Antibacterial resistance and the cost of affecting demand: the case of UK antibiotics [†]

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Abstract

Consumption of broad-spectrum antibiotics is associated with rising antimicrobial resistance (AMR) levels. The use of broad-spectrum drugs, particularly of cephalosporins, quinolones, and co-amoxiclav contributes the most to the rise in AMR. We use aggregate sales data on antibiotics from the UK to estimate structural demand models and reveal drug substitution patterns. We then simulate alternative tax schemes to evaluate the effectiveness of shifting demand from broad- to narrow-spectrum drugs. Our estimates suggest that these policies can be highly effective in demand management and come at a relatively low cost regarding changes in consumer and producer surplus.

Key words: antimicrobial resistance, demand estimation, antibiotics, policy simulation, welfare change

JEL Classification: I11, I18, L11, L65

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1. Introduction

Since the accidental discovery of penicillin by Alexander Fleming in 1928 and the first widespread use of antibiotics in the 1940s, they remain today among the most essential class of drugs worldwide. However, resistance to antibiotics was also identified as early as the 1940s, and indeed the negative externality was recognized in Fleming's 1945 Nobel Prize speech.[1] For the 150 million annual prescriptions written in the early 1980s in the US, one estimate places the unaccounted costs due to resistance to be between $.35-$35 billion (Phelps, 1989). Significantly high costs and welfare losses have also been estimated for EU/UK, and 23K-25K annual deaths in the US and EU each are attributed to resistance (Elbasha, 2003, Smith et al., 2005, ETAG, 2006, ECDC/EMEA, 2009, CDC and Prevention, 2013). Today antimicrobial resistance (AMR) has become a global threat with an estimated 700K deaths worldwide annually and has prompted calls for a global response (WHO, 2001, CMO, 2013, O'Neill, 2016). Based on these concerns, the British government commissioned a review of AMR, which was tasked with identifying causes of rising drug resistance and proposing policy actions that can be taken internationally. The final report of the commission warns that if the problem goes unchecked, as many as 10 million lives a year, and as much as cumulatively $100 trillion in output worldwide would be at risk by 2050 (O'Neill, 2016). A key issue identified in this report, and relevant to this paper, is stewardship of demand management towards appropriate/optimal use.

Antibiotics can be classified as narrow- or broad-spectrum, where narrow-spectrum drugs work against a select group of bacteria and will not kill other microorganisms in the body and thus help in slowing AMR. However, they can only be prescribed when the causative organism is known. On the other hand, broad-spectrum antibiotics are prescribed more generally and when the causative organism is unknown, but they also exacerbate the AMR problem the most (Steinman et al., 2003b,a, Wood et al., 2007, Kaier and Moog, 2012, CMO, 2013).

[1] "*... Mr. X. has a sore throat. He buys some penicillin and gives himself, not enough to kill the streptococci but enough to educate them to resist penicillin. He then infects his wife. Mrs. X gets pneumonia and is treated with penicillin. As the streptococci are now resistant to penicillin the treatment fails. Mrs. X dies.*" Fleming, Nobel Lecture, December 11, 1945.

The O'Neill (2016) report makes several recommendations to tackle the rise of AMR. For instance, it recommends taxing pharmaceutical firms that manufacture these drugs. However, firms that invest in research and development (R&D) beneficial for controlling AMR can deduct their investments from the imposed tax. It also recommends demand management via testing for pathogens before prescribing, and where appropriate, using narrow-spectrum drugs. If there is a cost to finding which narrow-spectrum antibiotic is appropriate, broad-spectrum antibiotics will be overprescribed relative to the narrow-spectrum antibiotics and contribute to AMR. In the same vein, a cost-side intervention could tax broad-spectrum drugs as well as aim to reduce testing time and costs. This intervention could potentially help manage the demand for antibiotics by adjusting the relative pricing of these drugs and encouraging the use of narrow-spectrum agents.

In this paper, we test the feasibility of such cost-side interventions to affect demand. We focus on human use of antibiotics as it has been identified as the primary driver of antibiotic resistance in Adda (2020). Giubilini (2019) makes a case for antibiotic tax for human use for mild and self-limiting cases, and Ribers and Ullrich (2023) make a similar suggestion when evidencing the large heterogeneity in physicians' prescribing decisions for antibiotics. To that end, we use sales data from 2003 to 2013 from the UK and estimate demand via discrete choice models. We combine demand estimation with Nash-Bertrand pricing behavior and jointly estimate the supply-side equations where multi-product firms maximize their profits in an oligopolistic setting. We then simulate and compute the effect of various tax-based interventions where the tax is imposed on physician practices. Specifically, we inquire about the extent to which a tax on broad-spectrum antibiotics would shift the demand from broad- to narrow-spectrum antibiotics and the associated societal costs in terms of short-term reductions in consumer and producer surplus.

There is a large theoretical literature on the role of taxes in dealing with the high use of antibiotics as well as empirical studies focusing on the rise in prescriptions due to competitive pressures and/or financial incentives linked to physicians. We contribute to this literature by providing computation of counterfactual price equilibria within oligopoly markets under alternative taxes. This helps us evaluate the effects of different cost-saving measures in addressing the rising use of antibiotics and the problem of AMR.

We find that at the individual drug level, demand is elastic.[2] The share-weighted mean own-elasticity is −2.58 with a standard deviation of 1.61 and the unweighted mean is −3.73. The weighted mean cross-price elasticity is 0.10 with a standard deviation of 0.17 and the unweighted mean is 0.02 and a max of 4.08. In general, drugs within the same spectrum class are more easily substituted than those across different spectrum classes. A 1% increase in the price of a broad-spectrum drug leads to a 0.14% increase in demand for another broad-spectrum drug, while it only leads to a 0.08% increase in demand for a narrow-spectrum drug. Our estimates also suggest that there is significant heterogeneity in individual taste parameters for the associated spectrum of a drug and switching patients from broad- to narrow-spectrum would have implications on short-run consumer welfare over and above any price effects.

We estimate the effect of ad valorem and unit taxes for all and by sub-group of drugs. In the former case, we impose a 5 or 20% tax either on (i) all antibiotics, (ii) on all broad-spectrum antibiotics, or (iii) a subset of broad-spectrum drugs that have been identified in the public health literature as contributing the most to the AMR problem. These alternative taxes generate a range of effects on consumption. For instance, a 20% tax on all antibiotics reduces the overall antibiotics consumption by 12.71% while the consumption

[2]Two other papers also estimate demand for antibiotics and report elasticities, though those are for groups of drugs rather than for individual brands as in our case. In the context of how new drugs impact the calculations for a price index, Ellison et al. (1997) use sales data from the US for the cephalosporins which belong to the class of antibiotics, and estimate an AIDS demand model. They report group-wide elasticities by brand and generic groups, where each group itself consists of individual drugs aggregated across different manufacturers and alternative forms of the drug, but all within the same molecule. The own-elasticities range from −4.34 to +1.06. Alternatively, in the context of the impact of TRIPS on welfare, Chaudhuri et al. (2006) use data on quinolones, which too is a class of antibiotics, from India and also estimate AIDS demand by product groups. Their focus is on foreign versus domestic manufacturers and so they also provide group-wide elasticities by molecule and domestic and foreign status of manufacturers, where individual brands and forms are grouped to that level. Most of the own-price elasticities are lower than −2 but range from −5.94 to −0.08. While these estimates are at the group level, there are examples of estimates at the brand level as well, albeit not for antibiotics, which are more in line with our estimates. For instance, Duso et al. (2014) estimate nested logit models at the brand level for anti-diabetic drugs from Germany, and reports a range from −37.349 to −0.991 with a mean value of −6.65, while Björnerstedt and Verboven (2016) estimates nested-logit and random coefficients models using brand-level data from the Swedish analgesics market and report own-elasticities in the range of −15.45 to −5.16 for the nested logit and −6.5 to −1.99 from the random coefficients models.

of the latter sub-group of broad-spectrum drugs is reduced by 29.35%. By contrast, imposing a similar 20% tax on just the sub-group of broad-spectrum with the highest AMR contribution reduces the consumption for this group by 37.73% with an overall reduction of only 2.38% as most patients are switched to narrow-spectrum and other broad-spectrum antibiotics.

For the 20% tax, the yearly consumer welfare loss is £322 per 1,000 inhabitants if it is levied on all antibiotics. If the same tax is imposed on just the sub-group of antibiotics identified above, the loss in consumer surplus is £78.2 per 1,000 inhabitants. Multiplied by the average UK population of 61.8 million over the same period, this translates to £19.9m and £4.8m per year. We also compare the effectiveness of the ad valorem tax to flat unit tax on a sub-group of drugs where the unit tax is bench-marked to the estimated marginal cost differential between broad- and narrow-spectrum drugs. Here we find that the total welfare cost if such a tax is imposed on the sub-group of broad-spectrum drugs is £252.5 per 1,000 inhabitants, i.e., £15.6m in total per year, while the reduction in their quantity is 69.60%.

Our total welfare calculations account for the change in consumer surplus, firm profit, tax revenue, and additional testing costs. However, we do not account for any long-term benefits that accrue to consumers due to a reduction in AMR, which would further reduce long-term loss in consumer surplus. Thus our estimates should be interpreted as an upper bound on the total cost of such a supply-side intervention. Considering the societal cost of AMR, which includes 10 million lives lost annually and a cumulative $100 trillion in lost output by 2050 cited earlier, this may not be a high price to pay for reducing AMR. Thus, the cost-side intervention as suggested in O'Neill (2016) seems well worth it.

The rest of the paper is structured as follows. The next section describes how our paper is related to prior literature. The section following that describes the antibiotics UK market and the data. Section four outlines the model as well as discusses estimation issues. Section five has all the main results including the regression coefficients, substitution patterns, and simulations. The last section concludes.

2. Related Literature on AMR

There is a small but growing empirical literature in economics related to the use of antibiotics. In Denmark, which shares similarities with the UK health care system, Huang and Ullrich (2024) find that physicians' preferences play a substantial role in driving the use of second-line broad-spectrum antibiotics. A higher prescription rate is linked to physician age, while it is negatively associated with the availability of diagnostic tools and the staff size of clinics. Ribers and Ullrich (2023) provide further evidence that both the variation in diagnostic information and physicians' awareness of the social cost of increasing antibiotic resistance are associated with antibiotic overuse. This paper finds that improving diagnostic information is important to help avoid negative health consequences, but it also supports the motivation for an antibiotic tax. In the context of Taiwan health care, Bennett et al. (2015) find that antibiotic prescriptions increase with the level of competition among health providers, largely due to pressure from patients, but antibiotic prescriptions decreased when physician's cost of prescribing drugs increased due to a policy reform targeting antibiotic consumption. On the other hand, for a field experiment conducted in China, Currie et al. (2011) and Currie et al. (2014) find that misuse of antibiotics is not driven by pressure from patients, but rather by financial incentives linked to prescribing drugs. Similarly, others have investigated the link between appropriate antibiotic prescription and physician incentives. For instance, Ellegård et al. (2018) report that relative to broad-spectrum, the share of narrow-spectrum prescriptions increased significantly among children diagnosed with respiratory tract infection after physicians were exposed to pay-for-performance schemes tied to the use of narrow-spectrum antibiotics. Others have also reported positive results relating to pay-for-performance and more appropriate antibiotic prescriptions (Mullen et al., 2010, Yip et al., 2014, Gong et al., 2016).

By comparison to the above empirical literature, there is a much more substantial but mostly theoretical literature that discusses the role of taxes, subsidies, tradable permits, and optimal patent designs in addressing problems associated with AMR. Several studies highlight differences between optimal levels of antibiotic use chosen by a social planner versus those that may emerge in different settings, including, but not limited to, single versus multiple periods,

farm versus human use, choice of drugs within a hospital or community settings, global versus single country, competitiveness of the health care system, and when antibiotics may be renewable or a non-renewable resource (Tisdell, 1982, Brown and Layton, 1996, Laxminarayan and Brown, 2001, Rudholm, 2002, Laxminarayan and Weitzman, 2002, Herrmann and Gaudet, 2009, Herrmann and Nkuiya, 2017, Albert, 2021). For instance, since antibiotic use lowers the burden of treatable infections but also increases the resistance to antibiotics, Albert (2021) highlights the tradeoffs in incentives among fee-for-service healthcare providers among different market structures. Relative to a social planner, the providers over-prescribe in a competitive system and under-prescribe in a monopoly as they earn a profit on two margins due to an increased efficacy over the long run, but also by maintaining a higher infection rate in the population. He finds a Goldilocks zone in the oligopolistic markets and suggests subsidies at the low level of competition and a tax when the market is more competitive.

In parallel, others have considered the role of various instruments into account for the negative externality such as direct regulation, user charges, physician charges, and tradable permits when physicians are subject to defined drug budgets, as in the case of the UK (Coast et al., 1998, Smith and Coast, 1998, Smith et al., 2006, Herrmann and Nkuiya, 2017). For instance, Rudholm (2002) considers a Pigouvian tax to eliminate the departure of market equilibrium from the global optimal resource allocation problem, while in a simulation-based study to control resistance to anti-malaria treatments, Laxminarayan et al. (2006) study the impact of global subsidies for artemisinin-based combination therapy (ACT) over artemisinin monotherapy (AMT), and find that even a partial subsidy can have a significant impact on delaying the emergence of artemisinin resistance. There is a third strand of literature that highlights the role of markets and optimal patent designs to address problems associated with AMR. We do not review that here but refer the interested reader to Gallini (2017) for a review of that literature.

3. Background, Data, and the sample

3.1. **Background.** Antibiotics are prescription-only medicines in the UK, and about 74% are prescribed via general practitioners (GPs), followed by 18% use in hospitals (PHE, 2015). With some exceptions for certain groups, after a

physician issues a prescription, patients can have it filled at a pharmacy and pay a fixed co-pay, regardless of the drug's actual cost. The National Health System (NHS) will reimburse pharmacies based on a set tariff as long as the drug has been approved for reimbursement. Rules for setting the tariffs are different for branded versus generic/unbranded drugs. For the latter, NHS reimbursement is based on the weighted average of wholesale prices supplied by main generic manufacturers or wholesalers. For branded drugs, the UK does not directly control prices but instead regulates profit on sales of drugs dispensed to NHS-covered patients under its Pharmaceutical Price Regulation Scheme (PPRS), and the terms are updated roughly every five years. Generally, manufacturers can set the price of new drugs without pre-approval by the Department of Health (DH), but any increases over the years need to be justified and approved by the DH (see Habl et al., 2006).

Prior literature shows that GPs are aware of prices and that they may be sensitive to them. See for instance, NAO (2007), Scoggins et al. (2006), Carthy et al. (2000) for the case of the UK, and Hauschultz and Munk-Nielsen (2020) for a comparable healthcare system in Denmark. In the UK this is enforced by NHS's budgeting strategy which has been in place since April 1999 and aims to achieve cost savings and efficiency where the NHS sets an annual prescribing budget for each Primary Care Trust (PCT) at the beginning of a financial year (Jacobzone, 2000). PCTs in turn set individual prescribing budgets for each contracted GP in their group who are then responsible for keeping their prescription payment within the budget.[3] PCTs track GPs' spending and

[3]See for instance Majeed (2000), which is an editorial in BMJ, a journal widely read by practitioners, explaining the relationship between a GP's prescribing budget and that of the PCT. PCTs have since been replaced by Clinical Commissioning Groups (CCGs) but the prescribing budgets exist even now. See also the NHS's Business Services Authority webpage about Prescribing Budgets at https://www.nhsbsa.nhs.uk/sicbls-icbs-and-other-providers/organisation-and-prescriber-changes/prescribing-budgets which states, "CCGs are responsible for setting a prescribing budget against each GP practice within their organisation" (Last accessed Aug/20/2023). Similarly, the Vale of York's CCG states on its website, "Groups of GPs taking part in this work are asked to manage the prescribing budget in line with the York and Scarborough formulary, and by using cost-effective medicines and prescribing in line with local policies" (see https://www.valeofyorkccg.nhs.uk/gps-take-over-budgets-to-help-manage-scarce-resources/. (Last accessed Aug/20/2023.) On the other hand, the cost of pathology services is not integrated and could be covered by doctor's offices, laboratory services, or outpatient services in hospitals. Only if the phlebotomy is done in a primary care setting, the cost would fall on the provider (see p.28 DH, 2006).

report it to the NHS Prescription Services. Some PCTs also reward GPs who underspend their budget to achieve cost-saving goals (Ashworth et al., 2004). Thus, drug prices may affect the GPs' decision.

3.2. **Data Source.** Our data comes from the British Pharmaceutical Index (BPI) data series by IMS Health Inc, which provides monthly sales information for pharmacies in the UK between 2003 and 2013. It covers all antibiotic prescriptions from general practices and outpatient hospital use. Residual consumption in hospital inpatient use, dental practices, and other community settings are not included. A drug is defined as a unique combination of manufacturer, molecule, product name, and formulation, and we aggregate over different pack sizes and strengths so that drugs in different strengths/sizes are not counted as different products. A limitation of our data is that generic manufacturers are not separately identified in the IMS database. Thus, if multiple manufacturers are producing a drug by a non-proprietary name within the same molecule and formulation, and in the same anatomical therapeutic chemical (ATC) class, then they are lumped into one product. We also standardize quantity as daily defined dosage (DDD), which is an assumed maintenance dose per day for a specific molecule-route-of-administration combination used for its main indication among adults.[4] Prices are computed as sales divided by quantity in DDD units and revenues and prices are deflated using UK CPI and are reported in 2003 real terms.

We separate the sales into two main broad- and narrow-spectrum groups based on the classification of molecules given in PHE (2014), EARS (2015), or Madaras-Kelly et al. (2014, 2015). We further subdivide the broad-spectrum into two subgroups, henceforth labeled as broad-A and broad-B. The latter distinction is based on a Department of Health's AMR strategy document that highlights a subset of broad-spectrum drugs that should be targeted to reduce their consumption to less than the median number of scripts relative to the total number of antibiotic scripts per year (see DH, 2016, Annex E). Accordingly, we label these targeted classes, i.e., cephalosporins (antibiotics with molecules cefalexin and cefixime), quinolones (molecules ciprofloxacin, levofloxacin, and ofloxacin), and co-amoxiclav as broad-A to distinguish them

[4]Defined daily doses (DDD) adjustment is a measurement that allows for comparability of quantity across drugs and is maintained by the World Health Organization (WHO). Note also that our data is at ATC4 level, and that combined with molecule is effectively ATC5.

from all other broad-spectrum antibiotics, broad-B. Similarly, (PHE, 2015) states that broad-spectrum drugs are more likely to drive antibiotic resistance than narrow-spectrum antibiotics, but their list of broad-spectrum drugs just consists of what we refer to as the broad-A group.[5]

The total market for all antibiotics in our data is £160m per year and in real terms has decreased from £208.6m in 2004 to £126.7m in 2012. This drop is driven primarily by a decrease in average real prices, which declined from £0.65 to £0.29 per DDD over the same period. By contrast, sales by volume have increased over time, both in absolute units as well as per capita. For example, in 2012, approximately 60 million packs of antibiotics were dispensed, compared to 44.5 million packs in 2004. This is equivalent to 0.44 billion and 0.32 billion DDD units of active ingredients, respectively. This increase is only partially explained by the rise in the UK population from 60m to 64m over this period as the average DDD unit of antibiotic consumption per resident per year also increased from 5.36 to 6.94 between 2004 and 2012.

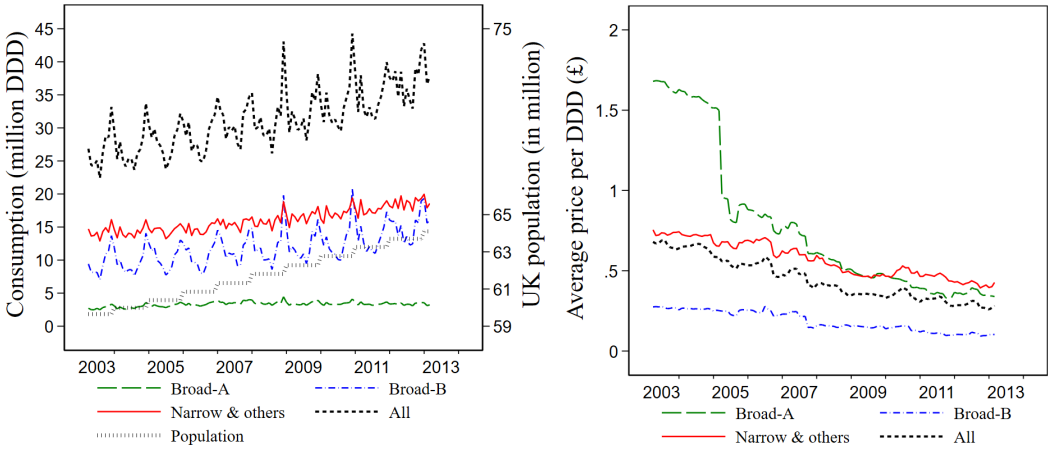


FIGURE 1. Antibiotic consumption and average prices in the UK

Sales by volume and prices per DDD are given in Figure 1. Two things stand out. First, the largest drop in prices was for broad-A drugs and came about in 2004 at the time of the new PPRS scheme and yet we do not see a corresponding increase in the quantity at that time. Second, antibiotic consumption

[5]Table 0.2 in PHE (2015) defines broad-spectrum antibiotics as (i) penicillins and enzyme inhibitors, which are co-amoxiclavs, (ii) cephalosporins, (iii) quinolones and (iv) carbapenems. Of these, carbapenems is a parenteral drug and we do not include it in our analysis since we restrict the analysis to eternal drugs.

fluctuates seasonally, with peaks in winter and dips in summer. The seasonality is predominantly influenced by the consumption of broad-spectrum antibiotics, particularly penicillins, and macrolides. This pattern is likely attributed to the increase in respiratory tract infections and virus-induced secondary bacterial infections during colder seasons (Suda et al., 2014, Hendaus et al., 2015). Figure A-1 in Appendix A plots the average relative shares of broad- vs narrow-spectrum drugs by month and shows that relative shares of the broad-spectrum also increase in the winter months.

TABLE 1. Relative shares and average prices by molecule

	ATC J01	Spectrum	DDD (g/d)	# Drug	2004 Share (%)	2004 Price (£)	2008 Share (%)	2008 Price (£)	2012 Share (%)	2012 Price (£)
Broad-spectrum					58.57	0.56	60.12	0.25	59.07	0.15
Broad-A					13.46	1.58	13.77	0.56	10.88	0.36
Co-amoxiclav	C	29.50	1.0	11	5.59	1.66	6.25	0.69	6.41	0.38
Cefalexin	D	19.25	2.0	15	4.03	0.69	3.73	0.46	1.80	0.29
Cefixime	D	19.50	0.4	2	0.06	3.64	0.04	3.07	0.02	2.34
Ciprofloxacin	G	39.75	1.0	5	3.20	2.39	3.34	0.30	2.36	0.24
Levofloxacin	G	39.75	0.5	2	0.20	2.78	0.16	2.11	0.07	1.46
Ofloxacin	G	39.75	0.4	3	0.38	1.98	0.26	0.90	0.22	1.20
Broad-B					45.11	0.26	46.35	0.16	48.19	0.10
Doxycycline	A	38.75	0.1	7	8.75	0.30	9.45	0.11	12.26	0.07
Tetracycline	A	38.75	1.0	1	0.78	0.14	0.58	1.12	0.33	0.99
Amoxicillin	C	13.50	1.0	13	35.55	0.26	36.3	0.15	35.55	0.10
Pivmecillinam	H	19.50	0.6	1	0.02	1.31	0.02	1.07	0.05	0.83
Neomycin	K	19.50	1.0	1	0.02	0.22				
Narrow-spectrum					41.43	0.70	39.88	0.53	40.93	0.42
Trimethoprim	E	4.25	0.4	5	8.78	0.12	8.08	0.08	7.52	0.10
Azithromycin	F	12.25	0.3	10	0.49	2.62	1.00	1.98	1.84	1.18
Clarithromycin	F	12.25	0.5	10	4.23	1.61	5.65	0.63	9.50	0.34
Clindamycin	F	10.75	1.2	3	0.16	4.4	0.2	8.22	0.21	2.01
Erythromycin	F	12.25	1.0	22	14.85	0.58	12.36	0.42	8.64	0.27
Flucloxacillin	H	4.25	2.0	8	7.45	0.96	7.52	0.72	8.38	0.62
Penicillin V	H	13.50	2.0	12	5.47	0.56	5.08	0.53	4.84	0.58
Combined Inside (18)					39.66	0.62	46.56	0.36	53.76	0.26

Shares are relative to the total quantity (in DDD) of all the 1st/2nd line molecules (inside option). Prices are weighted averages per DDD. "Combined Inside" refers to the share of these drugs relative to the potential size of the market. Penicillin V has the same spectrum score as amoxicillin but is typically classified as a narrow-spectrum antibiotic.

3.3. **Sample.** Enteral/oral drugs cover over 90% of the market in value, consisting of 44 different molecules. Parenteral antibiotics, i.e., those injected or infused, are used in more limited and serious situations. Of the oral drugs, Public Health England (PHE, 2014) recommends 18 different molecules as first- and second-line drugs to treat common primary community-acquired diseases, while others are to be used more sparingly. Table A-1 in Appendix A gives a mapping between these 18 molecules included in our analysis and if they are first- or second-line treatments for specific primary indications such as Urinary Tract Infection (UTI), Gastro-Intestinal Tract Infection (GITI), etc. Hence, we model the demand for oral drugs that contain these 18 molecules as the main active substances. The remaining 26 molecules, approximately 10% of the potential market, are included in the outside option in our econometric specification. The final data set consists of 11,417 observations of sales of 131 distinct products over 120 months and spanning across 18 molecules and 14 different formulations such as tablets, capsules, etc. Overall, the number of products reduced slightly over the years.

Relative shares and average prices of antibiotic molecules are summarized in Table 1. The top-selling broad-spectrum antibiotic is amoxicillin, whose shares stayed stable at around 36% over the years while that of co-amoxiclav and doxycycline increased slightly over time. Other broad-spectrum drugs listed in the table lost market shares. There was also a movement of relative shares within the narrow-spectrum drugs. For instance, erythromycin-based products lost shares at the expense of clarithromycin. Remarkably, however, the broad- to narrow-spectrum molecule share stayed relatively constant at 60/40 while the relative prices changed significantly. Specifically, the ratio of the average price of narrow- to broad-spectrum increased from 1.25 (= .70/.56) in 2004 to 2.80 (= .42/.15) in 2012. Overall, average prices declined from 0.62/DDD in 2004 to 0.26/DDD as shown in the last row of the table, while the total quantity consumed increased: the last row also shows the share of all drugs for these 18 molecules relative to the potential size of the market, which we will describe later, increased from 39.7% to 53.8%. Further, Table 1 also lists the ATC3 class of the molecule, the spectrum score of a drug, the conversion factor between grams and DDD, and importantly, the number of individual drugs by molecule. This additional information is used for both, informing

our empirical specification, as well as for interpreting some of the results that follow.

4. Empirical Specification

In this section, we first briefly describe our demand and supply-side equations, and then focus on issues related to identification and estimation.

4.1. **Demand.** We consider $t = 1, \ldots, T$ markets, each having a mass M_t of patients that have contracted a bacterial infection in the period. In our model, the decision-maker is a physician and patient hybrid who cares about the patient's well-being and is sensitive to drug prices, but not to the price of a test as that may not fall on the physician's budget.[6] While there is no direct financial cost of the test on either the patient or the physician, there may be some disutility with prescribing the test. To that end, we introduce a random coefficient for the spectrum variable to capture the inherent variability in disutility around the mean spectrum value. This modeling framework recognizes the possibility that certain consumers may experience disutility associated with the test. The decision-maker i faces the choice of $j = 1, \ldots, J_t+1$ drugs belonging to G_t groups of antibiotics, where the groups are defined at the third level of ATC (ATC3 hereafter) and the $+1$ denotes the outside option of no antibiotic treatment.[7] Thus the decision-maker i in market t gets indirect utility u_{ijt} from choosing drug j given by

$$u_{ijt} = x_{jt}\beta_i + \xi_{jt} + \zeta_{igt} + (1-\rho)\epsilon_{ijt}. \tag{1}$$

In the equation above, x_{jt} is a $(1 \times k)$ vector of observed drug characteristics, including price, count of pack varieties, and product dummies. Some drug characteristics are invariant over markets. For instance, formulation, branded/generic type, age of the molecule, or spectrum value, and hence they are selectively included in the non-linear part of the specification via the random coefficients which are described shortly. This vector also includes the mean temperature during the month, monthly dummies for seasonality, and a linear time trend. In some specifications, we use annual dummies instead of a

[6] A typical patient pays a flat co-pay for a prescription but the cost of the drug falls on GP practice and hence they would be sensitive to its price as discussed earlier in Section 3.

[7] The third level of ATC classification corresponds to pharmacological similarities and groups the 18 molecules in our data into eight nests.

linear time trend. The scalar error term ξ_{jt} captures the drug characteristics that are unobserved by the econometrician, such as the availability of the drug in the local dispensary, the knowledge of the physician about the effectiveness of the drug to treat the infection, localized detailing to the physician about the specific brand, etc. The term ζ_{igt} is common to all the drugs that are part of the same nest (ATC3 group) in the market and is a random variable with a probability distribution function that depends on the within-group correlation parameter ρ, with $0 \leq \rho < 1$. The idiosyncratic error term ϵ_{ijt} is assumed to be identically and independently distributed extreme value, and so is the composite term $\zeta_{igt} + (1-\rho)\epsilon_{ijt}$ (see Cardell, 1997).

The β_i are vectors of $k \times 1$ random coefficients and can be expressed as the sum of means, β, and dispersion around these means. These dispersions are represented by $k \times 1$ unobservable random variables of individual heterogeneity v_i, drawn from a multivariate standard normal, and so $\beta_i = \beta + \Sigma v_i$ will be a vector sampled from a multivariate normal distribution. The matrix Σ has a vector of standard deviations σ along its diagonal and takes a value zero outside of the diagonal. In our empirical analysis, the vector of standard deviations sigma will be allowed to differ from zero only for the constant, the price, the number of packages, and the spectrum, i.e., we will account for four random coefficients that enter the non-linear part of the model.[8]

[8]Since physician budgets are fixed, there is a potential concern that physicians' prescribing may change over the year as the budget constraint may start to bind. Specifically, budgets are annual and more likely to bind near the end of the financial year, GPs may start switching to cheaper drugs at that time. For instance, our data shows that broad-spectrum drugs are on average cheaper than narrow-spectrum drugs, and this in turn could create seasonality in the relative shares of broad- vs. narrow-spectrum drugs. First, to check if this is a major issue in the data, in Figure A-1 we plot the relative shares by month which are averaged over all the years in the data. While there is a clear pattern of seasonality, the peak in the broad-spectrum shares does not coincide with the end of the NHS fiscal year which is 31st March for years of our data. The peak is in fact in the winter months. Second, such a seasonality in relative shares could also arise due to the seasonal nature of underlying health issues if certain diseases are more likely in some seasons than others and require specific types of antibiotics. Thus, even if we were to include seasonal dummies, a variable for the spectrum value of a drug, and their interactions in the demand model, the dynamic aspect of GP's annually binding budget and its impact on demand and hence on the substitution patterns would remain unidentified. Thus, to be parsimonious we do not include these additional interaction terms but note that a random coefficient for prices in the model could alleviate this concern, if it exists, to some extent.

Equation (1) and $\beta_i = \beta + \Sigma v_i$ characterize the random coefficients nested logit (RCNL) model described by Verboven and Grigolon (2014). The decision-maker of the patient i in market t chooses the product j that gives the highest utility. In the case of the RCNL model, the conditional probability of that choice is,

$$\phi_{ijt}(x_t, \xi_t, v_i, \theta_1) = \frac{\exp\left(\left(x_{jt}\beta_i + \xi_{jt}\right)/\left(1-\rho\right)\right)}{\exp\left(I_{igt}/\left(1-\rho\right)\right)} \frac{\exp\left(I_{igt}\right)}{\exp\left(I_{it}\right)}, \tag{2}$$

where $\theta_1 = \{\beta, \sigma, \rho\}$. McFadden's (1980) inclusive values I_{igt} and I_{it} used in equation (2) are the natural log sums:

$$\begin{aligned} I_{igt} &= (1-\rho) \ln \sum_{l=1}^{J_{gt}} \exp\left(\left(x_{lt}\beta_i + \xi_{lt}\right)/\left(1-\rho\right)\right), \\ I_{it} &= \ln\left(1 + \sum_{g=1}^{G_t} \exp\left(I_{igt}\right)\right). \end{aligned} \tag{3}$$

The market share of the drug j in market t, s_{jt}, can be obtained by integrating equation (2) with respect to the distribution of the vector of random variables v_i, whose solution can be approximated by Monte Carlo simulations (see Nevo, 2001, Berry et al., 1995) with the adjustment for the nested structure explained in Verboven and Grigolon (2014).

One could also potentially use the UK income distribution and interact it with the price coefficient to better understand the distributional implication of the tax policies we later analyze in the counterfactual exercises. For instance, one could proceed as in Nevo (2001) if we had data at sub-national markets and we took income distribution drawn from different geographic markets to get better identification. Unfortunately, our data is at the national level and hence that is not possible. Alternatively, one could proceed as in Berry et al. (1995), i.e., take a single draw of income from the national market. However, all individuals pay the same co-pay regardless of income (with some exceptions) and it is the GP practices drug budgets that are more relevant. These budgets are (1) not financed by local council taxes in the UK but rather at the national level and hence are not based on local incomes but rather on catchment and population size and (2) not easy to track down by local areas even if we had the data at the sub-national level. Thus we do not pursue the distributional effects in this paper.

4.2. **Supply Side.** Drugs are assumed to have asymmetric constant marginal cost c_{jt}. Each firm $f = 1, \cdots, F$ controls the set of prices (p_{ft}) that maximizes its profit, given the prices of all drugs produced by the other firms p_{-ft}. Thus, the firm maximizes

$$\max_{p_{ft}} \Pi_{ft}\left(p_{ft}, p_{-ft}\right) = \max_{p_{ft}} \sum_{l \in \mathcal{J}_{ft}} \left(p_{lt} - c_{lt}\right) q_{lt}\left(p_t\right), \tag{4}$$

where $\mathcal{J}_{ft}$ is the set of products produced by firm f in market t. Since the total unit sales can be expressed as $q_{jt} = s_{jt} M_t$, we can derive the first-order conditions in each market t, leading to a system of J_t equations per market as

$$p_t = c_t + \underbrace{\Delta_t^{-1} s_t}_{m_t}, \tag{5}$$

where m_t is the vector of mark-ups and Δ_t is the Jacobian matrix whose element j, k equals to $-\partial s_{kt}/\partial p_{jt}$ if j and k belong to the same firm and zero otherwise.

We rewrite the pricing equation (5) in econometric form and it is estimated jointly with the system of demand functions obtained by numerically deriving the market shares (s_{jt}) from equation (2) as

$$\ln(p_{jt} - \underbrace{\Delta_{jt}^{-1} s_{jt}}_{m_{jt}}) = \ln(c_{jt}) \equiv w_{jt}\gamma + \omega_{jt}. \tag{6}$$

In the equation above, ω_{jt} is the error term, γ is the vector of coefficients and w_{jt} is the vector of observable product characteristics.[9] These include the number of packages, a dummy for generic drug production, and formulation dummies for liquid and capsule formulation where the baseline is tablets. We include these variables in the cost side because, for instance, drugs with a higher pack variety may have different unit marketing costs. We also include in

[9]Equation (6) is in log form but since marginal costs can be negative when markup is greater than price, we used the transformation $\ln(1+p-m) = \ln(1+c)$ so as not to lose these observations. In our case, since the DDD prices in this market are often significantly below one pound, it is common to encounter small values of $(p-m)$ so that $1+p-m$ is positive and we can take the logs. This transformation does not cause a problem as $\ln(1+p-m) \approx (p-m)$ for small values of $(p-m)$ as in our case. Note that negative marginal costs are still possible. In the econometric script, we address instances of negative marginal costs by applying a slight penalty to the GMM function. This precaution ensures that the parameters steer clear of excessive occurrences of negative marginal costs, which would not be theoretically justifiable.

w_{jt} other cost shifters such as the price of diesel as it may affect transportation costs, the exchange rate to account for the cost of imported material, as well as a time trend.

4.3. **Potential market and outside good.** We rely on the WHO's report on antibiotic consumption in the Europe region to define the potential antibiotic market for the UK (WHO, 2018). The report suggests that the median consumption of antibiotics was 17.9 DDD per 1000 inhabitants per day in 2015, ranging from 7.7 DDD to 38.2 DDD. Most European countries had antibiotic consumption of less than 30 DDD per 1000 inhabitants per day, and the UK's antibiotic consumption was around 20 DDD. Based on this, we define the potential UK market as 30 DDD per 1000 inhabitants per day, which is roughly twice the EU median and 1.5 times the UK antibiotic consumption in 2015. Therefore, the total potential UK market in our model is 30 DDD $\times$ 30 days (in a month) $\times$ UK population in thousands in a given year. Accordingly, the share of each product is relative to this potential market, so $s_{jt} = q_{jt}/M_t$, and the share of the outside good is then $s_{0t} = 1 - \sum_j s_{jt}$, where q_{jt} is the quantity of drug j measured in DDD units. We provide robustness checks around this measure of the potential market.

4.4. **Descriptive Statistics.** Table 2 provides summary statistics of all the relevant variables used in the model. The mean share of a drug is 0.48% but varies from almost 0% to 26%. The mean price is £1.16 per DDD, also with significant variation. The outside option varies from 32% to 67% with a mean value of 54%. The dependent variable has a mean of -7.13 and that of the logarithm of within-nest market shares is -4.92. Pack variety ranges from 1 to 10 with a mean of 2.68, and the mean spectrum score is 18.3 with a minimum of 4.25 and a maximum value of 39.75. Note that the spectrum does not vary by individual drugs but rather by molecules. The majority of observations, around 57%, are on generics. The mean age of a molecule, computed as the difference between 2003 and the earliest launch year of the molecule anywhere in the world, is 39.58 years. About one-third of the sample consists of drugs in liquid form while 66% are tablets or capsules.

Descriptive statistics for market-level variables, such as time and temperature and number of products per market are also given in Table 2, along with cost side shifters. We omit descriptive statistics for monthly or annual dummies.

Due to entry and exit, there is significant variation in the number of drugs in a market. Accordingly, we categorize the markets as high, medium, and low based on the 25th and 75th percentile values of the total number of products in a market. The mean values of these dummy variables are 0.31, 0.42, and 0.27 respectively, and are labeled as labeled as x_{10t}, x_{11t} and x_{12t} in the table. We discuss them further in the context of identification in the next subsection.

TABLE 2. Summary statistics and between and within variation of variables.

Variable	Description	Mean	sd_O^2	sd_B^2	sd_W^2	Min	Max
s_{jt}	Share of drug j (%)	0.48	1.67	0.08	1.66	0.00†	25.7
s_{0t}	Share of outside option (%)	54.0	6.95	7.01	0	31.80	67.0
	Endogenous variables						
$\ln(s_{jt}/s_{0t})$	Dependent variable	-7.13	2.47	2.35	1.10	-17.2	-0.21
$\ln(s_{(j\in g)t})$	Within nest ln(share)	-4.92	2.55	2.50	1.09	-16.2	0.00
p_{jt}	Price (in £) per DDD	1.16	1.23	0.99	0.62	0.04	11.5
	Demand shifters						
x_{1jt}	Spectrum-score / 10	1.83	1.07	1.04	0	0.43	3.98
x_{2jt}	Pack varieties	2.68	1.72	1.50	0.65	1	10
x_{3jt}	Dummy: generics	0.57	0.50	0.50	0	0	1
x_{4jt}	Dummy: tablet	0.43	0.50	0.50	0	0	1
x_{5jt}	Dummy: capsule	0.23	0.42	0.42	0	0	1
x_{6jt}	Dummy: oral liquid	0.34	0.47	0.47	0	0	1
x_{7jt}	Age of molecule / 10	3.96	1.22	1.22	0	1.5	5.8
x_{8jt}	Temperature	10.2	4.59	0.63	4.58	-0.27	19.3
x_{9jt}	Time trend / 10	5.97	3.42	2.20	3.14	0.1	12
x_{10t}	Dummy: high #drugs	0.31	0.46	0.11	0.46	0	1
x_{11t}	Dummy: medium #drugs	0.42	0.49	0.16	0.48	0	1
x_{12t}	Dummy: low #drugs	0.27	0.45	0.19	0.43	0	1
	Cost shifters						
z_{1t}	Price of diesel (log)	0.56	0.15	0.09	0.14	0.34	0.81
z_{2t}	Exchange rate (log)	1.58	0.39	1.17	1.96	2.69	10.3
z_{3jt}	#other drugs by the same firm	4.06	5.55	5.31	0.96	0	19
z_{4jt}	#other drugs by the same firm & within the same nest	1.35	1.29	1.25	0.40	0	5
z_{5jt}	#packs over other products by the same firm and in the same nest	3.54	3.67	3.54	1.22	0	17
z_{6jt}	#packs by competitors in the same nest as reference drug	45.3	23.2	23.0	4.68	0	92

Total 11,417 obs of 131 distinct products over 120 months spanning 18 molecules and 14 formulations. †The minimum is small but not zero.

4.5. **Identification.** The mean price coefficient can be identified via the exogenous cost shifters on the supply side. However, these are not sufficient to identify other coefficients. The random coefficients, with no observable individual demographics, can be identified with repeated cross-sections if there is sufficient variation in product characteristics or in the number of products over markets (Ackerberg and Rysman, 2005).

Table 2 shows variations in drug characteristics between and within drugs, i.e. cross-sectionally across drugs as well as over time. For example, the number of packs has an overall sample variance of 1.72, which is the result of both between and within dispersion, 1.50 and 0.65, respectively. Most of the drug characteristics vary more across drugs than over time. However, the exchange rate, the price of diesel, and the mean monthly UK temperature only vary over time.[10] The dummy variable generic, the variable spectrum, and the dummies of the formulation are time-invariant, and therefore, the between variation is merely driven by the entry and exit of drugs.

Table 3 shows the variation in the number of drugs due to entry and exit over time. Among the 131 drugs identified in the data, an average market has 95 of them, while an average drug is found in 87 out of 120 markets. There are instances of drugs that are available in a much lower number of markets. For example, one drug is observed in only five markets. These changes in the number of products produce variations in the prices and the number of pack varieties which are essential to identifying their coefficients in our analysis. However, Ackerberg and Rysman (2005) demonstrate that variations in the number of products can result in inaccurate price elasticities. This issue arises from the presence of symmetric unobserved product differentiation (SUPD) in logit errors. Logit models inherently assume that the introduction of an additional product merely contributes one dimension to the SUPD space with minimal congestion effects. Consequently, the price coefficient may be identified through changes in the number of products, even when prices remain consistent. This susceptibility of SUPD can potentially lead to unreliable substitution patterns. In response to this critique, the authors recommend an

[10]The exchange rate is a weighted average of rates between the UK and the top five countries/regions from where the UK imports antibiotics or APIs for antibiotics. These are China, India, Singapore, the US, and the EU, and the weights are based on import shares of antibiotics.

approach that involves incorporating additional functions to address the influence of the number of products in the market to mitigate the problem. Thus we adopt their proposed solution by categorizing the number of products into three distinct groups: 'small', 'medium', and 'large' which vary over time.

TABLE 3. Entry and exit of drugs

Variable	Obs	Mean	Std. Dev.	Min	Max
Number of drugs in a market	120	95.14	4.17	88	104
Number of markets a drug is on sale	131	87.15	37.82	5	120

Additionally, the ρ coefficient in the nested logit versions also needs to be identified. If patients switch drugs within the same ATC3 class across markets, their behaviour can produce changes in within nest market shares. Variation in the within nest share ($\ln s_{(j\in g)t}$) can allow for the identification of this parameter. However, this may be correlated with the error term as patients may choose to switch drugs within an ATC3 class in response to shocks on unobserved drug characteristics. When an unobserved drug characteristic such as quality is high, the market share of that drug is high, but so is the within-nest market share. The switchers can either be patients from the same ATC3 class or from other ATC3 classes. Thus, the within nest share needs to be instrumented for which we use variation in the number of drugs and packs by the reference firm or competitors within the nest.

The random coefficients models use the nonlinear method of moments estimator which requires orthogonality conditions between the observed drug characteristics and the demand error term. Berry et al. (1995) suggest using the sum of product characteristics of other products of the same firm, and the sum of product characteristics of products of other firms to generate additional instruments. Björnerstedt and Verboven (2016) suggest adding the count of other products of the same firm, and the count of products of other firms as instruments as they capture the intensity of competition. Further, they also suggest generating additional instruments by nests. We construct our additional instruments following the same procedure. For a given drug j by firm f in nest g we count the number of other drugs by the same firm, z_{3jt}, and the number of other drugs by the same firm within the same nest, z_{4jt}. Similarly, we also count the number of packs by the reference firm over other drugs within the nest, z_{5jt}, as well as the number of packs by all competitors within

the same nest, z_{6jt}. In some models, we also included the squared terms or interactions of these additional variables. Further details on the construction of the instruments and their interactions are described in Section A.3.

Finally, following Reynaert and Verboven (2014), we generate and use optimal instruments for estimation. Briefly, Reynaert and Verboven (2014) show through Monte Carlo simulations that the optimal instruments are more efficient than other instruments and that they are also helpful in attenuating bias when there is limited product characteristic variation across markets. To that end, we follow Chamberlain (1987) and construct optimal instruments that are the expected value of the gradient of the structural error term (the product-specific unobservable) for the parameter vector. In the case of linear parameters and exogenous regressors, the gradient would be (minus) the covariates. In the case of nonlinear parameters, the optimal instruments are nonlinear predicted variables. In the presence of multiproduct firms and differentiated products, the joint estimation of demand and supply of the nonlinear (predicted) prices can be approximated by regressing the prices on a polynomial of demand and cost shifters and possibly BLP-type instruments. A similar logic applies to the supply-side error, with the markup variable replacing the price variable. For further details on the GMM estimator and the use of optimal instruments in our context, see Appendix D.

5. Results

5.1. **Regression Coefficients.** Table 4 provides selected regression coefficients from alternative demand models, i.e., simple logit as OLS and 2SLS/IV followed by a joint estimation of the demand and the supply-side moment conditions in equation (6). We then estimate the nested logit model (Nlogit) and then our final preferred specification as the random coefficients nested logit (RCNL) model. All except the first two specifications are jointly estimated with the supply-side and the RCNL additionally employs optimal instruments as described earlier. The 2SLS/IV and the joint estimation with equation (6) for the simple logit case are used to gauge the model's incremental improvement attributed to the use of price instruments and the efficiency gains derived from supply-side moments. Appendix B provides additional estimates

from the random coefficients logit model, as well as the coefficients of the associated supply-side equation when we use joint estimation (see Table B-1 and Table B-2 respectively).

Starting first with the OLS estimation of the simple logit in column (1), the price coefficient is positive and not statistically significant.[11] When we re-estimate the model using instrumental variables via simple two-stage least squares, the price coefficient becomes negative -0.872 and is significant at the 1% level (see column (2)). The first-stage regression is in column (3) and shows that the four excluded instruments are individually significant and the joint F-test for the excluded instruments is 11.17 indicating that the instruments are not collectively weak. Nonetheless, the demand is in the inelastic region for most of the sample and the implied marginal costs are negative for about 66% of the observations. Column (4) provides estimates from the joint estimation with the supply side. The price coefficient is negative -7.069 and significant. The average price-cost margin for the joint estimation is 0.235 with only 3.83% of the sample obtaining negative marginal costs, showing further improvement in the estimates. Other coefficients of interest indicate that demand increases with pack variety, is not statistically significant for generics and that the coefficient on the spectrum is positive but not statistically significant.

Column (5) shows the impact of adding a nesting structure to the model. The coefficient on price decreases to -4.838 but the nesting coefficient ρ on $\ln(s_{ig})$ is 0.348 and is significantly different from zero and one, suggesting that drugs in the same nests (ATC3 classes) are more similar than drugs in other groups. The coefficient on the spectrum also becomes negative and significant though the number of observations with negative marginal costs increases to 5%. Finally, Columns (6) and (7) provide estimates from RCNL that overcome the restrictive substitution patterns imposed due to the independence of irrelevant alternatives (IIA) property for the simple logit models. The nesting coefficient ρ increases to 0.456 and is again significantly different from zero and one. Further, only 1.85% of the observations have a negative implied

[11] Note that all the regressions include product dummies and hence time-invariant product characteristics like age of molecule or formulation, etc. drop out of the regressions. We retrieve the coefficients for these product characteristics using Chamberlain's GLS regression of product dummies on fixed product characteristics. See Section D.3 for details or refer to Nevo (2000).

TABLE 4. Demand estimation

	Logit				**NLogit**	**RCNL**	
	OLS	IV/2SLS		IV-Joint	IV-Joint	IV-Joint	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
	β	β	1st-stage	β	β	β	σ
‡Constant	-4.654^a	-2.786^a	1.372^a	-2.786^b	0.113	0.240	0.111
	(1.099)	(1.073)	(0.094)	(1.132)	(0.591)	(0.733)	(0.528)
Price	0.015	-0.872^a		-7.069^a	-4.838^a	-8.241^a	4.168^a
	(0.016)	(0.309)		(0.278)	(0.234)	(0.053)	(0.071)
$\ln(s_{(j\in g)})$					0.348^a	0.456^a	
					(0.066)	(0.021)	
‡Spectrum	0.161	0.257^b		0.26	-0.242^a	-0.017	0.150^b
	(0.119)	(0.123)		(0.185)	(0.083)	(0.155)	(0.062)
Pack	0.542^a	0.530^a	-0.009	0.464^a	0.287^a	0.379^a	0.131^a
	(0.025)	(0.025)	(0.008)	(0.012)	(0.036)	(0.027)	(0.03)
‡Age	0.169	0.072		0.07	0.010	-0.082	
	(0.130)	(0.125)		(0.153)	(0.066)	(0.059)	
‡Generic	1.240^a	0.120		0.120	-0.034	-0.077	
	(0.296)	(0.306)		(0.329)	(0.157)	(0.166)	
‡Capsule	0.291	-0.171		-0.171	0.184	0.046	
	(0.395)	(0.395)		(0.373)	(0.175)	(0.194)	
‡Liquid	-0.684^b	-0.388		-0.388	-0.036	0.133	
	(0.300)	(0.314)		(0.353)	(0.163)	(0.163)	
Temperature	-0.000	0.001	0.001	0.007	0.008	-0.002	
	(0.009)	(0.010)	(0.005)	(0.008)	(0.008)	(0.008)	
Time	-0.013^b	-0.067^a	-0.089^a	-0.451^a	-0.307^a	-0.317^a	
	(0.005)	(0.020)	(0.009)	(0.018)	(0.017)	(0.008)	
Med #drugs	-0.012	-0.034	-0.016	-0.041^c	-0.082^a	0.02	
	(0.025)	(0.028)	(0.014)	(0.022)	(0.021)	(0.022)	
Low #drugs	0.161^a	0.184^a	0.027	0.586^a	0.300^a	0.419^a	
	(0.032)	(0.039)	(0.023)	(0.033)	(0.033)	(0.033)	
z_1:Price of diesel (log)			0.537^a				
			(0.166)				
z_2: Exchange rate (log)			0.051				
			(0.053)				
z_3 #drugs by firm j			0.045^a				
			(0.008)				
z_4 #packs by firm j in nest g			-0.023^a				
			(0.006)				
pseudo-Rsq	0.828	0.783	0.771	0.179	0.357	0.993	
avg $(p-c)/p$		0.598		0.235	0.228	0.315	
% mc<0		66.48		3.83	4.99	1.85	
F-stat			11.17				

Total 11,417 obs of 131 distinct products over 120 months spanning 18 molecules and 14 formulations (with three main characteristics, tablet, capsule, and oral liquid). All regressions include product dummies and monthly dummies. Robust standard errors are in parentheses. Superscripts (a), (b), and (c) imply significance at 1, 5 or 10% respectively.‡The mean β coefficients are retrieved from the minimum distance method as product dummies are included.

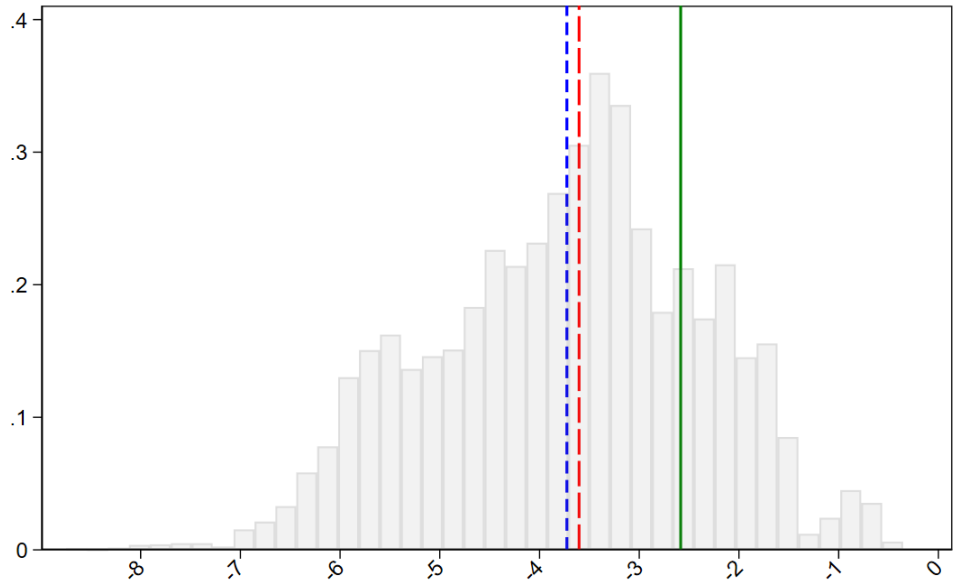
marginal cost and the average price-cost margin for the remaining sample is 0.315. The mean coefficient on price is -8.241 and significantly different from zero, while the distribution parameter σ_p is 4.168 and is also significant, which indicates that there is variation in marginal (dis)utility of price around the mean value. Thus, price sensitivity varies in the underlying population and may stem from the fact that practitioners have uneven professional experience, and react differently to national media and guidelines on cost-saving (Scoggins et al., 2006).

Similarly, the coefficient on the number of pack varieties is positive and significant, indicating higher marginal utility if a drug is available in multiple dosages and pack sizes. The variance coefficient is also significant, indicating that there is some heterogeneity in the marginal valuation of pack variety. The time trend is negative across all estimations, which implies that the utility of consuming common antibiotics is reducing over time compared to the outside option which may be induced by increasing resistance level. The coefficient on average temperature which varies seasonally is not significant as we include monthly dummies in all the estimates. However, the pattern of coefficients on the monthly dummies shown in Figure B-1 in the appendix shows the demand increases in winter months, perhaps due to a preference for using antibiotics to treat respiratory tract infections, and virus-induced secondary bacterial infection in cold seasons (Suda et al., 2014, Hendaus et al., 2015).

Among the coefficients recovered using the minimum distance method, the mean marginal utility associated with the spectrum is not significant. However, the variance parameter is significant so there is considerable heterogeneity in the taste parameter for the spectrum. This suggests that although on average patients and doctors do not exhibit strong preferences for broad- or narrow-spectrum antibiotics, some individuals do derive higher marginal utility from narrow- or broad-spectrum antibiotics, and hence, all else equal, their utility level would change if they were given drugs with different spectrum values.

5.2. **Substitution Patterns.** Before turning to the tax simulations and their effect on demand and upper-bound measures of welfare, we provide here estimates of substitution patterns as they help contextualize the results from the simulations. Based on the estimates for RCNL, we computed own- and cross-price elasticities for all the antibiotics in our sample. The distribution

FIGURE 2. Own price elasticity (RCNL Model)



The green solid line, the blue short-dashed line, and the red long-dashed line are the share-weighted mean, simple mean, and median values of own-price elasticity.

of the own price elasticity is shown graphically in Figure 2. Weighted means and standard deviations are given in columns (1) and (2) of Table 5 where the weights are based on shares. The weighted mean own- and cross-price elasticities are -2.58 and 0.10 with standard deviations of 1.61 and 0.17 respectively. Column (3) provides the simple mean elasticities. We delay the discussion of the results in the last three columns till the next subsection.

Aggregate own-price elasticities for all 18 molecules, along with a full 18×18 matrix of cross-price elasticities is summarized in Table B-3 in the appendix. Here instead, to understand the substitution possibilities across drugs with different antibacterial resistance, we partitioned cross-price elasticities by broad- and narrow-spectrum groups, and within those, substitution to the same or different molecules. From here on we only refer to the weighted mean values.

A 1%increase in the price of a broad-spectrum drug gives, on average, a 0.14% increase in the quantity of other broad-spectrum drugs. The substitution to drugs with the same molecule is, on average, higher than the substitution to other broad-spectrum drugs with a different molecule. The cross-price elasticities for the two cases are 0.27 and 0.09 respectively. This of course makes sense given that there are typically lots of different products within the same

molecule (see Table 1). Further, substitution into a narrow-spectrum drug, which would always be a different molecule, for a 1% increase in the price of a broad-spectrum drug is 0.08%.

TABLE 5. Price elasticities (alternative models)

	RCNL			RCL	Mol	22D
	Mean	Std.	Mean	Mean	Mean	Mean
	(1)	(2)	(3)	(4)	(5)	(6)
Own-price elasticity $\%\Delta s_j/\%\Delta p_j$	-2.58	1.61	-3.73	-2.46	-2.74	-2.57
Cross-price elasticity $\%\Delta s_j/\%\Delta p_k$	0.10	0.17	0.02	0.11	0.10	0.12
Cross-price elasticity wrt p_{Bk}, the price of a broad-spectrum drug						
$\%\Delta s_{Bj}/\%\Delta p_{Bk}$ (within broad)	0.14	0.20	0.03	0.15	0.15	0.17
$\%\Delta s_{Bj}/\%\Delta p_{Bk}$ (j,k same molecule)	0.27	0.32	0.11	0.08	0.74	0.27
$\%\Delta s_{Bj}/\%\Delta p_{Bk}$ (j,k different molecules)	0.09	0.11	0.01	0.14	0.04	0.12
$\%\Delta s_{Nj}/\%\Delta p_{Bk}$ (j in narrow)	0.08	0.08	0.01	0.13	0.05	0.11
Cross-price elasticity wrt p_{Nk}, the price of a narrow-spectrum drug						
$\%\Delta s_{Nj}/\%\Delta p_{Nk}$ (within narrow)	0.13	0.28	0.04	0.05	0.18	0.14
$\%\Delta s_{Nj}/\%\Delta p_{Nk}$ (j,k same molecule)	0.21	0.31	0.10	0.03	1.03	0.21
$\%\Delta s_{Nj}/\%\Delta p_{Nk}$ (j,k different molecules)	0.11	0.24	0.02	0.06	0.02	0.12
$\%\Delta s_{Bj}/\%\Delta p_{Nk}$ (j in broad)	0.04	0.04	0.01	0.06	0.03	0.06

Columns (1) and (2) provide the weighted mean and standard deviation of elasticities based on the RCNL model in Table 4 while column (3) gives the unweighted mean from the same model. Columns (4)-(6) give weighted mean elasticities based on alternative specifications given in Table B-1. Column (4) is the weighted mean price elasticities from the RCL model, column (5) is again the RCNL model with molecule level nesting, and column (6) gives mean elasticities from an RCNL specification with ATC3 level nesting when the potential size of the market is changed from baseline value to 22 DDD.

Next, a 1% increase in the price of a narrow-spectrum drug gives, on average a 0.13% increase in the quantity of another narrow-spectrum drug, with further refined cross-elasticities being 0.21% and 0.11% into the same or different molecules that are also with narrow-spectrum. The substitution to a broad-spectrum drug on the other hand is only 0.04%. These patterns suggest that broad-spectrum drugs are closer substitutes to each other, particularly to drugs with the same molecule, than drugs in the narrow-spectrum. Similarly, narrow-spectrum drugs are closer substitutes for each other, first to other narrow-spectrum drugs with the same molecule, then to other narrow-spectrum drugs, and least substitutable with broad-spectrum drugs.

At first glance, these results seem odd. Substitution from a narrow-spectrum drug to a broad-spectrum drug is surprisingly low, given that narrow-spectrum drugs target specific pathogens. If their price increased, one would expect substitution to broad-spectrum drugs. Indeed, as Table A-1 shows, Urinary Tract Infection (UTI) can be treated by only one narrow-spectrum drug in our dataset, trimethoprim, but by several broad-spectrum drugs. However, this is not the case for several other indications. For instance, for Upper Respiratory Tract Infection (URTI), there are six different narrow-spectrum molecules available. If one of them is unavailable, it is conceivable that substitution would occur within the narrow-spectrum category. Nonetheless, we further examine whether these substitution patterns result from our nesting design, which was based on ATC3 classes.

5.3. **Alternative specifications.** We also estimated the main RCNL model summarized in columns (6) and (7) in Table 4 with some alternative specifications, and the results are given in Table B-1 in Appendix B. First, we experimented with the nesting structure. We removed the ATC3 level nesting and estimated an RCL model that does not impose any ex-ante substitution pattern. The overall fit seems reasonable and as it turns out, the overall price sensitivity is not very different.

Second, we replaced the ATC3 level nesting with a more restrictive molecule level nesting (recall from Table 1 that there can be multiple molecules within an ATC3 class). This increases the nesting parameter value from 0.456 to 0.843 and reduces the magnitude of the price coefficients from -8.241 and 4.168 (mean and sigma respectively) to -3.569 and 1.820. However, it also increases the number of observations with negative marginal costs from 1.85% to 4.49%.

Third, we went back to the ATC3 level nesting and replaced the linear time trend with annual dummies to check if a linear time trend is sufficient to capture the overall change in demand over the observed time period. The price coefficients are similar to those in the main RCNL model, the nesting parameter value drops to 0.160, and the percent of observations with negative marginal costs increases to 4.93%. In most other respects the results are similar so we do not think there is any significant difference between the preferred model in the main analysis versus the one with annual dummies.

Fourth, as an additional robustness check, we reduced the potential market from 30 DDD per 1000 inhabitants per day to 22 DDD per 1000 inhabitants per day.[12] The model, using this revised definition of market size, yields results that closely resemble our current model (see Table B-1). With the alternative market size, the price coefficient is -7.324 as opposed to -8.241 in our main model. The standard deviation of the random coefficient on price is 3.578 instead of 4.168 in the main model. Finally, the nesting coefficient ρ for $\ln(s_{jg})$ is 0.425 compared to the 0.456 in the main model.[13]

We also compared weighted mean elasticities from our preferred specification, i.e. RCNL with ATC3 nesting, with some of the additional ones discussed above. The results are summarized in columns (4)-(6) in Table 5. The RCL model does not impose any nesting structure. Compared to the baseline model, RCL allows for slightly greater substitution from broad- to narrow-spectrum, i.e., 0.08 in RCNL vs 0.13 in RCL (compare columns (1) and (4) in Table 5) but similar substitution from narrow- to broad-spectrum, i.e., 0.04 in RCNL vs 0.06 in RCL.

Next, we consider the case with molecule-level nesting rather than at the ATC3 level. Note that the value of the nesting parameter increases from 0.456 to 0.843 and hence by construction, there is greater substitution within the molecule than outside. We can see the effect of this nesting in the cross-price elasticity matrix discussed above. Both within broad- and narrow-spectrum drugs, the cross-price elasticity to other drugs in the same molecule increases in

[12] To ensure the outside share is always positive in all periods, we can only reduce the potential market to 22 DDD. The average UK antibiotic consumption was around 20 DDD per 1000 inhabitants per day. By doing so, the mean outside share is 0.37 with min as 0.07 and max as 0.55. Values beyond 22 DDD would encounter negative market shares.

[13] We also estimated the original RCNL model using the "differentiation instruments" proposed by Gandhi and Houde (2020). In addition to our initial BLP type of and other instruments, we incorporated the sum of differences in product characteristics among competing firms within the same market segment. Specifically, we utilized pack varieties and the generic indicator variable to create these supplementary instruments. The findings closely mirrored the primary specifications detailed in columns (6) and (7) of Table 4 (the mean price coefficient changed from -8.241 to -7.470, and the σ_p coefficient changed from 4.168 to 3.707). These additional instruments had minimal impact on the instances of negative marginal costs and did not significantly enhance the first-stage F-value in the basic 2SLS-logit model. Notably, the substitution patterns highlighted in Table 5 in the subsequent section showed minimal deviation from those of the baseline RCNL model. This suggests that the ensuing policy implications and calculations remain robust even with the inclusion of differentiation instruments.

magnitude. Importantly, the cross-price elasticity between narrow and broad-spectrum drugs decreases even more. For instance, the number 0.08 decreases to 0.05, and 0.04 decreases to 0.03 (these numbers are in columns (1) and (5) in Table 5). Finally, the last column reverts to the original specification of the nesting structure but uses an alternative definition for the potential size of the market based on 22 DDD per 1000 inhabitants per day, and once again, the estimated elasticities remain remarkably consistent (compare columns (1) and (6) in Table 5).

In terms of model choice, we believe RCNL estimates provide a more reasonable substitution pattern relative to RCL by imposing some nesting structure. But between nesting at ATC3 vs molecule level, it is not clear which is necessarily superior. Because ATC3 contains multiple molecules, it is less restrictive than nesting at the molecule level, and based on this as well as on Table A-1, which gives the mapping between molecules and indications, we prefer the ATC3 level nesting. Between these two models, ATC3 level nesting also gives better fits in terms of the number of negative marginal costs. Thus we focus on this model in the next section on policy simulations, but it is clear from the forgoing comparisons, that the results are fairly robust to these alternatives.

5.4. **Policy Simulations.** We next ask if we change the relative prices of broad- and narrow-spectrum drugs via taxation, what would be the impact on demand and on consumer and total welfare? The source of price sensitivity is due to the NHS setting the annual prescribing budgets for each PCT, which in turn sets budgets for individual physicians so that GPs are responsible for keeping their prescription payments within those budgets.

To that end, we undertake two related tax exercises where we either impose an ad valorem tax or a unit tax. For the ad valorem tax, we impose 5% and then 20% on either (i) all antibiotics, (ii) all broad-spectrum antibiotics, or (iii) the subset of broad-spectrum antibiotics labeled 'broad-A'. As discussed earlier, this latter group consists of molecules that have been identified in government AMR strategy documents as those that should be especially targeted for reduced consumption due to their higher contribution to the rise in AMR (PHE, 2015, DH, 2016). Accordingly, in the third exercise, we impose a tax on just these drugs to see how much of a substitution is to the rest of the broad-spectrum drugs, i.e., 'broad-B' versus narrow-spectrum antibiotics as

well as to the outside option. We also use these tax simulations to compute how much is the associated welfare loss from such a tax. In these calculations, we account for the short-run change in consumer and producer surplus, as well as any additional costs due to testing if more patients are switched to narrow-spectrum costs.[14]

For these tax exercises, we use the estimated demand parameters and back out marginal cost vector c_t in market t. We then calculate the new equilibrium net price vector p_t^* and market shares $s_t(p_t^* \odot (1+\tau_t))$ as,

$$p_t^* = c_t + \Delta_t^{-1}(s_t(p_t^* \odot (1+\tau_t))) \cdot s_t(p_t^* \odot (1+\tau_t)).$$

In our three simulation exercises, we let τ be 5% and 20% for some drugs. While not the focus of our paper, the marginal costs by broad- and narrow-spectrum drugs are given in the appendix and show that (i) the marginal costs are lower for broad-spectrum relative to narrow-spectrum drugs, and (ii) that while average prices fell over the ten years, the marginal costs fell by even more leading to greater margins and profitability. The tax simulation algorithm, the marginal costs, and accompanying welfare calculations are explained further in Appendix C.

We repeat the exercise where we impose a unit tax on all broad-spectrum drugs. The unit tax is pegged to the average difference in estimated marginal costs between broad- and narrow-spectrum drugs. Since we do not provide an

[14]We account for the testing cost in our simulations as follows. We assume that each infection would be first tested for pathogens before prescribing any narrow-spectrum drugs. We convert the change in the quantity of each drug due to the simulated policy (which is measured in defined daily dosages) to bouts of illnesses under the assumption that an antibiotic script is prescribed either for 7 or 14 days. Thus, conservatively, we divide the change in quantity by seven and then multiply it by the NHS tariff for microbiology as our measure of testing cost. The cost for microbiology was obtained from the NHS Reference cost page https://www.gov.uk/government/collections/nhs-reference-costs which provides data for 2009 onwards (earlier years data is archived but not available). We used the national average cost for "currency code" DAP831 for Microbiology/Virology or for DAPS07 for Microbiology (the code changes across the years). For all the years from 2009-10 to 2011-12, the national average unit cost is £8 with the interquartile range from £5-10 or £6-10, and the national average unit cost for 2012-13 is £7 with an interquartile range of £4-9. Since it does not change much by year, we kept the testing cost to £8 until April 2012 and then changed it to £7 for the observations after that. However, we also converted these costs to 2003 value to be consistent with the rest of the data. The data sources mentioned here do not indicate if the pathology cost varies by drug spectrum.

optimal tax calculation, these sets of exercises can be used to gauge the likely effects of alternative options. The detailed results from the second exercise are relegated to the appendix, and only the main conclusions are discussed here.

It should be noted that the change in welfare in these exercises is only a partial analysis: it captures the change in demand and welfare loss associated with cost-side interventions but do not measure aggregate societal benefits accrued in the long run from the increase in demand for drugs that do not exacerbate the AMR problem as much. Thus, these exercises provide an upper bound on the costs and change in demand from implementing such tax policies but does not fully quantify the long-term welfare benefits of slowing AMR. Nonetheless, given the dire predictions in the O'Neill (2016) if AMR goes unchecked, it is well worth exploring these options.

TABLE 6. Ad valorem tax (5 or 20%)

		Tax on all antibiotics		Tax on all broad-spectrum		Tax on broad-A	
		5% (1)	20% (2)	5% (3)	20% (4)	5% (5)	20% (6)
%Δ price	Broad-A†	5.22	21.95	5.22	22.60	5.19	22.72
	Broad-B‡	4.45	17.66	4.37	17.62	-0.30	-0.89
	Broad	4.96	20.52	4.94	20.94	3.35	14.83
	Narrow	5.30	20.73	-0.13	-0.59	-0.12	-0.43
	Combined	5.14	20.63	2.33	9.85	1.56	6.97
% Δ quantity	Broad-A	-8.69	-29.35	-11.18	-36.01	-11.83	-37.73
	Broad-B	-0.36	-1.04	-1.75	-6.37	0.75	2.55
	Broad	-2.17	-7.19	-3.80	-12.81	-1.98	-6.20
	Narrow	-5.47	-18.96	1.60	5.64	1.02	3.55
	Combined	-3.73	-12.71	-1.71	-5.68	-0.79	-2.29
Δ CS		-91.9	-322.5	-33.5	-117.0	-22.3	-78.2
Δ profits (PS)		-41.3	-144.6	-20.9	-68.8	-7.7	-21.4
Δ tax revenue (TR)		92.6	298.8	40.2	121.6	20.9	57.0
Δ testing cost (TC)		-114.7	-396.6	34.5	121.5	21.8	75.5
Δ Total welfare (TW)		74.1	228.3	-48.7	-185.7	-30.9	-118.1

The monetary change of welfare is measured as pounds per 1000 inhabitants per year and is the average value from all years. All figures are converted to 2003 real value. For equivalent values for 2012 only, see Table C-5. TW = CS + PS + TR − TC. †Broad-A group consists of co-amoxiclav, quinolones (ciprofloxacin, levofloxacin, and ofloxacin) and cephalosporins (cefalexin, cefixime). ‡All other broad-spectrum drugs.

The tax exercises use all years' data where monetary values are set to 2003 real terms and the welfare calculations are expressed per 1,000 inhabitants using the UK population of that year. Table 6 provides annual average values related to the ad valorem tax of 5% and 20% tax under the three scenarios described above. For comparison, the equivalent numbers for 2012, the last full year of observations in our data, are given in the appendix in Table C-5.

Starting with the ad valorem tax of 5% on all antibiotics (column (1), Table 6), it leads to a 4.96% increase in the price of broad-spectrum drugs and a 5.30% increase in the price of narrow-spectrum drugs, for a combined price increase of 5.14%. However, the reduction in quantity for narrow-spectrum drugs is 5.47% while that for broad-spectrum drugs is only 2.17% for an overall reduction of 3.73% in quantity (recall that the baseline relative shares of broad- and narrow-spectrum are around 60% and 40%, see Table 1). This leads to an average loss in consumer and producer surplus of £91.9 and £41.3, for a total of £133.2 per 1,000 inhabitants. In turn, this is offset by a tax revenue of £92.6 and an additional £114.7 in avoided testing costs, for net positive change. The testing costs decline because fewer patients are given narrow-spectrum drugs. Overall, it leads to an increase in total welfare of £74.1.

Column (2) provides estimates when tax is set to 20%. Again there is an overall decrease in the use of antibiotics, but once again the percentage decline in narrow-spectrum drugs is more than twice that of broad-spectrum antibiotics. There is a large drop in consumer and producer surplus. However, the total welfare change becomes positive again, considering the changes in tax revenue and the savings due to avoided testing costs associated with prescribing narrow-spectrum prescriptions.

By contrast, an ad valorem tax on just the broad-spectrum antibiotics changes the calculus quite a bit (columns (3) and (4)). The drop in consumer surplus with either a 5% or a 20% tax is less than a third of that when it was on all drugs. Moreover, the usage of broad-spectrum drugs declines, while that of the narrow-spectrum increases (for the 20% tax rate, by -12.81% and 5.64% respectively). The total change in consumer and producer surplus net of tax revenue and testing costs is a decrease of £185.7.

Note that in the foregoing cases, the decline in broad-spectrum prescriptions is not even across the subgroups of the broad-spectrum drugs. For instance,

in column (4), the decline in a subset of broad-spectrum antibiotics that are associated with contributing the most to the rise in AMR is 36.01% ('broad-A') while that of the other broad-spectrum drugs is 6.37% ('broad-B'). As the last two columns show (columns (5) and (6)), this balance changes even further if the tax is imposed on only this subset of broad-spectrum antibiotics. This tax allows for more substitution within broad-spectrum antibiotics from 'broad-A' to 'broad-B'. With a 20% tax levied on the broad-A group of antibiotics, their consumption declines by 37.73% with some increase in the broad-B group as well as a smaller increase in narrow-spectrum drugs relative to that in the column (4) scenario. The total decline in all antibiotics is only 2.29% and consequently, the change in consumer surplus and change in total welfare net of tax revenue and testing costs are also much smaller than before.[15]

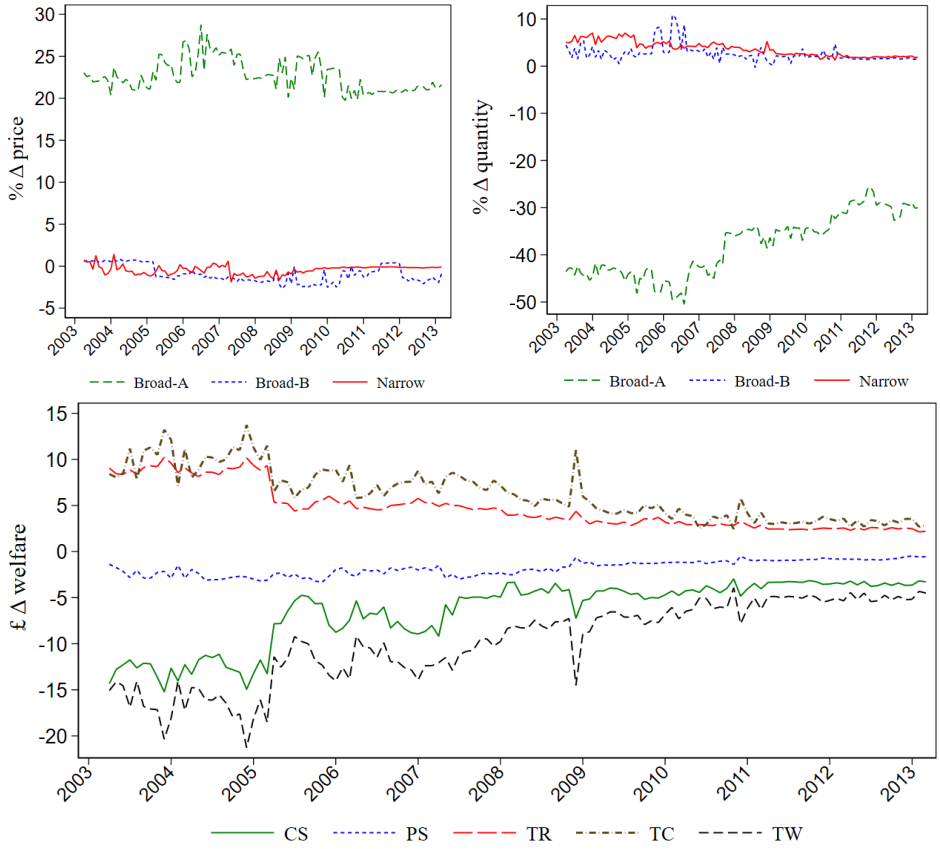


FIGURE 3. 20% Ad valorem tax on broad-A antibiotics

[15]Table C-7 in Appendix C.2 compares the results of these counterfactual tax exercises with those based on simpler logit and nested logit models. The implied substitution to the imposed tax per the simpler models is quite unrealistic and, accordingly, we think that our RCNL-based simulations are more plausible.

Figure 3 shows the effect of the 20% ad valorem tax under the third scenario of taxing only broad-A antibiotics for the entire data series, i.e., without aggregating to a year and average over all years. Under this tax, for the entire duration, the percentage change in narrow-spectrum and broad-B drugs is positive (see the top right panel) while that on broad-A is negative but is uneven as the change is larger in earlier years, i.e., before 2007 and somewhat less in later years. In part, this is due to the observed price drop in the broad-A group of drugs noted earlier in Figure 1. The lower panel of Figure 3 shows the evolution of consumer surplus and other components in the calculation of the total welfare effects. Again the effects are larger pre-2005 when the base prices of broad-A were higher and lower post the change in these prices. An equivalent exercise with a 5% tax is given in the appendix in Figure C-2.

As these counterfactual exercises show, it is possible to shift demand from broad-spectrum to narrow-spectrum, or at least away from the broad-A group by up to around 35-40% with a relatively modest drop in short-run welfare or total consumption. An alternative tax exercise where a unit tax is imposed on either all broad-spectrum drugs or again on the same subset of 'broad-A' leads to a similar conclusion (exact numbers are given in Table C-6 in the appendix). In this exercise, we impose a unit tax which is equal to the difference in marginal costs between broad- and narrow-spectrum drugs and is of the order of £0.10 for all periods but varies slightly for each month and year.

6. Summary and Discussion

In this paper, we studied the market structure of first- and second-line antibiotics in the UK between 2003 and 2013. Using aggregate levels of sales data, we estimated discrete choice demand models. We find that while prices have declined over the last decade, marginal costs have declined even more and the marginal costs of broad-spectrum antibiotics are lower than that of the narrow-spectrum antibiotics. The weighted mean own- and cross-price elasticities are -2.58 and 0.10 with standard deviations of 1.61 and 0.17 respectively. Importantly, a 1% increase in the price of a broad-spectrum drug shifts the demand to narrow-spectrum drugs by 0.08%. In general broad-spectrum drugs are closer substitutes to each other than drugs in the narrow-spectrum and vice versa and greater substitution is to other drugs in the same molecule.

Demand estimates reveal that there is a dispersion in tastes for antibiotics that varies by the antibiotic spectrum of the drug (the marginal utility of the spectrum). Price increases in one drug do lead to significant substitution towards other cheaper drugs, but most of the substitution is within groups by the spectrum of the antibiotics. This implies that while switching from broad- to narrow-spectrum is possible via changes in relative prices, it will have significant implications for consumer surplus. For an ad valorem tax of 20% on all antibiotic drugs, the cost in terms of loss in consumer welfare is £322.5 per 1000 residents, and the reduction in quantity consumed is due to both broad-spectrum drugs (7.19%) and narrow-spectrum drugs (18.96%). Alternatively, a 20% ad valorem tax on a subset of drugs that contribute the most to the AMR problem, i.e., the broad-A (co-amoxiclav, quinolones, and cephalosporins) in our sample, leads to a cost of £78.2 per 1000 residents in terms of reduction in consumer surplus while the demand of broad-A declines by 37.73% and that of narrow-spectrum increases by 3.55%. While our simulations show how much demand is shifted from broad- to narrow-spectrum, and at what cost, it does not calculate the long-term benefits of switching to drugs with a lower AMR footprint. In addition, it is clear that the estimated loss in welfare is much smaller than the estimates of worldwide costs in O'Neill (2016) and it may be well worth our effort to consider such remedies to shift demand to narrow-spectrum drugs.

Our analysis focuses on quantifying trade-offs from taxing by type of antibiotics because certain drugs contribute more to the AMR problem than other drugs as highlighted by various public health documents discussed earlier. Giubilini (2019) makes an ethical case for taxing individuals for antibiotics in cases when the disease is mild and self-limiting, that is, where a patient eventually recovers from a disease even without antibiotic treatment with sufficiently high probability. Our drug level analysis and the taxation policies in the counterfactual do not account for the severity of the disease and hence, may miscalibrate the welfare impacts to some extent.

Nonetheless, in our analysis, the financial burden of the tax is not on the patients but rather on the GP practices who may be overprescribing in some cases, as also highlighted in Giubilini (2019) and other places. Moreover, as Table A-1 shows, for each of the seven indications there is a choice of

prescribing broad- and narrow-spectrum drugs, and the tax on broad or broad-A would encourage prescribing the narrow-spectrum drugs. Thus, while our analysis ignores the disease severity, we believe our counterfactual exercise captures the main first-order effects of such policies. Also, we do not think that such tax policies should be implemented without allowing for exemptions based on the severity of the disease which the physicians could certify.

As discussed earlier, there is also no direct financial cost of the pathology test on either the patient or the physician. Nonetheless, there may be some disutility with prescribing the test. This is because susceptibility testing takes time. If decisions are time-critical and it is not an option to wait for a precise diagnostic to know which narrow-spectrum antibiotic to prescribe, this may slow the switch from broad-spectrum to narrow-spectrum. Further, these can vary by type of disease, a dimension of heterogeneity that is not considered in the analysis. Susceptibility testing is also done when prescribing broad-spectrum antibiotics because it can inform about the further course of action in case the first antibiotic treatment is not successful. These issues can be difficult to fully tease out in an aggregate demand analysis. To that end, our model includes a random coefficient for the spectrum variable and estimates show that consumers (patient-physician combination) exhibit strong variation in tastes by the spectrum.

In principle, this could also be exploited to modify tastes in such a way as to reduce the consumption of broad-spectrum drugs. Currently, demand-side interventions are mainly educational campaigns, including raising awareness of antibiotic resistance to the public, professional education to prescribers as well as stewardship of preferred prescription in primary care and in hospitals (DH, 2013, Scoggins et al., 2006). However, those campaigns may not be sufficient. Since part of the preference over broad-spectrum antibiotics may stem from fear of treatment failure, especially in primary care when there is no clear clue of the specific type of bacterial pathogen, a quick and cheap diagnosis test may completely solve the puzzle. Although these tests are expensive, time-consuming, and rarely used in primary care now, scientists have made progress in reducing the cost and time of diagnostic methods. For example, Schmidt et al. (2017) have successfully reduced the time of testing to four hours by direct DNA sequencing. If the uncertainty of bacteria type or level of susceptibility could be reduced by widely used accurate diagnosis, the inappropriate

consumption of antibiotics would be calibrated. That combined with cost-side interventions that we highlight above would imply shifting to narrow-spectrum antibiotics with much lower distortions and lower loss in consumer welfare.

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Appendices

These appendices are for the paper titled, "**Antibacterial resistance and the cost of affecting demand: the case of UK antibiotics**" and optionally can be made available online only.

Appendix A. Further details on Data and instruments

A.1. **Mapping molecules to indications.** Table A-1 maps molecules to their indications and recommendations for 1st or 2nd use. If a molecule is suggested for patients with allergies to the 1st/2nd line molecules, it is marked as '3'. Some molecules have special instructions based on patient characteristics like age, gender, pregnancy, and breastfeeding, which are noted in the table. Table A-1 is not a comprehensive mapping based on pathogens but rather based on indications and importantly, our reading of the various guidelines related to antibiotic use.

Table A-1. Selected antibiotics and their recommended indications

	ATC3 J01	# of Drugs	Spec-trum	URTI	LRTI	UTI	GITI	GTI	SKIN
Broad-spectrum									
Selected-broad									
Co-amoxiclav[abc]	C	11	29.5	2	2	1,2	1	1	1,2
Cefalexin[abc]	D	15	19.25		2	1,3	3	3	3
Cefixime[b]	D	2	19.5			1		1	
Ciprofloxacin[abc]	G	5	39.75	1	1	1,2	2,3	1	1
Levofloxacin[bc]	G	2	39.75		2	1	2,3		2
Ofloxacin[abc]	G	3	39.75			1		1	2
Other-broad									
Doxycycline[abc†]	A	7	38.75	3	1,2			1	1,2,3
Tetracycline[abc]	A	1	38.75			2	2,3		2
Amoxicillin[abc]	C	13	13.5	1	1,2	1,2	1,2	1	1,2
Pivmecillinam[bc]	H	1	19.5			1,2			
Neomycin[bc]	K	1	19.5						1
Narrow-spectrum									
Trimethoprim[abc]	E	5	4.25			1,2	2		2
Azithromycin[abc]	F	10	12.25	2	2			1,2,3	2
Clarithromycin[abc]	F	10	12.25	3	1,2,3		1,2,3	3	3
Clindamycin[abc*]	F	3	10.75	3	2			2,3	1
Erythromycin[abc‡]	F	22	12.25	2,3	1,2			1,2,3	2,3
Flucloxacillin[abc]	H	8	4.25	1	2			1	1
Penicillin V[abc]	H	12	13.5	1	1				

Notes: Notes: Indications are URTI (Upper Respiratory Tract Infection), LRTI (Lower Respiratory Tract Infection), UTI (Urinary Tract Infection), GITI (Gastro-Intestinal Tract Infection), GTI (Genital Tract Infection), and SKIN (Skin Infection). Numbers (1) and (2) indicate 1st/2nd line use (highest option is listed when it may be used in multiple ways for the same indication); (3) indicates use in case of allergies. For example, if the indication is URTI and the patient is allergic to 1st/2nd line drugs, Doxycycline may be prescribed.

*Clindamycin is listed for GTI only for women.

†Doxycycline is listed as not suitable for pregnant and breastfeeding patients.

‡Erythromycin is listed for treatment of URTI and LRTI only when there is a penicillin allergy and pregnancy. More suitable for pregnant or breastfeeding patients. Sources: Superscripts a, b, c indicate PHE (2014), BNF (2023), and Pan Mersey APC (2023) respectively. Disclaimer: This table is to guide the authors' econometric choices and not to impart medical advice to anyone. No one should use this or any other economics journal for medical advice.

A.2. **Seasonality by spectrum.** Figure A-1 plots the relative shares of broad- vs. narrow-spectrum drugs by months averaged over the ten years of data. As discussed in the main text, there is seasonality in the relative shares and the peak for broad-spectrum is in the winter months. The NHS fiscal year is from April/1 to March/31 the following year.

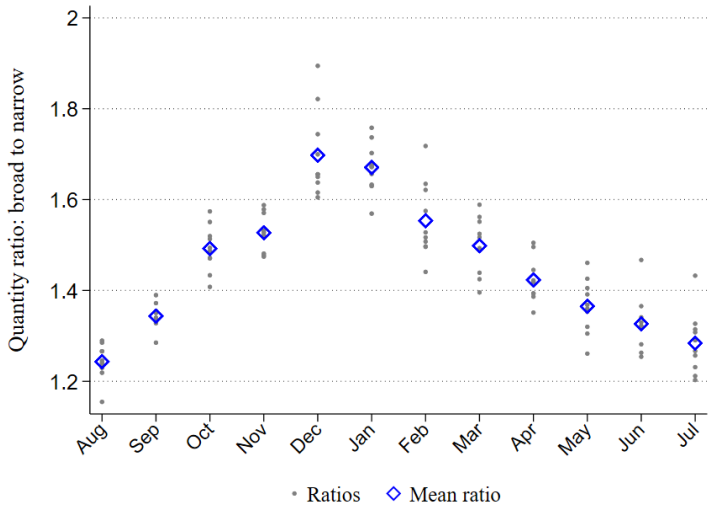

FIGURE A-1. Relative antibiotics consumption by month: the total quantity of broad-spectrum to narrow-spectrum molecules

A.3. **Instruments.** We first describe all the excluded instruments, and then how they were used in different models along with other exogenous variables and counts of moment restrictions. The variables z_{1t} and z_{2t} are the log of the price of diesel and of exchange rate and are not specific to any drug and vary only by markets (average monthly values). The next set is BLP-style instruments: z_{3jt} is the total number of other drugs produced by the manufacturer of the reference drug j and z_{4jt} is the total number of other drugs by the reference firm of j restricted to the nest of the drug j. Similarly, z_{5jt} is the total number of packs across other products by firm producing drug j within the nest of drug j, and z_{6jt} is the total number of packs by competitors within the reference nest of drug j. Interactions and higher powers include $z_7 = z_4^2$, $z_8 = z_5^2$, and $z_9 = z_4 z_5$.

For the logit model, the exogenous variables are constant, pack varieties, a time trend, the weather temperature, and drug dummies (131 minus one reference). Note that the invariant product characteristics such as spectrum value, formulation type, etc. do not enter this equation. Therefore, when the logit specification is estimated via OLS, it has 4+130 = 134 demand-side instruments. We back out those coefficients on spectrum, age, generic, capsule, liquid, and constant using Chamberlain's method, which we describe below. Further, when we estimate it via 2SLS, we use four additional instruments: z_1, z_2, z_3, and z_4 for a total of 138-moment restrictions.

Next, we estimate the logit jointly with the supply side equation. The supply equation includes a constant, pack variety, the log of the price of diesel (z_1), the log of the exchange rate (z_2), a time trend, a dummy variable for broad-spectrum molecules, a dummy variable for generic, a dummy variable for capsule, a dummy variable for liquid, for a total of nine instruments (the supply side does not include drug dummies). Summing up, in the logit model when estimated jointly with the supply side, there are 136 demand-side instruments (134 plus z_3 and z_4) and nine cost-side instruments (including z_1 and z_2) for a total of 145-moment restrictions.

Finally, for the RCNL estimation, we additionally use z_5 and z_6 (which provide nest-specific counts) as well as z_7 and z_8 for a total of 149 moment conditions (140 for the demand side and nine for the supply side). In the RCL model, we drop z_6 and z_8 and instead use z_9 for a total of 139+9=148 restrictions.

In the versions with optimal instruments, following Reynaert and Verboven (2014) we further compute six instruments: four optimal instruments for the random coefficients for the constant, price, pack variety, and spectrum, one for the price in the linear part, and one for the within-group market share. The optimal instruments for other variables are the exogenous variables themselves. The optimal instruments replace the original instruments.

Appendix B. Additional results

B.1. **Monthly dummies.** Figure B-1 plots the coefficients of monthly dummies from the baseline RCNL model given in columns (6) and (7) of Table 4. The error bar indicates the 95% confidence interval, and the base month is March.

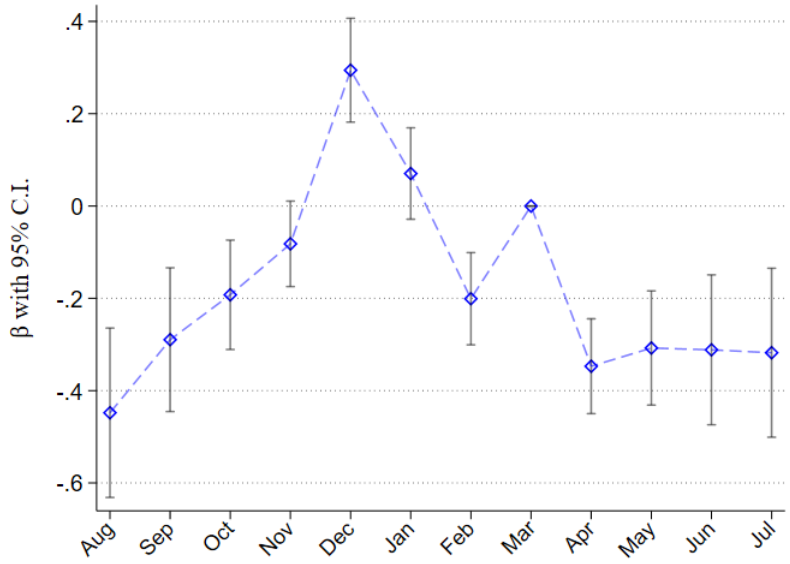

Figure B-1. Coefficients of monthly dummies in the RCNL model

B.2. **Robustness - Alternative specifications.** The baseline model in the main text Table 4 uses RCNL with ATC3 level nesting. Table B-1 provides results from some alternative specifications. Columns A is an RCL specification, (B) is RCNL but with molecule-level nesting, (C) is like the baseline model but with annual dummies instead of linear time trend, and (D) is also like the baseline but with the alternative definition of the potential market based on 22 DDD per 1000 inhabitant per year.

TABLE B-1. Estimation results: Variations of RNCL and RCL

	(A) RCL		**(B)** Molecule nesting		**(C)** Year dummies		**(D)** 22D	
	β	σ	β	σ	β	σ	β	σ
‡Constant	-2.93^a	1.712^a	-2.198^a	0.711^b	-0.285	0.792	0.409	0.532
	(1.11)	(0.31)	(0.557)	(0.324)	(0.64)	(0.503)	(0.655)	(0.714)
Price	-9.270^a	4.698^a	-3.569^a	1.820^a	-7.841^a	4.031^a	-7.324^a	3.578^a
	(0.082)	(0.082)	(0.054)	(0.032)	(0.033)	(0.082)	(0.137)	(0.068)
$\ln(s_{(j\in g)})$			0.843^a		0.160^a		0.425^a	
			(0.071)		(0.023)		(0.033)	
‡Spectrum	0.243	0.564^a	-0.070	0.084	0.190^b	0.825^a	-0.059	0.187^b
	(0.19)	(0.085)	(0.096)	(0.076)	(0.088)	(0.06)	(0.133)	(0.094)
Pack	0.515^a	0.019	0.142	0.032^c	0.491^a	0.169^b	0.373^a	0.115^b
	(0.028)	(0.049)	(0.096)	(0.017)	(0.037)	(0.076)	(0.032)	(0.046)
‡Age	0.132		0.223^a		0.064		-0.024	
	(0.13)		(0.06)		(0.069)		(0.062)	
‡Generic	0.306		0.063		-0.333^c		-0.034	
	(0.33)		(0.14)		(0.181)		(0.157)	
‡Capsule	-0.568		-0.281^c		-0.049		0.058	
	(0.384)		(0.16)		(0.205)		(0.187)	
‡Liquid	-0.634^c		0.076		0.074		0.029	
	(0.324)		(0.151)		(0.175)		(0.164)	
Temperature	-0.003		-0.012		-0.016^c		-0.023^a	
	(0.008)		(0.008)		(0.009)		(0.008)	
Time	-0.393^a		-0.142^a				-0.305^a	
	(0.007)		(0.006)				(0.01)	
Med #drugs	0.102^a		-0.011		0.024		0.007	
	(0.022)		(0.023)		(0.029)		(0.023)	
Low #drugs	0.626^a		0.129^a		0.215^a		0.511^a	
	(0.034)		(0.033)		(0.055)		(0.042)	
pseudo-Rsq	0.98		0.98		0.97		0.98	
avg $(p-c)/p$	0.34		0.28		0.36		0.27	
% mc<0	1.49		4.49		4.93		2.26	

Total 11,417 obs. of 131 distinct products over 120 months spanning 18 molecules and 14 formulations (with three main characteristics, tablet, capsule, and oral liquid). All regressions include product dummies. Robust standard errors are in parentheses. Superscripts (a), (b), and (c) imply significance at 1, 5 or 10% respectively. ‡The mean β coefficients are retrieved from the minimum distance method as product dummies are included.

B.3. **Supply Side Coefficients.** Table B-2 provides supply-side coefficients for equation (6) when jointly estimated with the demand models.

TABLE B-2. Supply Side equation (log(mc+1))

Supply-side	Logit	NLogit	RCL	RCNL			
				Main	Mol	Year D	22D
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Constant	0.789^a	0.794^a	0.466^a	0.470^a	0.663^a	0.362	0.663^a
	(0.107)	(0.107)	(0.108)	(0.113)	(0.139)	(0.341)	(0.114)
‡Broad-spectrum	-0.037^b	-0.037^b	0.003	-0.013	-0.071^a	0.012	-0.002
	(0.018)	(0.018)	(0.018)	(0.021)	(0.022)	(0.093)	(0.021)
Pack	-0.031^a	-0.032^a	-0.011^b	-0.021^a	-0.017	0.002	-0.024^a
	(0.006)	(0.006)	(0.005)	(0.007)	(0.013)	(0.008)	(0.007)
Generic	-0.195^a	-0.197^a	-0.157^a	-0.146^a	-0.093^a	-0.120	-0.183^a
	(0.019)	(0.019)	(0.019)	(0.022)	(0.035)	(0.107)	(0.02)
Capsule	0.047^c	0.047^c	-0.068^a	-0.045^c	0.049	-0.076^a	-0.047^c
	(0.027)	(0.027)	(0.024)	(0.025)	(0.03)	(0.025)	(0.025)
Liquid	0.239^a	0.242^a	0.147^a	0.180^a	0.127^a	0.081	0.211^a
	(0.021)	(0.021)	(0.022)	(0.024)	(0.038)	(0.063)	(0.024)
Time	-0.028^b	-0.028^b	-0.061^a	-0.066^a	-0.033^b	-0.058	-0.043^a
	(0.013)	(0.013)	(0.013)	(0.013)	(0.014)	(0.069)	(0.013)
z_1:Price of	0.051	0.051	0.617^a	0.606^a	0.114	0.553	0.319
diesel (log)	(0.227)	(0.227)	(0.226)	(0.227)	(0.243)	(2.333)	(0.229)
z_2: Exchange	0.034	0.033	0.042	0.080	0.028	0.080	0.002
rate (log)	(0.064)	(0.064)	(0.064)	(0.064)	(0.069)	(0.302)	(0.065)
Statistics							
Obs	11417	11417	11417	11417	11417	11417	11417
pseudo-Rsq	0.15	0.15	0.17	0.14	0.13	0.18	0.14

Total 11,417 obs of 131 distinct products over 120 months spanning 18 molecules and 14 formulations (with three main characteristics, tablet, capsule, and oral liquid). Robust standard errors are in parentheses. Superscripts a,b, and c imply significance at 1, 5, or 10% respectively.

‡broad-spectrum is a dummy variable that indicates if the drug has a broad-spectrum molecule. It is different from the Spectrum variable used in the demand equation.

B.4. **Elasticities by molecule.** Table B-3 provides the share-weighted own- and cross-price elasticities by molecule.

TABLE B-3. Share weighted own and cross-price elasticities by molecule

		Cross-price elasticity																	
	(0)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)
(1)	-3.87	0.39	0.05	0.02	0.06	0.06	0.11	0.02	0.05	0.09	0.12	0.01	0.02	0.05	0.10	0.02	0.04	0.06	0.05
(2)	-4.14	0.02	0.58	0.02	0.02	0.00	0.02	0.02	0.02	0.02	0.01	0.01	0.02	0.00	0.02	0.00	0.02	0.02	0.02
(3)	-1.68	0.00	0.00	0.16	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00
(4)	-2.63	0.06	0.03	0.02	0.12	0.26	0.66	0.03	0.01	0.03	0.05	0.01	0.03	0.04	0.07	0.02	0.03	0.03	0.02
(5)	-3.31	0.01	0.00	0.02	0.04	0.02	0.27	0.00	0.01	0.00	0.01	0.00	0.00	0.02	0.01	0.02	0.00	0.00	0.00
(6)	-4.76	0.01	0.00	0.00	0.07	0.18	0.37	0.00	0.01	0.00	0.01	0.00	0.00	0.01	0.01	0.00	0.00	0.01	0.00
(7)	-1.52	0.01	0.03	0.00	0.05	0.00	0.00	0.08	0.53	0.07	0.00	0.02	0.06	0.00	0.01	0.00	0.04	0.03	0.03
(8)	-2.88	0.01	0.01	0.01	0.00	0.02	0.02	0.07	.	0.00	0.02	0.00	0.00	0.01	0.01	0.01	0.01	0.01	0.01
(9)	-1.68	0.18	0.10	0.00	0.17	0.00	0.01	0.22	0.08	0.29	0.01	0.05	0.19	0.00	0.05	0.00	0.12	0.09	0.10
(10)	-4.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	.	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
(11)	-0.45	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	.	0.00	0.00	0.00	0.00	0.00	0.00	0.00
(12)	-1.05	0.01	0.02	0.00	0.03	0.00	0.00	0.04	0.02	0.04	0.00	0.01	0.06	0.00	0.01	0.00	0.02	0.02	0.02
(13)	-2.66	0.02	0.01	0.05	0.01	0.05	0.02	0.00	0.02	0.00	0.03	0.00	0.00	0.10	0.06	0.16	0.02	0.01	0.01
(14)	-3.97	0.08	0.04	0.01	0.06	0.05	0.08	0.02	0.03	0.02	0.08	0.00	0.02	0.15	0.29	0.04	0.26	0.05	0.04
(15)	-2.50	0.00	0.00	0.03	0.00	0.02	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.07	0.01	0.09	0.00	0.00	0.00
(16)	-3.92	0.03	0.05	0.00	0.03	0.01	0.02	0.04	0.03	0.04	0.02	0.02	0.04	0.02	0.22	0.00	0.32	0.04	0.04
(17)	-3.64	0.11	0.11	0.01	0.08	0.04	0.10	0.08	0.07	0.08	0.55	0.02	0.08	0.03	0.11	0.01	0.11	0.06	1.18
(18)	-3.97	0.02	0.03	0.01	0.02	0.01	0.02	0.02	0.03	0.02	0.15	0.01	0.02	0.01	0.02	0.01	0.03	0.30	0.31

The 18 molecules are as follows: (1) Co-amoxiclav, (2) Cefalexin, (3) Cefixime, (4) Ciprofloxacin, (5) Levofloxacin, (6) Ofloxacin, (7) Doxycycline, (8) Tetracycline, (9) Amoxicillin, (10) Pivmecillinam, (11) Neomycin, (12) Trimethoprim, (13) Azithromycin, (14) Clarithromycin, (15) Clindamycin, (16) Erythromycin, (17) Flucloxacillin, (18) Penicillin V.

The column marked (0) lists the weighted mean own-price elasticity for any drug. The rest of the 18×18 provides the weighted mean cross-price elasticities. Note that the leading diagonal in this part of the table is not the own-price elasticity. For instance, 0.39 on the leading diagonal is the mean cross-price elasticity of a co-amoxiclav-based drug with respect to a 1% change in the price of any other co-amoxiclav-based drug. Similarly, 0.02 is the mean percent change in the quantity of a co-amoxiclav-based drug associated with a 1% change in the price of a cefalexin-based drug while 0.05 is the mean percent change in the quantity of a cefalexin-based drug associated with a 1% change in the price of a co-amoxiclav based drug. The rest of the matrix should be read the same way.

Appendix C. Tax Simulations

C.1. **Tax simulation algorithm.** We use the demand and pricing equations to conduct a tax simulation exercise. We impose the tax rate τ on groups of drugs of interest. Given the estimated demand parameters and the estimated marginal cost vector in market t, c_t, we calculate the new equilibrium price vector p_t^* and market shares $s_t(p_t^* \odot (1+\tau_t))$ as,

$$p_t^* = c_t + \Delta_t^{-1}(s_t(p_t^* \odot (1+\tau_t))) \cdot s_t(p_t^* \odot (1+\tau_t)).$$

In our simulation exercises, we let τ be 5% and 20% for some drugs. The surplus gained by individual i in market t is

$$cs_{it} = \frac{1}{\beta_{pi}} \max_{j \in \mathcal{J}_t} u_{ijt},$$

where β_{pi} is the value of the random coefficient on prices (in absolute value) associated with individual i. By diving by β_{pi} we monetise the indirect utility function.

This money metric utility varies across consumers and by markets, and we can take its expectation to compute the average consumer welfare (Small and Rosen, 1981). For the random coefficients nested logit model, the expression of interest for the market t is

$$\max_{j \in \mathcal{J}_t} u_{ijt} = \ln \left[1 + \sum_{g=1}^{G_t} \left[\sum_{l=1}^{J_{gt}} \exp\left(\frac{x_{lt}\beta_i + \xi_{lt}}{1-\rho} \right) \right]^{1-\rho} \right].$$

Refer to Train (2009), among others, for an explanation of the procedure. The expected consumer surplus can be simulated in the following way,

$$E(cs_{it}) \approx \frac{1}{ns} \sum_{i=1}^{ns} \frac{1}{\beta_{pi}} \ln \left[1 + \sum_{g=1}^{G_t} \left[\sum_{l=1}^{J_{gt}} \exp\left(\frac{x_{lt}\beta_i + \xi_{lt}}{1-\rho} \right) \right]^{1-\rho} \right] + K_t$$

where K_t is a period-specific constant and the expected value is computed over the cross-section of individuals. We do not know the value of this constant. However, it drops out of calculations when we study the change in expected consumer surplus associated with a variation in the price vector in the counterfactual situation relative to the observed factual condition. The total monetary consumer surplus is $E(cs_{it})$ times the potential market size.

We also account for the cost of testing incurred to diagnose the pathogen before prescribing narrow-spectrum drugs. This step is not necessary when prescribing broad-spectrum drugs. As a conservative estimate of the additional cost of testing, we divide the narrow-spectrum drug quantity by seven

and convert it to bouts of illnesses under the assumption that an antibiotic script is prescribed for seven days. We then multiply it by the NHS tariff for microbiology testing that is in place that year.

The total welfare in a period t is the sum of consumer surplus, producer surplus, the tax revenue, net of the testing cost

$$\text{TW}_t = \text{CS}_t + \text{PS}_t + \text{Tax revenue}_t - \text{Testing cost}_t.$$

As mentioned above, we focus on changes in total welfare. We convert the monetary change of welfare to pounds per 1000 inhabitants, knowing that the UK population between 2003 and 2013 was 61.8M.

C.2. **Marginal costs.** As described above, the first step for tax simulations is to back out the marginal costs for each drug. Figure C-1 provides the marginal costs aggregated by broad- and narrow-spectrum categories.

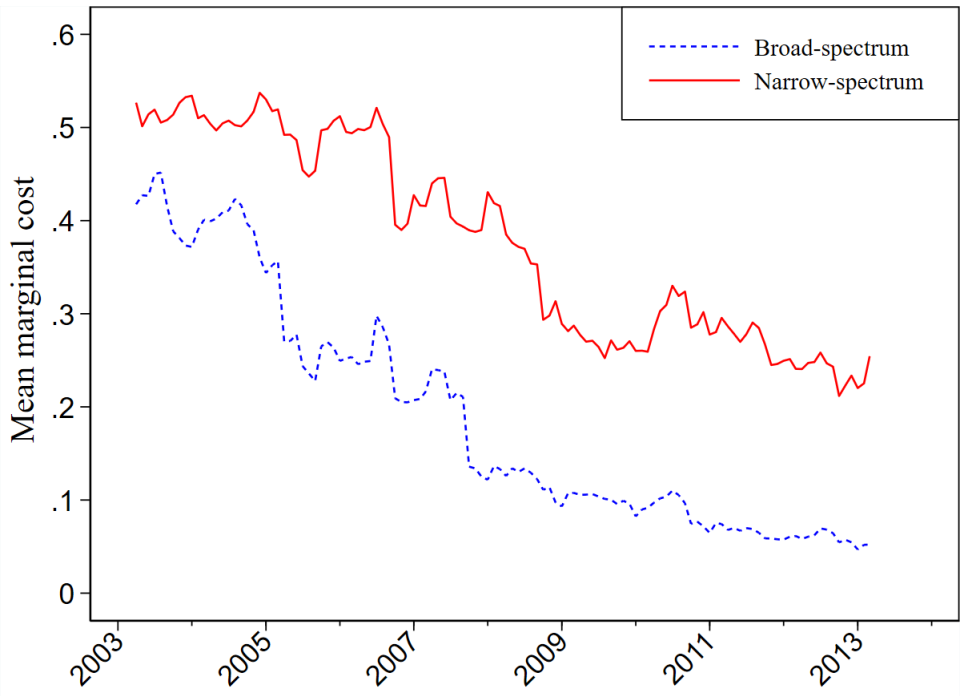

FIGURE C-1. Estimated marginal cost

The marginal cost of producing antibiotics is decreasing over time, perhaps because of improvements in production technologies (Arcidiacono et al., 2013).

We also back out the price-cost margins for all drugs in all years. Table C-4 provides weighted averages by molecules for select years and overall. Note that the implied margin is between the retail price and the marginal cost of production and hence it contains margins earned by manufacturers, wholesalers, and retailers. Our data and estimation strategy does not allow these to be separated into individual components in the supply chain. There is considerable variation in profitability across individual molecules, ranging from as low

as 13.3% to 99.5%. For some generics in the UK, margins can be considerably high as noted elsewhere as well: by one estimate, the margin at the retail level alone can be as high as 76.6% (Kanavos, 2007). Overall broad-spectrum drugs are slightly more profitable (46% vs 43.8%), with the difference being larger in the earlier years than later.

TABLE C-4. Average margins by molecule

Margins $(100 \times (p-c)/p)$	2004	2008	2012	All Years
broad-spectrum	30.0	51.0	60.0	41.9
Narrow-spectrum	26.4	31.1	42.0	33.2
Overall	28.3	39.4	48.2	37.0

Means weighted by market shares

C.3. **Ad valorem tax, year 2012 only.** Table C-5 is the analog of Table 6 and provides the estimates from the ad valorem tax exercises for just the year 2012.

TABLE C-5. Ad valorem tax (5 or 20%). 2012

		Tax on all antibiotics		Tax on all broad-spectrum		Tax on broad-A	
		5% (1)	20% (2)	5% (3)	20% (4)	5% (5)	20% (6)
% Δ price	Broad-A†	4.99	21.5	4.84	21.1	4.80	21.1
	Broad-B‡	4.51	17.2	4.38	16.7	-0.60	-1.47
	Broad	4.84	20.2	4.70	19.8	3.14	14.2
	Narrow	5.01	20.4	-0.05	-0.16	-0.05	-0.16
	Combined	4.93	20.3	2.22	9.38	1.48	6.71
% Δ quantity	Broad-A	-7.47	-25.7	-9.09	-29.3	-9.07	-30.0
	Broad-B	1.22	4.48	0.30	1.34	0.57	1.62
	Broad	-0.38	-1.08	-1.43	-4.31	-1.21	-4.21
	Narrow	-3.44	-12.2	0.65	2.12	0.54	2.01
	Combined	-1.63	-5.65	-0.58	-1.68	-0.49	-1.66
Δ CS		-55.3	-201	-14.4	-49.8	-11.0	-42.1
Δ profits (PS)		-39.0	-135	-14.4	-49.4	-3.8	-9.7
Δ tax revenue (TR)		70.3	234	23.8	75.7	10.3	30.0
Δ testing cost (TC)		-66.5	-236	12.6	40.9	10.4	38.9
Δ Total welfare (TW)		42.5	134	-17.6	-64.4	-14.9	-60.7

The monetary change in welfare is measured as pounds per 1000 inhabitants per year for 2012. All figures are converted to 2003 real value. For equivalent values for the average from all years, see Table 6. $TW = CS + PS + TR - TC$. †Broad-A group consists of co-amoxiclav, quinolones (ciprofloxacin, levofloxacin, and ofloxacin), and cephalosporins (cefalexin, cefixime). ‡All other broad-spectrum drugs.

C.4. **5% Ad valorem tax on broad-A only, all years.** Figure C-2 is the analog of Figure 3 given in the main text. Whereas the figure in the main text provides welfare calculations by period for the ad valorem tax of 20% on broad-A drugs, Figure C-2 does so for a 5% ad valorem tax on broad-A drugs.

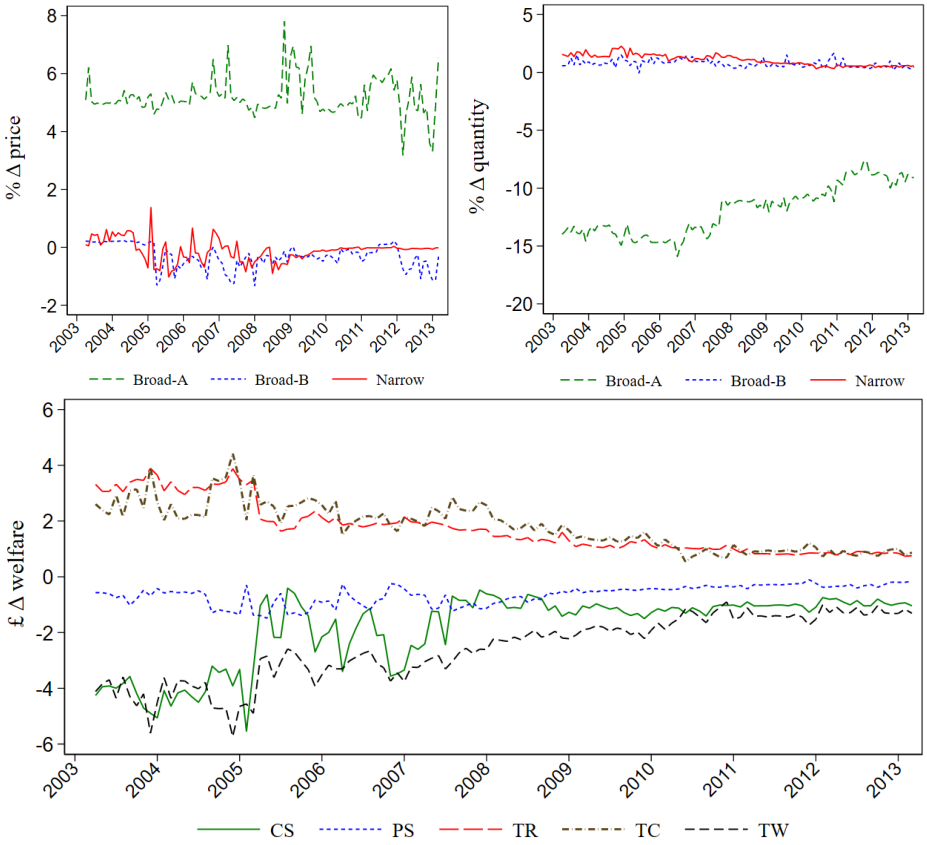

FIGURE C-2. 5% Ad valorem tax on broad-A antibiotics

C.5. **Per unit tax.** Table C-6 gives the results of imposing a unit tax on either all broad-spectrum drugs or just on broad-A drugs as described in the main text. The unit tax is equal to the difference in the marginal costs between broad- and narrow-spectrum drugs and is of the order of £0.10 for all periods but varies slightly for each month and year.

TABLE C-6. Per unit tax

		2012		All years	
		Tax on all broad (1)	Tax on broad-A (2)	Tax on all broad (3)	Tax on broad-A (4)
%Δ price	Broad-A†	49.40	54.71	35.64	38.09
	Broad-B‡	87.64	-1.646	67.38	-1.134
	Broad	61.13	37.42	46.24	24.99
	Narrow	-1.740	-0.466	-1.411	-0.660
	Combined	28.38	17.68	21.71	11.78
% Δ quantity	Broad-A	-63.83	-76.24	-56.24	-64.86
	Broad-B	-71.59	4.260	-73.26	4.324
	Broad	-70.16	-10.57	-69.56	-10.70
	Narrow	32.56	4.924	26.32	5.250
	Combined	-28.22	-4.268	-30.42	-4.174
Δ CS		-17.11	-23.55	-114.3	-57.4
Δ profits (PS)		-134.6	-14.43	-144.6	-20.9
Δ tax revenue (TR)		611.0	103.5	526.8	109.4
Δ testing cost (TC)		631.5	95.30	520.4	106.2
Δ Total welfare (TW)		-172.2	-29.80	-252.5	-75.1

The monetary change of welfare is measured as pounds per 1000 inhabitants per year either for 2012 or as the average from all years. All figures are converted to 2003 real value. TW = CS + PS + TR − TC. †Broad-A group consists of co-amoxiclav, quinolones (ciprofloxacin, levofloxacin, and ofloxacin), and cephalosporins (cefalexin, cefixime). ‡All other broad-spectrum drugs.

C.6. **Logit/Nested logit vs RCNL in ad valorem taxes.** Substitution to narrow-spectrum or broad-B drugs under the IV-logit model is very different from our preferred RCNL model. For instance, a 5% or 20% tax on broad-A drugs decreases the quantity of broad-A drugs by 11.83% or 37.73% (see the last two columns of Table C-7). For the same tax, the logit model predicts a decrease in quantities by 0.79% and 2.95% respectively. By contrast, the nested-logit model gives results that are not too different from the RCNL when the tax is imposed on just broad-A drugs (again, see the last two columns). However, they differ quite substantially and do not generate plausible results when we compare the tax on all antibiotics (first two columns of Table C-7) or on all broad-spectrum drugs (columns 3 and 4 of Table C-7). In both of these cases, the nested logit model predicts an increase in the quantity of broad-B drugs whereas RCNL predicts a decrease in consumption of broad-B drugs.

Accordingly, we think there is a benefit to using the RCNL model as it can overcome IIA and at least in this application seems to generate more plausible substitution patterns relative to the logit or nest-logit models.

TABLE C-7. Ad valorem tax. Comparing models

		Tax on all antibiotics		Tax on all broad-spectrum		Tax on broad-A	
		5% (1)	20% (2)	5% (3)	20% (4)	5% (5)	20% (6)
RCNL							
% Δ quantity	Broad-A†	-8.69	-29.35	-11.18	-36.01	-11.83	-37.73
	Broad-B‡	-0.36	-1.04	-1.75	-6.37	0.75	2.55
	Broad	-2.17	-7.19	-3.80	-12.81	-1.98	-6.20
	Narrow	-5.47	-18.96	1.60	5.64	1.02	3.55
	Combined	-3.73	-12.71	-1.71	-5.68	-0.79	-2.29
Nlogit							
% Δ quantity	Broad-A	-12.88	-37.44	-14.21	-39.38	-14.15	-38.70
	Broad-B	2.19	5.78	0.80	2.93	0.84	2.26
	Broad	-1.09	-3.61	-2.46	-6.26	-2.41	-6.63
	Narrow	-5.78	-18.18	0.82	2.05	0.85	2.36
	Combined	-3.28	-10.30	-1.28	-3.32	-1.19	-3.23
Logit IV demand§							
% Δ quantity	Broad-A	-0.69	-2.63	-0.78	-2.93	-0.79	-2.95
	Broad-B	0.09	0.30	-0.01	-0.01	0.04	0.13
	Broad	-0.15	-0.58	-0.24	-0.89	-0.21	-0.80
	Narrow	-0.54	-1.81	0.04	0.16	0.04	0.15
	Combined	-0.34	-1.19	-0.12	-0.45	-0.11	-0.40

The change is the average value from all years. †Broad-A group consists of co-amoxiclav, quinolones (ciprofloxacin, levofloxacin, and ofloxacin), and cephalosporins (cefalexin, cefixime). ‡All other broad-spectrum drugs. §In this simulation, negative marginal costs are replaced by 0.

Appendix D. Estimation details

D.1. **The nonlinear GMM estimator.** To explain the estimator, we begin by summarizing the demand and pricing equations. We establish a relationship between the observed market shares, denoted as s_{jt}, and the approximated market shares derived from 100 simulations based on four independent standard normal distributions. These distributions are associated with the constant, price, spectrum, and pack variety, respectively. The simulated market share is then expressed as follows:

$$s_{jt}(\delta_t, \sigma, \rho) = \frac{1}{100} \sum_{i=1}^{100} \phi_{ijt}(\cdot). \tag{D-1}$$

We utilize the previously defined ϕ_{ijt} from equation (2) from the main text, along with $\delta_t = X_t\beta + \xi_t$, which represents the $J_t \times 1$ vector of mean utilities. Notably, one of the columns in the matrix X_t corresponds to the (minus) price vector $(-)p_t$. It is important to address the mean price coefficient separately, denoted as β_p, as its entry in our estimator follows a non-linear relationship.

The compact form for each market t is a system of J_t equations. On the left-hand side, we have the observed market shares, and on the right-hand side, we represent the simulated market shares. This system of equations can be expressed as:

$$s_t = s_t(\delta_t, \sigma, \rho). \tag{D-2}$$

By applying an inversion technique to the market share function with respect to the corresponding mean utility, we obtain the following:

$$\delta(s_t, \sigma, \rho) = s_t^{-1}(s_t, \sigma, \rho). \tag{D-3}$$

In the context of RCL and RCNL, the inversion of market share functions necessitates the utilization of a contraction mapping technique, as detailed in Berry 1994. By employing this inversion process, we can effectively determine the demand-side residuals that play a pivotal role in characterizing the demand side of the estimator. These residuals hold crucial information regarding the relationships between market shares and the underlying demand factors, i.e.,

$$\xi_t(\theta_1) = \delta(s_t, \rho, \sigma) - X_t\beta, \tag{D-4}$$

with $\theta_1 \equiv \{\beta, \rho, \sigma\}$.

Likewise, we can reframe the system of J_t pricing equations (6) from the main text in terms of the residuals, resulting in the following representation:

$$\omega_t(\theta) = \ln(p_t - m_t(\theta_1)) - W_t\gamma. \tag{D-5}$$

Each demand and pricing residual can be represented compactly as $\eta_{jt}(\theta) \equiv (\xi_{jt}(\theta_1), \omega_{jt}(\theta))'$, where θ denotes the set of all parameters.

For identification, we rely on the moment restrictions given by:

$$E(\eta_{jt}(\theta)|Z_t) = 0, \tag{D-6}$$

where Z_t includes the non-overlapping exogenous variables X_t (excluding the price), W_t, and the additional instruments discussed in the main text.

Following the approach in Berry et al. (1995), we standardize the residuals of the demand and pricing equations, denoted as η_{jt}. Assuming homoscedasticity in the variance-covariance of the residual pair, i.e., $\Omega = E(\eta_{jt}(\theta)\eta_{jt}(\theta)')$, we perform the Cholesky decomposition to obtain:

$$T(Z)'T(Z) = \Omega(Z)^{-1}. \tag{D-7}$$

Next, let $H_{jt}(Z_t)$ be the $L \times 2$ matrix of instruments. Utilizing the moment restrictions from equation (D-6) and the standardization from equation (D-7), we can express the $L \times 1$ moment restrictions, assumed to be *iid* over T markets, as follows:

$$g(\theta) \equiv E\left(H_{jt}(Z_t)T(Z)\eta_{jt}(\theta)\right) = 0. \tag{D-8}$$

The objective is to minimize the sample-equivalent of the nonlinear (in some parameters) general method of moments function:

$$\arg\min_{\theta} g'(\theta)Wg(\theta), \tag{D-9}$$

where W represents an $L \times L$ weighting matrix.

D.2. **The optimal instruments.** Reynaert and Verboven (2014) propose the use of optimal instruments to enhance the efficiency of the random coefficients and provide insights into their application. In this section, we adapt their explanation to suit our model.

Optimal instruments refer to the conditional expectations (based on a specific set of instruments) of the gradients of the residual functions concerning the parameters. These instruments aim to improve the precision and accuracy of our estimation, and are expressed as:

$$E\left(\frac{\partial \eta_{jt}(\theta)}{\partial \theta'}|Z_t\right), \tag{D-10}$$

whose elements are:

$$\begin{pmatrix} E\left(\frac{\partial \xi_{jt}(\theta)}{\partial \beta'_{-[p]}}|Z_t\right) & E\left(\frac{\partial \xi_{jt}(\theta)}{\partial \beta_p}|Z_t\right) & E\left(\frac{\partial \xi_{jt}(\theta)}{\partial \sigma'}|Z_t\right) & E\left(\frac{\partial \xi_{jt}(\theta)}{\partial \rho}|Z_t\right) & 0 \\ 0 & E\left(\frac{\partial \omega_{jt}(\theta)}{\partial \beta_p}|Z_t\right) & E\left(\frac{\partial \omega_{jt}(\theta)}{\partial \sigma'}|Z_t\right) & E\left(\frac{\partial \omega_{jt}(\theta)}{\partial \rho}|Z_t\right) & E\left(\frac{\partial \omega_{jt}(\theta)}{\partial \gamma'}|Z_t\right) \end{pmatrix},$$

and denoting with $\beta_{-[p]}$ all the parameters β but the coefficient associated with (minus) the price, β_p. With Δ_t defined in equation (5), the elements of the matrix are:

- $E\left(\frac{\partial \xi_{jt}(\theta)}{\partial \beta'_{-p}}|Z_t\right) = -E(x_{[-p]jt}|Z_t) = -x_{[-p]jt}$
- $E\left(\frac{\partial \omega_{jt}(\theta)}{\partial \gamma'}|Z_t\right) = -E(w_{jt}|Z_t) = -w_{jt}$
- $E\left(\frac{\partial \xi_{jt}(\theta)}{\partial \beta_p}|Z_t\right) = E(p_{jt}|Z_t) \approx \widehat{p}_{jt}$

- $E\left(\frac{\partial \omega_{jt}(\theta)}{\partial \beta_p}|Z_t\right) = -E\left(\frac{\left[\Delta_t^{-1}\left(\frac{\partial \Delta_t}{\partial \beta_p}+\frac{\partial \Delta_t}{\partial \xi_t}\frac{\partial \xi_t}{\partial \beta_p}\right)\Delta_t^{-1}s_t\right]_j}{c_{jt}}|Z_t\right)$
- $E\left(\frac{\partial \xi_{jt}(\theta)}{\partial \sigma'}|Z_t\right) = E\left(\frac{\partial \delta_{jt}(s_t,\sigma)}{\partial \sigma'}|Z_t\right)$
- $E\left(\frac{\partial \xi_{jt}(\theta)}{\partial \rho}|Z_t\right) = E\left(\frac{\partial \delta_{jt}(s_t,\sigma)}{\partial \rho}|Z_t\right)$
- $E\left(\frac{\partial \omega_{jt}(\theta)}{\partial \sigma'}|Z_t\right) = -E\left(\frac{\left[\Delta_t^{-1}\left(\frac{\partial \Delta_t}{\partial \sigma'}+\frac{\partial \Delta_t}{\partial \xi_t}\frac{\partial \xi_t}{\partial \sigma'}\right)\Delta_t^{-1}s_t\right]_j}{c_{jt}}|Z_t\right)$
- $E\left(\frac{\partial \omega_{jt}(\theta)}{\partial \rho}|Z_t\right) = -E\left(\frac{\left[\Delta_t^{-1}\left(\frac{\partial \Delta_t}{\partial \rho}+\frac{\partial \Delta_t}{\partial \xi_t}\frac{\partial \xi_t}{\partial \rho}\right)\Delta_t^{-1}s_t\right]_j}{c_{jt}}|Z_t\right)$

The sample equivalent of the transpose of equation (D-10) involves introducing a new variant of the matrix H of instruments, while the GMM procedure explained in equations (D-8) and (D-9) remains unchanged. The only distinction between our estimator and the approach described by Reynaert and Verboven (2014) and Conlon and Gortmaker (2020) lies in the standardization of the optimal instrument functions. Instead of using variance, we standardize with respect to the Cholesky matrix, which corresponds to a standard deviation in the univariate case. This approach aligns with the non-optimal instrument variants of estimators used throughout the rest of the paper. For detailed procedure steps, refer to Appendix A of Reynaert and Verboven (2014). Additionally, we fit the approximation of $E(p_{jt}|Z_t)$, denoted as $\hat{p}_{jt}$, as described in Berry et al. (1999). When we divide the elements of the system of equations (D-10) by the marginal cost, we adjust it for our transformation, $1 + c_{jt}$.

D.3. **Chamberlain's Method.** Due to the presence of product dummies, some characteristics that remain constant over time cannot be discerned in the linear part of the model due to multicollinearity. Following the approach of Chamberlain (1982) and Nevo (2000), we employ the minimum distance method to recover their coefficients.

Let $d = (d_1, d_2, ..., d_J)'$ represent the $J \times 1$ vector of coefficients for the product dummies, X denotes the $J \times K$ matrix containing K product characteristics we aim to estimate, and ξ stand for the $J \times 1$ vector of unobserved product attributes. The minimum distance method essentially projects the values of the product dummies onto X.

Formally, we have the equation: $d = X\beta + \xi$. Assuming $E[\xi|X] = 0$, the estimated coefficients β associated with the K characteristics in X can be calculated as $\hat{\beta} = \left(X'\hat{V}_d^{-1}X\right)^{-1}X'\hat{V}_d^{-1}\hat{d}$, where $\hat{d}$ represents the estimated coefficients of the product dummies from the main regression, and $\hat{V}_d$ is the estimated variance-covariance matrix associated with them.