year of scientific publication lest it fails a prior art search at the patent office.

[10] The only way left to get this information would be via individual Medicare Part A claims data which requires significant funding to obtain.

of the observed DRG weights as I do currently. But the short time horizon of 4 years post-treatment, and the lack of disambiguation of the hospital charges across cost centers at the DRG-level will be an inevitable weakness of this work.

Notwithstanding these shortcomings, the evidence presented here is policy-relevant. In the 117th Congress, the DISARM Act of 2021 aimed to make additional payments via Medicare for antibiotic drugs to combat the threat of Antimicrobial Resistance. The 2007 DRG restructuring incidentally created a similar policy change, and hence my study should be directly valuable to AMR policymakers. It should also be valuable to policymakers interested in the impact of pull incentives in general. Further, the data attribution process I describe in this paper of using SureChEMBL (Papadatos et al. 2016) to attribute patents to DRGs should also open the doors for future research attempting to understand the impact of Inpatient Prospective Payment Systems (IPPS) on patent innovation.

7 Appendix

7.1 Medicare Part A payment mechanism

Borrowing notation from Azoulay, Heggeness, and Kao (2025) (See their supplementary material), the payment from the Prospective Payment System (PPS) received by a hospital h for providing the product bundle represented by Diagnostic Related Group (DRG) d for a discharge completed in fiscal year t can be denoted as the function:

$$PPS_{h,d,t} = f\left(\text{Base rate}_t, \text{DRG weight}_{d,t}, \text{Wage index}_{h,t}, \text{Adjustments}_{h,t}\right)$$

The Base rate_t is a standardized national rate set prospectively each year by the CMS separately for the labor and non-labor related charges. The $\text{Wage index}_{h,t}$ factor adjusts the labor-related standardized rate for local wages at the hospital's locality. The $\text{Adjustments}_{h,t}$ factor corresponds to adjustments made to the reimbursements for hospitals with disproportionately higher share of economically poorer patients, and to hospitals who do teaching/research in addition to treating patients. Note that the adjustment factor is studied extensively by Azoulay, Heggeness, and Kao (2025) while I focus on the $\text{DRG weight}_{d,t}$ factor. To quote the CMS (72 Fed. Reg. 47130 (Aug. 22, 2007)), "Each

DRG weight represents the average resources required to care for cases in that particular DRG, relative to the average resources used to treat cases in all DRGs." This can be written as:

$$DRG_{d,t} = \frac{\text{Average cost}_{d,t-1}}{\sum_i \text{Average cost}_{i,t-1}}$$

where i indexes the set of all DRGs. To compute Average $\text{cost}_{d,t-1}$ uses data from the MedPAR claims files. Specifically, CMS aggregates the provider-DRG-level total claims from last FY, factors out the wage indexes, weights and adjustments, to back out a standardized charge. Then they use a hospital level Cost-To-Charge ratio to convert the charges back to costs. Then they divide the costs by the number of discharges in that DRG to arrive at Average $\text{cost}_{d,t-1}$. For my identification, I approximate this process with data from NIS. Specifically, instead of backing out the standardized charge from claims, I propose to use the last FY's standardized rate, base DRG weights, and the number of discharges at a DRG-level from NIS data to approximate the standardized charge and use that to compute counterfactual DRG-weights. I check the quality of my approximation with the observed data and perform sensitivity analyses accordingly to provide robustness checks.

Table 7.1 provides an illustrative hypothetical example of a patient at a generic Hospital in San Francisco, CA who underwent Hip & Femur Procedures (DRG 482). Notice how wage index, DRG weights, and adjustments get applied to the national standardized rates for arriving at the final reimbursement rate for this patient.

Table 1: Hypothetical patient at a generic Hospital in San Francisco, CA, DRG 482, HIP & FEMUR PROCEDURES EXCEPT MAJOR JOINT W/O CC/MCC (2001)

Hypothetical patient at Generic Hospital in San Francisco, CA, DRG 482 HIP & FEMUR PROCEDURES EXCEPT MAJOR JOINT W/O CC/MCC (2001)	
Description	**Value**
Average length of stay	3.8
Large urban labor-related rate	$2,809.18
Large urban non-labor-related	$1,141.85
Wage index	1.4193
Standard Federal Rate: labor × wage index + non-labor rate	$5,128.92
DRG relative weight (RW) factor	1.8128
Weighted payment: Standard Federal Rate × DRG RW	$9,297.71
Disproportionate Share Payment (DSH)	0.1413
Indirect medical education (IME)	0.0744
Total cost outlier reimbursement	$0
Total operating payment: Weighted payment × (1 + IME + DSH)	$11,303.23

Source: The Office of Evaluation and Inspections (2001)

7.2 A brief history of the Inpatient Prospective Payment System, and the 2007 DRG restucturing

The book by Mayes and Berenson (2006) recounts the origins of the IPPS within the Medicare Part A reimbursement system. The book narrates how policy concerns over soaring Medicare costs in the 1970s, and the contemporaneous "conceptual innovation" (Pg. 21, Chapter 1, Mayes and Berenson (2006)) of research into prospective reimbursement (Dowling 1974) precipitated in the adoption of the IPPS. This happened alongside the developments at Yale where the technical solution required to take that research idea to the ground was created (Fetter, Thompson, and Mills 1976; Mills et al. 1976). This technical solution was born out of the need of researchers to design a system for comparing hospitals' performances which in turn requires that "one must identify the specific products they provide" (Fetter 1999). This is done by a DRG classification system which groups bundles of intermediate products/services - such as lab tests, beds, meals etc. - a

hospital would provide to deliver a final product (such as midwifery or heart transplant) to the average patient into a specific DRG and thus identifying it as a specific product. Following the initial example set by the experiments with a DRG classification system in New Jersey (Iglehart 1982), Congress mandated the use of DRGs in Medicare Part A as part of the Tax Equity and Fiscal Responsibility Act of 1982 (TEFRA).

The DRG classification system underwent a major overhaul in 2007. The set of events surrounding this change is described in Table 7.2. This table also provides the rationale for the study period used in this study.

Table 2: Legislative timeline establishing the study period

2003	Medicare Modernization Act passes and establishes an 18 month moratorium on Physician-Owned Specialty hospitals.
2005	The Medicare Payment Advisory Commission (MedPAC) unanimously recommends changing the DRG system to adjust for severity in order to remove perverse incentives for Physician-Owned Speciality hospitals. But CMS only adopts minor changes for FY 2006.
2006	CMS proposes CS-DRGs (Consolidated Severity-DRGs) for FY 2007 but public comments in the rulemaking process oppose it. CMS drops the proposal and promises to hire a contractor to do more analyses of changes.
2007	**CMS proposes MS-DRGs, and adopts it successfully for FY 2008.** RAND Corp. provides ex-ante analyses of the change (Wynn and Scott 2007).
	...
2011	Congress introduces the Generating Antibiotic Incentives Now (GAIN) Act which extends market exclusivity for Qualified Infectious Disease Products (QIDP) by 5 years and fast-tracks their FDA review process.
2012	Congress passes the GAIN Act

Source: Until 2007, see 72 Fed. Reg. 47130 (Aug. 22, 2007). For more on 2012, see the manuscript of Kong and Zhao (2025).

While the DRG weights change every year, note that the events shown in Table 7.2 are the relevant events for the DRG restructuring of 2007 which established version 25 of the DRG classification system. The same is clarified by the following quote from the DRG definitions manual for Version 33.0A published by 3M (the vendor of CMS in charge of

maintaining the DRG system) about the stability of the CC list since 1984 until 2007 when the change happened:

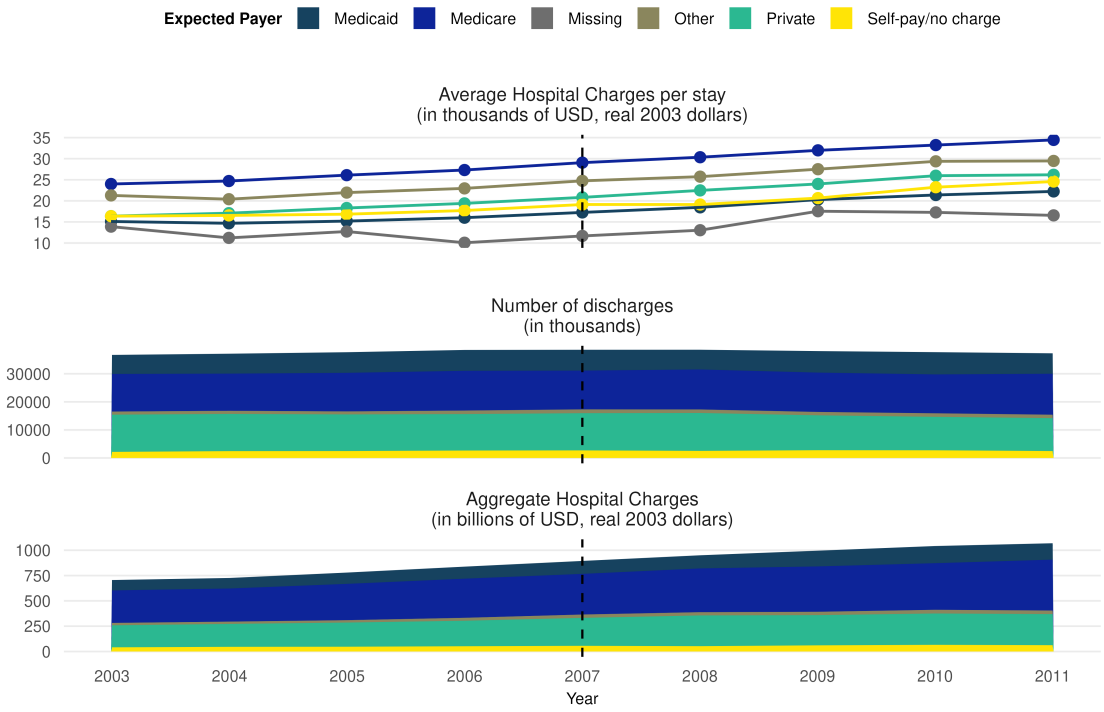
> "Except for new diagnosis codes that were added to ICD-9-CM after FY 1984 (e.g., HIV), the CC list of diagnoses used in the DRGs remained virtually identical to the original CC list used in FY 1984. As a result of the changes that occurred in hospitals during the first 22 years of PPS, the CC list had lost much of its power to discriminate hospital resource use. Better coding of secondary diagnoses, stricter criteria for extended hospital stays, increased availability of post acute care services and the shift to outpatient care resulted in most patients (nearly 80 percent) admitted to hospitals having a CC. Therefore, in version 25 (MS-DRGs) the diagnoses comprising the CC list were completely redefined. The revised CC list is primarily comprised of significant acute disease, acute exacerbations of significant chronic diseases, advanced or end stage chronic diseases and chronic diseases associated with extensive debility. In general, most chronic diseases were not included on the revised CC list. For a patient with a chronic disease, a significant acute manifestation of the chronic disease was required to be present and coded for the patient to be assigned a CC. The revision of the CC list reduced the number of Medicare patients with a CC from approximately 80 percent to 40 percent."

8 Tables and figures

Figure 1:

Trends in usage of inpatient services in the US across Expected Payers, 2003-2011

Data was sourced annually, and aggregated at the Diagnostic Related Group (DRG) level



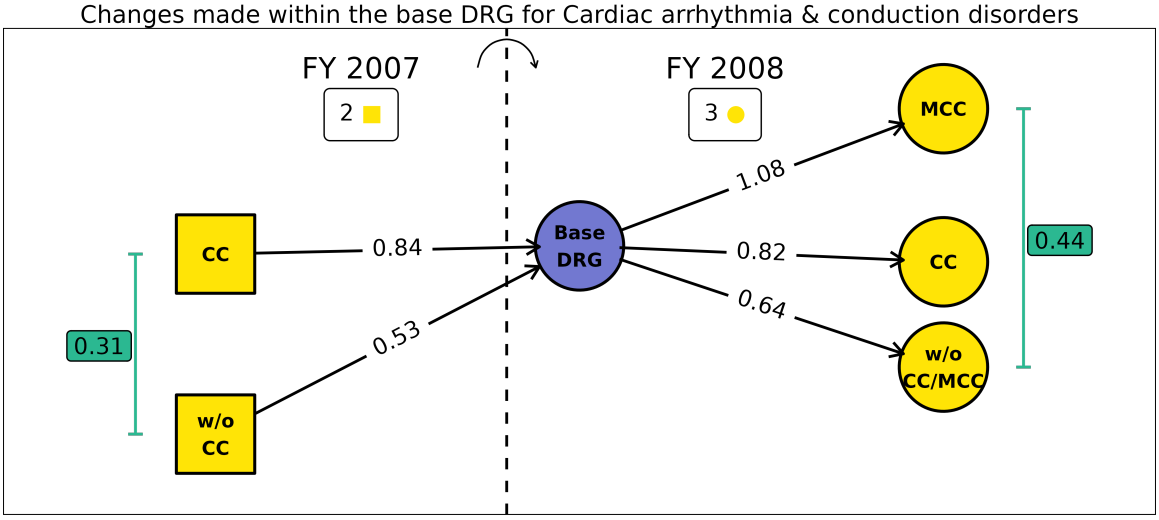
NOTE:
Dashed line marks the year 2007 when Medicare transitioned to the MS-DRG classification system.
Aggregate Hospital Charges were reckoned by multiplying the Average Hospital Charges per stay and the No. of Discharges.
All USD are inflation adjusted to base year 2003 using the CPI.
Survey errors could not be visualized since the plots were made using data already aggregated at the DRG-level.

SOURCE:
HCUPnet, Healthcare Cost and Utilization Project. Agency for Healthcare Research and Quality, Rockville, MD.

Figure 2:

An illustration of the 2007 DRG restructuring policy in Medicare Part A

Changes made within the base DRG for Cardiac arrhythmia & conduction disorders



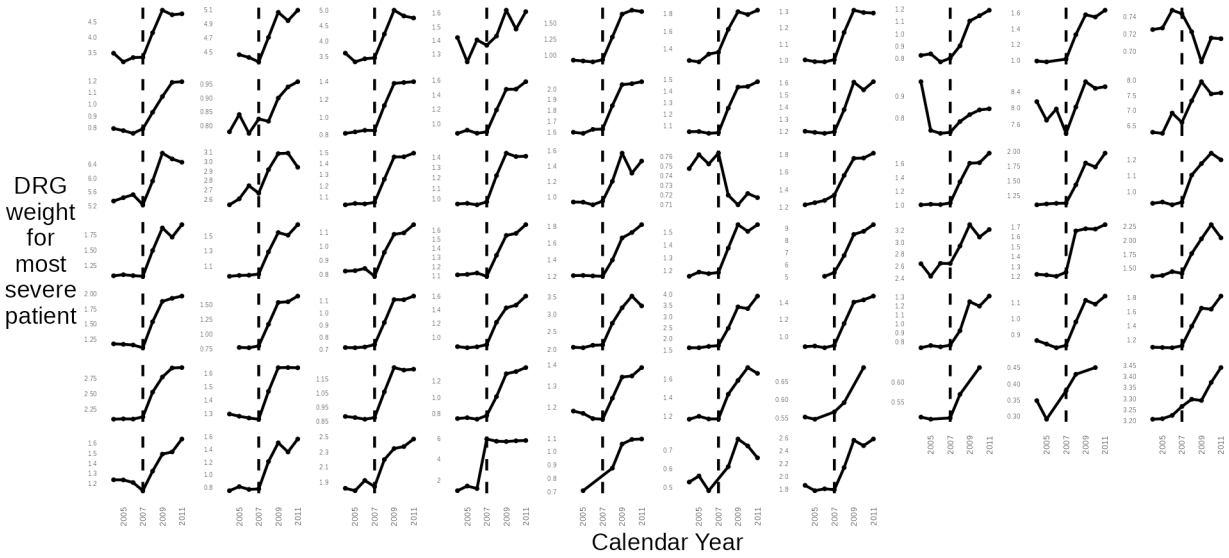
NOTE:
CC = Complication or Comorbidity
MCC = Major CC

SOURCE:
Final Rule for FY08 published in 72 Fed. Reg. 47130 (Aug. 22, 2007) by the Centers for Medicare & Medicaid Services

Table 3: List of DRGs related to bacterial infectious syndromes

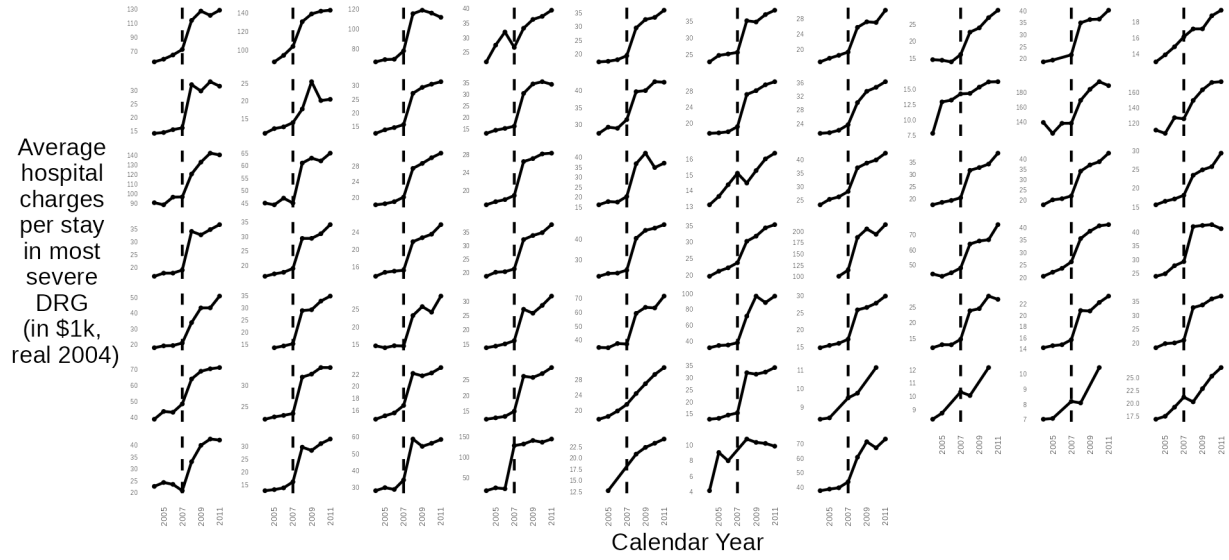
DRG code	DRG name
011	Tracheostomy for face,mouth & neck diagnoses w MCC
023	Cranio w major dev impl/acute complex CNS PDX w MCC or chemo implant
025	Craniotomy & endovascular intracranial procedures w MCC
052	Spinal disorders & injuries w CC/MCC
056	Degenerative nervous system disorders w MCC
070	Nonspecific cerebrovascular disorders w MCC
073	Cranial & peripheral nerve disorders w MCC
080	Nontraumatic stupor & coma w MCC
091	Other disorders of nervous system w MCC
123	Neurological eye disorders
124	Other disorders of the eye w MCC
152	Otitis media & URI w MCC
154	Nasal trauma & deformity w MCC
157	Dental & Oral Diseases w MCC
177	Respiratory infections & inflammations w MCC
193	Simple pneumonia & pleurisy w MCC
196	Interstitial lung disease w MCC
202	Bronchitis & asthma w CC/MCC
222	Cardiac defib implant w cardiac cath w AMI/HF/shock w MCC
224	Cardiac defib implant w cardiac cath w/o AMI/HF/shock w MCC
226	Cardiac defibrillator implant w/o cardiac cath w MCC
288	Acute & subacute endocarditis w MCC
291	Heart failure & shock w MCC
299	Peripheral vascular disorders w MCC
306	Cardiac congenital & valvular disorders w MCC
312	Syncope & collapse
314	Other circulatory system diagnoses w MCC
377	G.I. hemorrhage w MCC
380	Complicated peptic ulcer w MCC
383	Uncomplicated peptic ulcer w MCC
385	Inflammatory bowel disease w MCC
388	G.I. obstruction w MCC
391	Esophagitis, gastroent & misc digest disorders w MCC
393	Other digestive system diagnoses w MCC
441	Disorders of liver except malig,cirr,alc hepa w MCC
444	Disorders of the biliary tract w MCC
456	Spinal fus exc cerv w spinal curv/malig/infec or 9+ fus w MCC
485	Knee procedures w pdx of infection w MCC
488	Knee procedures w/o pdx of infection w CC/MCC
539	Osteomyelitis w MCC
548	Septic arthritis w MCC
551	Medical back problems w MCC
553	Bone diseases & arthropathies w MCC
557	Tendonitis, myositis & bursitis w MCC
573	Skin graft &/or debrid for skn ulcer or cellulitis w MCC
576	Skin graft &/or debrid exc for skin ulcer or cellulitis w MCC
602	Cellulitis w MCC
606	Minor skin disorders w MCC
640	Nutritional & misc metabolic disorders w MCC
643	Endocrine disorders w MCC
673	Other kidney & urinary tract procedures w MCC
682	Renal failure w MCC
689	Kidney & urinary tract infections w MCC
727	Inflammation of the male reproductive system w MCC
742	Uterine & adnexa proc for non-malignancy w CC/MCC
757	Infections, female reproductive system w MCC
774	Vaginal delivery w complicating diagnoses
781	Other antepartum diagnoses w medical complications
782	Other antepartum diagnoses w/o medical complications
793	Full term neonate w major problems
814	Reticuloendothelial & immunity disorders w MCC
865	Viral illness w MCC
867	Other infectious & parasitic diseases diagnoses w MCC
870	Septicemia w MV 96+ hours
947	Signs & symptoms w MCC
951	Other factors influencing health status
974	HIV w major related condition w MCC

Figure 3: Trends in weights of most severe DRG in each base DRG



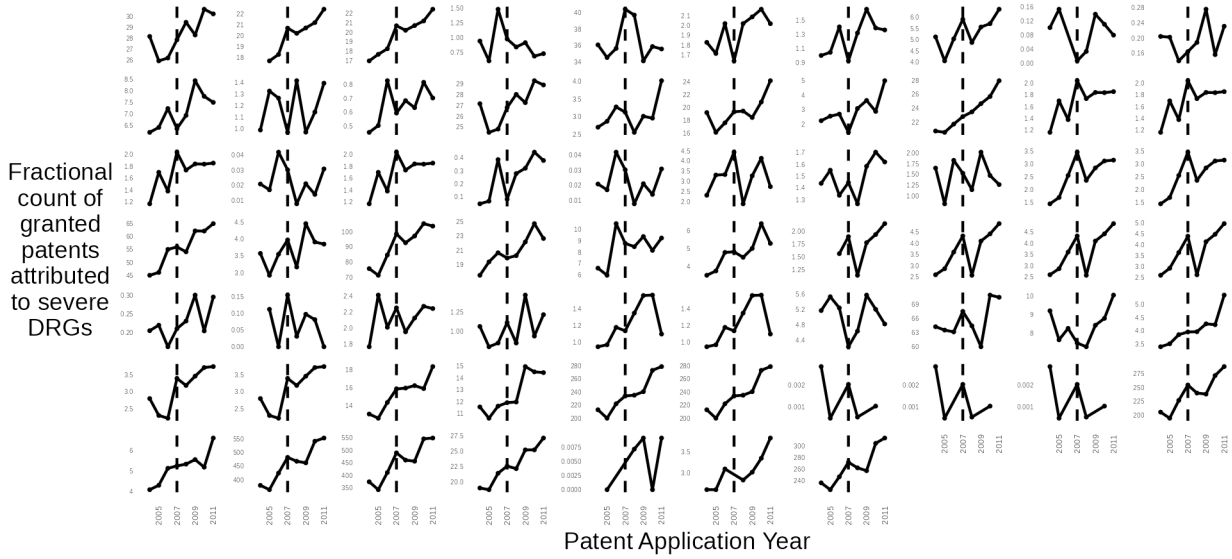
Note: Data was taken from Federal Register Final Rule documents on 'Changes to the Hospital Inpatient Prospective Payment Systems' published annually. Dashed line indicates 2007 when the DRG restructuring policy was enacted.

Figure 4: Trends in average hospital charges per stay for most severe DRG in each base DRG



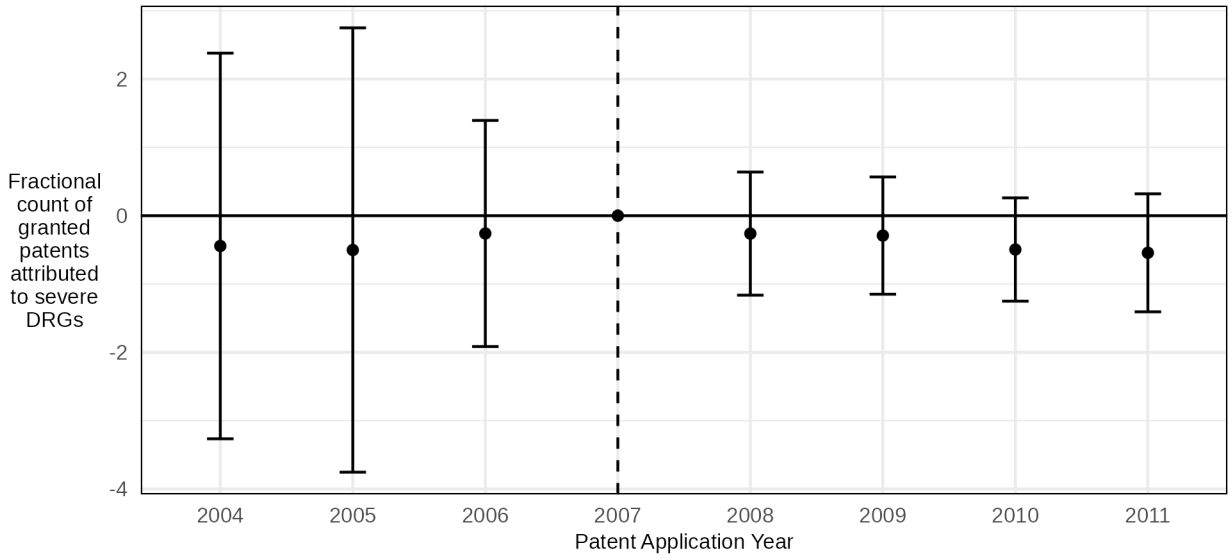
Note: Data was taken from the Nationwide Inpatient Sample (NIS) dataset. Dashed line indicates 2007 when the DRG restructuring policy was enacted. All dollar amounts were inflation-adjusted to 2004.

Figure 5: Trends in fractional count of patents attributed to most severe DRG in each base DRG



Note: US Patents data was taken from the SureChEMBL (NIS) dataset. Dashed line indicates 2007 when the DRG restructuring policy was enacted. Patents were attributed to each base DRG by mapping ICD codes to MeSH codes, and counts fractionalized to avoid double counting patents in multiple base DRGs. See section 3.3 for more details on the attribution process.

Figure 6: Reduced-form effect of DRG restructuring policy on patent outcomes



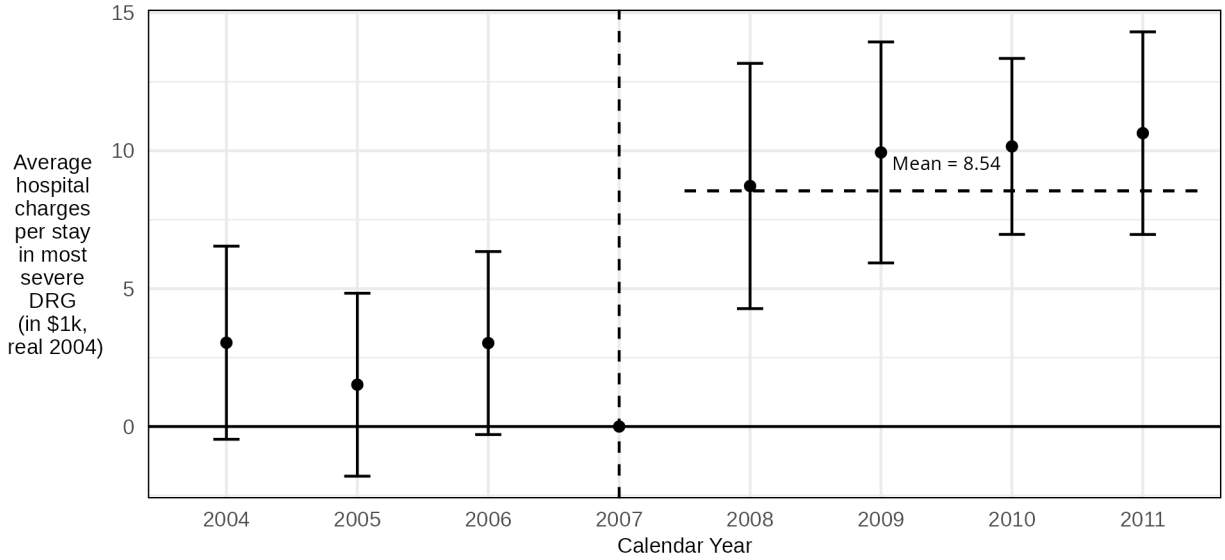
Note: Independent variable is the weight of the most severe DRG in each base DRG. Dashed line indicates the reference year 2007 when the DRG restructuring policy was enacted. Patents were attributed to each base DRG by mapping ICD codes to MeSH codes, and counts fractionalized to avoid double counting patents in multiple base DRGs. See section 3.3 for more details on the attribution process. Base DRG and Year Fixed effects are included. 95% confidence intervals based on standard errors clustered at base DRG level are shown.

Table 4: Reduced form effect

	Dep: Fractional count of granted patents attributed to severe DRGs		
	(1)	(2)	(3)
Weight of most severe DRG X 2008	-1.189	-0.767	-0.262
	(2.930)	(3.476)	(0.460)
Weight of most severe DRG X 2009	-1.078	-2.229	-0.291
	(2.449)	(2.807)	(0.438)
Weight of most severe DRG X 2010	0.082	-1.634	-0.495
	(2.772)	(3.421)	(0.386)
Weight of most severe DRG X 2011	0.694	-2.209	-0.543
	(2.793)	(3.438)	(0.441)
Year FE		X	X
Base DRG FE			X
Observations	518	518	518
R2	0.00	0.00	0.98
Outcome Mean (SDev)	37.9 (96.1)	37.9 (96.1)	37.9 (96.1)

Note: Independent variable is the weight of the most severe DRG in each base DRG. Patents were attributed to each base DRG by mapping ICD codes to MeSH codes, and counts were fractionalized to avoid double counting patents in multiple base DRGs. See section 3.3 for more details on the attribution process. Standard errors clustered at base DRG level are shown. *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

Figure 7: First stage effect of DRG restructuring policy on price of stay



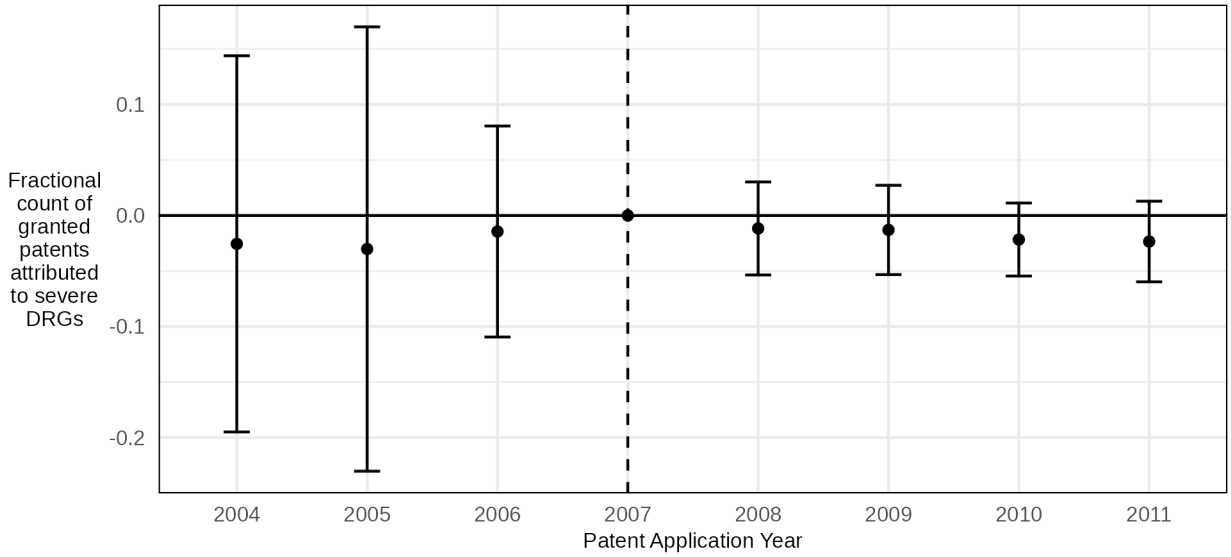
Note: Independent variable is the weight of the most severe DRG in each base DRG. Dashed line indicates the reference year 2007 when the DRG restructuring policy was enacted. Data on hospital charges was taken from the Nationwide Inpatient Sample (NIS) dataset. All dollar amounts were inflation-adjusted to 2004. Base DRG and Year Fixed effects are included. 95% confidence intervals based on standard errors clustered at base DRG level are shown.

Table 5: First stage effect on Average hospital charges

	Dep: Average hospital charges per stay in most severe DRG (real 2004, $1k)		
	(1)	(2)	(3)
Weight of most severe DRG X 2008	20.578 ***	22.767 ***	8.722 ***
	(0.949)	(1.382)	(2.269)
Weight of most severe DRG X 2009	20.034 ***	22.762 ***	9.939 ***
	(0.714)	(0.960)	(2.045)
Weight of most severe DRG X 2010	20.389 ***	23.095 ***	10.158 ***
	(0.578)	(0.620)	(1.628)
Weight of most severe DRG X 2011	20.831 ***	23.430 ***	10.638 ***
	(0.548)	(0.624)	(1.875)
Year FE		X	X
Base DRG FE			X
Observations	518	518	518
R2	0.79	0.87	0.97
Outcome Mean (SDev)	38.5 (36.3)	38.5 (36.3)	38.5 (36.3)

Note: Independent variable is the weight of the most severe DRG in each base DRG. Data on hospital charges was taken from the Nationwide Inpatient Sample (NIS) dataset. All dollar amounts were inflation-adjusted to 2004. Standard errors clustered at base DRG level are shown. *** p<0.01, ** p<0.05, * p<0.1

Figure 8: Second stage effect of DRG restructuring policy via price of stay on patent outcomes



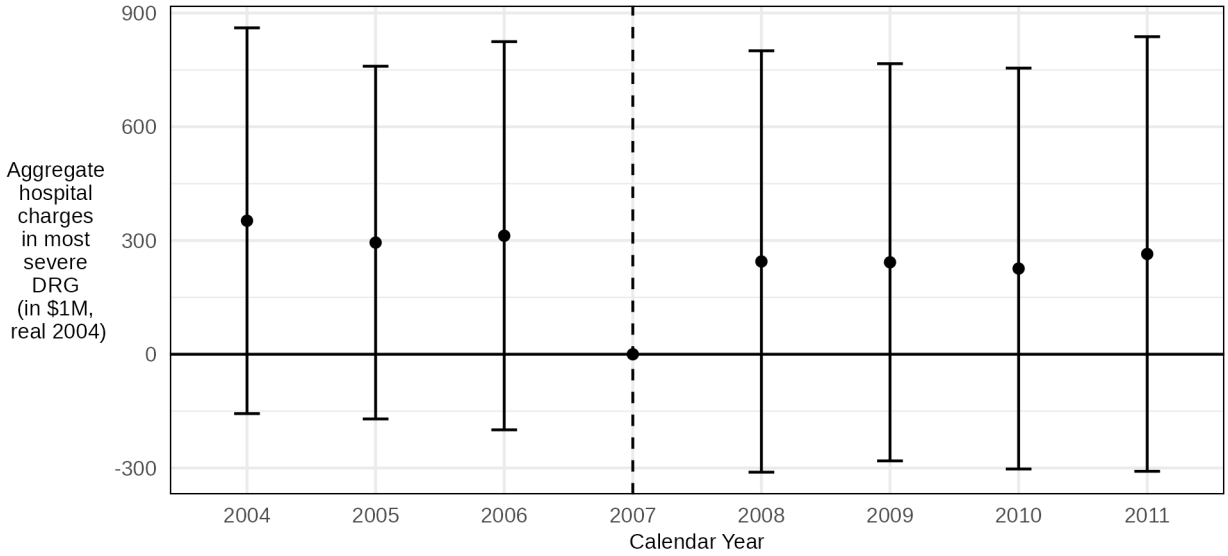
Note: Independent variable is the average hospital charges per stay in the most severe DRG instrumented by the weight of the most severe DRG in each base DRG. Dashed line indicates the reference year 2007 when the DRG restructuring policy was enacted. Data on hospital charges was taken from the Nationwide Inpatient Sample (NIS) dataset. Patents were attributed to each base DRG by mapping ICD codes to MeSH codes, and counts fractionalized to avoid double counting patents in multiple base DRGs. See section 3.3 for more details on the attribution process. All dollar amounts were inflation-adjusted to 2004. Base DRG and Year Fixed effects are included. 95% confidence intervals based on standard errors clustered at base DRG level are shown.

Table 6: Second Stage effect

	Dep: Fractional count of granted patents attributed to severe DRGs		
	(1)	(2)	(3)
Average hospital chargers per stay X 2008 (in real 2004, $1k)	0.471 **	-0.034	-0.012
	(0.195)	(0.153)	(0.021)
Average hospital chargers per stay X 2009 (in real 2004, $1k)	0.432 **	-0.098	-0.013
	(0.175)	(0.123)	(0.021)
Average hospital chargers per stay X 2010 (in real 2004, $1k)	0.487 **	-0.071	-0.022
	(0.202)	(0.148)	(0.017)
Average hospital chargers per stay X 2011 (in real 2004, $1k)	0.493 **	-0.094	-0.023
	(0.204)	(0.147)	(0.019)
Year FE		X	X
Base DRG FE			X
Observations	518	518	518
R2	-0.08	0.00	0.98
Outcome Mean (SDev)	37.9 (96.1)	37.9 (96.1)	37.9 (96.1)

Note: Independent variable is the average hospital charges per stay in the most severe DRG instrumented by the weight of the most severe DRG in each base DRG. Data on hospital charges was taken from the Nationwide Inpatient Sample (NIS) dataset. Patents were attributed to each base DRG by mapping ICD codes to MeSH codes, and counts fractionalized to avoid double counting patents in multiple base DRGs. See section 3.3 for more details on the attribution process. All dollar amounts were inflation-adjusted to 2004. Standard errors clustered at base DRG level are shown. *** p<0.01, ** p<0.05, * p<0.1

Figure 9: Effect of DRG restructuring policy on aggregate hospital charges



Note: Independent variable is the weight of the most severe DRG in each base DRG. Dashed line indicates the reference year 2007 when the DRG restructuring policy was enacted. Data on hospital charges was taken from the Nationwide Inpatient Sample (NIS) dataset. All dollar amounts were inflation-adjusted to 2004. Base DRG and Year Fixed effects are included. 95% confidence intervals based on standard errors clustered at base DRG level are shown.

Table 7: Effect on Aggregate hospital charges

	Dep: Aggregate hospital charges in most severe DRG (real 2004, $1M)		
	(1)	(2)	(3)
Weight of most severe DRG X 2008	-130.400	95.836	244.707
	(133.638)	(133.975)	(283.526)
Weight of most severe DRG X 2009	-78.024	79.193	242.604
	(117.451)	(130.965)	(267.252)
Weight of most severe DRG X 2010	-57.499	67.781	226.051
	(120.558)	(134.950)	(269.724)
Weight of most severe DRG X 2011	-70.996	92.429	264.455
	(128.685)	(155.805)	(292.411)
Year FE		X	X
Base DRG FE			X
Observations	518	518	518
R2	0.01	0.03	0.86
Outcome Mean (SDev)	2027.6 (2780.4)	2027.6 (2780.4)	2027.6 (2780.4)

Note: Independent variable is the weight of the most severe DRG in each base DRG. Data on hospital charges was taken from the Nationwide Inpatient Sample (NIS) dataset. All dollar amounts were inflation-adjusted to 2004. Standard errors clustered at base DRG level are shown. *** p<0.01, ** p<0.05, * p<0.1

Table 8: Robustness of effect to alternative operationalizations of patent outcomes

	Dep: Fractional count of granted patents attributed to severe DRGs containing...		
	...MeSH codes of antibiotic DRGs in claims or abstract or title only	...a chemical compound	...an antibiotic drug compound
Average hospital chargers per stay X 2008 (in real 2004, $1k)	-0.002	-0.011	-0.000
	(0.006)	(0.021)	(0.001)
Average hospital chargers per stay X 2009 (in real 2004, $1k)	-0.001	-0.019	-0.002
	(0.005)	(0.021)	(0.001)
Average hospital chargers per stay X 2010 (in real 2004, $1k)	0.001	-0.029	-0.001
	(0.004)	(0.022)	(0.002)
Average hospital chargers per stay X 2011 (in real 2004, $1k)	-0.001	-0.038	-0.002
	(0.003)	(0.029)	(0.005)
Year FE	X	X	X
Base DRG FE	X	X	X
Observations	518	518	518
R2	0.99	0.98	0.97
Outcome Mean (SDev)	6.5 (17.3)	39.9 (98.5)	2.6 (6.5)

Note: Independent variable is the average hospital charges per stay in the most severe DRG instrumented by the weight of the most severe DRG in each base DRG. Dashed line indicates the reference year 2007 when the DRG restructuring policy was enacted. Data on hospital charges was taken from the Nationwide Inpatient Sample (NIS) dataset. Patents were attributed to each base DRG by mapping ICD codes to MeSH codes, and counts fractionalized to avoid double counting patents in multiple base DRGs. See section 3.3 for more details on the attribution process. All dollar amounts were inflation-adjusted to 2004. Data on chemical compounds was taken from SureChEMBL. Data on antibiotic drug compounds was taken from AntibioticDB. Standard errors clustered at base DRG level are shown. *** $p<0.01$, ** $p<0.05$, * $p<0.1$

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