Substituting Patterns and Product Entry: Evidence from Abuse-Deterrent Drug Introductions in New Hampshire

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Word Count: 5,636

Abstract

In the years following OxyContin reformulation, there have been numerous abuse-deterrent formulations of opioid analgesics introduced into the market. How have these new formulations affected substitution patterns? Using a structural demand approach, I find that the introduction of Hysingla ER in 2015 diverted approximately 80,000 tablets from more abused alternatives for claims made local to New Hampshire drug providers. This theoretically diverted 1,000 out of 18,000 prescriptions away from opioids with higher abuse potential than Hysingla ER.

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1 Introduction

The saying goes that you can lead a horse to water, but you cannot make it drink. In other words, you can reformulate OxyContin for abusers but cannot force them to take it. In fact, it has been well documented that OxyContin reformulation coincided with a sharp spike in reported drug poisonings from other more lethal illicit street drugs like Fentanyl (Powell and Pacula, 2021) and Heroin (Evans et al., 2019). To my knowledge, however, there is not much literature looking into substitution patterns for other prescription drugs after an abuse-deterrent formulation is introduced.

Evans et al. (2019) utilized structural break analysis that provided suggestive evidence that OxyContin reformulation caused a spike in heroin overdoses and found that states with high pre-reformulation oxycodone and heroin use experienced disproportionately more heroin overdoses. Powell and Pacula (2021) showed similar results by looking at a longer time horizon using an event study approach. Both concluded that areas with higher levels of abusers tended to experience more drug overdoses. Based on the findings of the papers, understanding substitution effects should be considered highly important for the prevention of further fatal episodes of overdoses caused by drug reformulation.

The post-OxyContin reformulation era was characterized by a cascade of abuse-deterrent formulations being introduced into the market in a manner that presents numerous empirical challenges. Where numerous drug introductions coincide with and in time periods too close to one another. Thus, causing insufficient control periods for the two-way fixed effect approach, which was not an issue for Janssen and Zhang (2023) which looked at dispensing of retail pharmacies during the OxyContin reformulation. Hence, the structural approach that I am proposing will circumvent this issue by using counterfactual scenarios for abuse-deterrent drug introductions.

I will be using a Micro BLP approach similar to Berry et al. (2004) used in the car market, which allows me to ignore market segmentation. I found this to best exemplify the market as

prescription opioids of often dispensed cross-county and cross-state. From the structural model, I will be able to see how these elasticities vary over time as new formulations are introduced into the market. Additionally, with the estimated structural parameters I will be able to construct the counterfactual case where no new abuse-deterrent introduction to see the impact of the new formulations.

To further validate the model I will examine the association between the cosine similarity of drug labels and the cross-price elasticities from the structural model. In theory, drug products with similar labels should be more substituted, that higher similarity means higher cross-price elasticity. Therefore, if I find this to be the case, it is plausible that the structural model is valid to a limited extent.

2 Background - The Prescription Drug Market

Opioids are narcotic pain relievers only available through prescriptions for patients experiencing moderate-severe acute pain symptoms. It is the largest controlled substance in terms of units dispensed and is one of the most significant sources of drug poisoning alongside heroin in the United States. It has caused untold social and economic welfare loss for the United States which cannot be understated. The magnitude of the opioid crisis has spurred the development of numerous strategies to reduce the abuse potential of opioid analgesics. The development of abuse-deterrent formulations has been one such avenue to this endeavor which I will focus on in this study.

Abuse-deterrent reformulation can be defined as changes made to a drug that do not affect its medical use and pharmacological effects unless tampered with. The possible methods of tampering involve consuming the drug through unintended methods of intact. For example, OxyContin pre-reformulation[1], was typically crushed and subsequently snorted. This causes

[1]There is a difference between reformulation and formulation. Reformulation involves changes made to an existing product and formulation is often a new drug introduction.

the drug to be released more rapidly and thus, intensifies euphoric effects that would be more desirable for drug abusers. After reformulation, OxyContin was made to have abuse-deterrent properties, that made the drug more difficult to crush. However, the reformulation did not make any changes to its pharmacological effects in its intended form of use.

2.1 Obtaining a Prescription

Before someone can go into a drug store to obtain a controlled substance, they must first obtain a prescription. Typically, prescriptions are received from a doctor's visit or a nurse practitioner. The patient will then discuss their symptoms, and medical history, and may receive a medical examination. If deemed necessary, the healthcare provider will write a prescription for a specific medication to treat their conditions.

2.2 Prescription Details and Methods of Substitution

The relevant information on the prescription for my purposes is the medication details. It details the drug name, dosage instructions, quantity, and the number of refills allowed. Additionally, the prescription may allow for 'generic substitution' and 'therapeutic substitution'. Generic substitution occurs when a pharmacist dispenses a generic version of the prescribed medication instead of the brand-name product. Generic drugs are bio-equivalent to their branded counterpart. The FDA classifies bio-equivalence as 'absence of a significant difference between two or more products in the rate and extent of absorption at the site of drug action when administered at the same molar dose under similar conditions' (Food et al., 2003). However, this does not necessarily mean that a generic version of a branded drug will also hold the same abuse-deterrent qualities. It may be the case that upon the end of the patent period, there is substitution to less abuse-deterrent generic version of the abuse-deterrent branded one.

Therapeutic substitution involves substitution between different drug names within the same drug class. Much like generic substitution, this is done at the pharmacist's discretion with the

consent of the patient. Therefore, it is possible for other drugs of the same class to be dispensed that are distinct from the drug name on prescription. Therefore, the prescription itself does not necessarily restrict the choice set to a specific drug name but to a whole class of drugs. Substitutions in this case are quite different in that it requires the approval of the prescriber as well (Keely et al., 2002).

2.3 Pharmacy Options

With a prescription in hand, the patient has several options to obtain the medication. The traditional method would be through a retail pharmacy. They are publicly accessible and typically require the patient to go to the pharmacy with their prescription to obtain their medication. There is a licensed pharmacist there to fill prescriptions and provide other pharmacy-related services.

The other methods which are getting more popular are online and mail-order pharmacies[2], which do not require traveling to a location to obtain medication, cutting transportation costs. It is worth mentioning this now, as it is one of the key oversights of my analysis.

2.4 Purchase Options

Patients are faced with the choice of payment out-of-pocket or through insurance. This component will be observable given the data I have to some extent. That is because I will be using data on pharmacy claims, which means that we do not observe out-of-pocket purchases of prescription drugs. Nevertheless, given that I only observe prescription purchases through insurance claims, insurance coverage works through the following components:

1. **Co-payments:** also known as co-pays, are fixed amounts that insured individuals are required to pay out-of-pocket for certain prescription medications or medical services.

[2] Although, within more recent years, from 2005 - 2018, mail-order pharmacy decline from 17% to 15.7% in the United States (Do and Geldsetzer, 2021).

The specific co-payment amount may vary depending on the health insurance plan and the type of medication being prescribed. For example, a health insurance plan might have a co-payment of $10 for generic drugs and $30 for brand-name drugs.

2. **Coinsurance:** Coinsurance is a cost-sharing mechanism in health insurance where the insured individual is responsible for paying a percentage of the total cost of a prescription medication or medical service. Unlike co-payments, which are fixed amounts, coinsurance requires the insured to pay a percentage of the total cost, while the insurance company covers the remaining percentage. For instance, if the coinsurance rate is 20% and the prescription's total cost is $100, the insured would pay $20, and the insurance company would cover the remaining $80.

3. **Deductibles:** Deductibles refer to the initial amount that insured individuals must pay for covered medical services or prescription drugs before their insurance coverage kicks in. Once the deductible is met, the insurance company begins to pay a portion or all of the costs as outlined in the policy. Deductibles are typically assessed on an annual basis. For example, if a health insurance plan has a $500 deductible, the insured must pay the first $500 of medical expenses before the insurance starts covering the costs.

The fact that I do not observe out-of-pocket purchases may be problematic in a number of ways. It is reasonable to believe that those diverting drugs may choose to refrain from making insurance claims to avoid detection. However, there is also reason to assume that not everyone diverting will behave in this way. It may be the case that the patient legitimately needs the prescribed drug for medical purposes but will divert a fraction of the prescribed amount as street prices for prescription drugs are often many times more expensive than their retail counterparts (El-Aneed et al., 2009). This leads to the much-needed discussion on the methods of drug diversion.

2.5 Sources of Drug Diversion

Drug diversion, the acquisition of drugs for purposes other than medical use, can occur at various levels of the prescription drug market. It can first occur at the beginning of entry into this market, from the prescription itself. There are two distinct methods of diversion at this stage, forging prescriptions and illegal prescribing. Forgery of prescriptions can involve tampering with a legitimate prescription by changing what is already written on the prescription like increasing the number of refills, to theft and a purely fabricated prescription. This form of diversion may be subject to unobservability in the context of claims data.

On the other hand, illegal prescribing might be less detectable as the prescription itself is legitimate and diverters may be more confident in making an insurance claim. Therefore, any observed changes in substitution patterns may be more attributable to this form of diversion compared to forged prescriptions. The extent to which this occurs in New Hampshire is not apparent but in the context of Newfoundland and Labrador in Canada, El-Aneed et al. (2009) found that 98% of oxycodone prescriptions were prescribed by only 3% of all the physicians in the province. Thus, it is plausible that illegal prescribing may be a prominent source of diversion.

The next source of diversion will come in the pharmacy options, it is up to the pharmacist at a particular location to dispense the medication to patients. Pharmacists have a substantial degree of discretion with regard to the drugs they dispense. Through generic and to a lesser extent therapeutic substitution, patients may be given considerable choice as to which drug products they can choose.

2.6 Abuse-Deterrent Formulations of Interest

The following drugs are some key examples of abuse-deterrent drug introductions. Targiniq ER was approved in the United States in July 2014. This formulation combines Oxycodone with

Naloxone – an antagonist[3] that only activates when the tablet is tampered with. Hysingla ER is an abuse-deterrent formulation of Hydrocodone that was approved in the US in November 2014. MorphaBond ER is the first abuse-deterrent extended-release morphine product without an antagonist to be approved by the FDA (October 2015) in the United States. The aforementioned drugs have been labeled by the FDA as abuse-deterrent.[4]

Given the constraints related to the data, I will only be able to look into the impacts of Hysingla ER upon introduction. Containing Hydrocodone, Hysingla ER is one of the more potent opioid analgesics, being 10 times more potent than codeine and similar to morphine also in terms of adverse effects (O'Malley, 2015). The barrier formulation of Hysingla ER makes it more difficult to crush, break, or dissolve. Additionally, it has the property of turning into a viscous hydro-gel for those trying to inject it (O'Malley, 2015).

3 Data

The main data set comes from the New Hampshire Comprehensive Health Care Information System (NH CHIS) Public Use Data from 2012 to 2022, which provides me with all the pharmacy claims made within the state of New Hampshire.[5] The NH CHIS data provides information on both claimers and drug providers which will provide some individual-specific characteristics that will help define heterogeneous preferences.

To supplement the NH CHIS data, I will also retrieve more product characteristics from the NDC drug directory provided by the DEA.[6] For each drug, this data provides information on the chemical ingredients and their respective amounts, dosage method, market entry and exit dates, and more. This data will make up the product characteristic space for the structural demand

[3] An opioid antagonist will bind to an opioid receptor which will stop the receptor from producing a response, i.e. preventing euphoric effects desired by abusers.

[4] Aside, there are some other drugs that have been introduced that do not hold the FDA label that could also have abuse-deterrent properties.

[5] You can refer to the data dictionary here for more details on the columns.

[6] I retrieved it from here and file itself is located in the 'Additional References' section

model.

For the text analysis component, I data scraped all the product labels from DailyMed.[7] The product labels for prescription drugs are very comprehensive and contain many sections such as medication guides, warnings and precautions which are available to consumers when purchasing a prescription drug.

4 Model and Empirical Specification

4.1 Demand Estimation

The model in which I am employing is influenced by Berry et al. (2004). Due to the unique nature of my data, however, I will be utilizing a more simplistic version of their model which uses a Maximum Likelihood Estimator as opposed to General Methods of Moments. Additionally, how consumer characteristics enter the model is quite different.

To construct an individual i's utility function, let's start with the individual's choice vector over all schedule II prescription drugs. Where an individual i's choice vector is characterised by $(q_{i1}, q_{i2}, ..., q_{iJ_i})$, where:

$$q_{ij} = \mathbb{1}\{u_{ij} \geq u_{ik} \;\; \forall k \in \{0, 1, ..., J_i\}\}$$

which assumes that the observed choice has the highest utility among all other choices, which is the basic assumption made in all BLP estimations. The consumer-specific utility function will be defined as:

$$u_{ij} = \alpha \, I_i(p_{ij}) + \delta_j + \varepsilon_{ij} \tag{1}$$

$$\delta_j = x_j \beta + \xi_{ij} \tag{2}$$

[7] The data scraping code is available in my GitHub repository here.

For equation (1), δ_j is defined as the mean utility of a product, p_{ij} being a unique price faced by each individual i, and $I_i(\cdot)$ is is a function that transforms the billed price to the amount actually paid by the individual i given their insurance coverage. For equation (2), x_j will contain observed product characteristics with potential interactions with other individual characteristics such as age and gender. By assuming that ε will be distributed by Type 1 extreme-value distribution [8], we can construct the following multinomial logit approach for the market share for individuals i to be:

$$s_{ij} = \frac{exp(\delta_j + \alpha\, I_i(p_{ij}))}{1 + \sum_k exp(\delta_k + \alpha\, I_i(p_{ik}))} \tag{3}$$

Where, p_{ik} will be the average price of product k for $j \neq k$ subject to the observed insurance coverage, $I_i(\cdot)$, for j. This is a rather convenient expression to work with allowing me to use an MLE approach without worrying about integrals.

At this point, I would like to go into a little more detail as to why I constructed the price vector, $I_i(p_{ij})$. Given the structure of the claims data, I do not observe the prices of other drug products that each individual i is faced with. An even more complex issue that needs to be addressed is determining the appropriate choice set J_i for each i.

To address the choice set for each i, if I restrict the choice set to drugs available at the pharmacy where the claims were made. It assumes that each individual is restricted to drugs sold at a single pharmacy. This is an unreasonable assumption, given that the majority of claims are made out of state which suggests that pharmacy substitution may be subject to low costs.

Alternatively, I decided to include all schedule II drugs as the choice set which assumes that all individuals are faced with the same choice set. This assumption may be too general, however, this allows the inclusion of stimulants. Abusers are known to use both opioids and stimulants in tandem to mask the undesirable effects of each other (Compton et al., 2021). If we find that stimulants tend to have more inelastic cross-prices with respect to opioids, then it

[8] see Rasmusen (2007) under the multinomial logit section.

would suggest that abusers, to some extent, are influencing the results. If the inverse holds, it may suggest that abusers are diverting through other mediums.

Second, to explain the prices of other products more thoroughly, I used market-level prices for each alternative product for the billed amount.[9] Furthermore, by applying $I_i(\cdot)$ to each alternative product, I assume that the current observed coverage can also be applied to all other drugs of the same schedule. This gives me a unique price vector that depends on i and j, acting as an interaction between individual and product characteristics which will determine substitution patterns in this model (McFadden et al., 1977).[10]

For now, let us assume no endogeneity in prices. I will be using Maximum Likelihood Estimation, where I will maximize the joint probability of observing the choices made by all i to estimate α and δ:

$$L(\alpha,\delta) = \prod_{i=1}^{N} \mathbb{P}(q_{ij})$$
$$lnL(\alpha,\delta) = \sum_{i=1}^{N}\sum_{j=1}^{J} 1\{Y_i = j\} ln(s_{ij}) \tag{4}$$

Where $1\{Y_i = j\}$ means that we are only summing the logarithm of observed individuals i making claims for product j. This concludes the first-step estimation approach but in the Appendix, I outline a next-step estimation that will incorporate more interactions between product and individual characteristics.

[9] the price that would be paid out-of-pocket without insurance coverage

[10] Typically, prices are considered a product characteristic. Given that insurance coverage is unique to each i, this essentially acts as an interaction.

4.2 Estimation of Demand Elasticities

After maximizing equation (4) for α and δ, I will have $\hat{\delta}$'s and $\hat{\alpha}$ which I can back out estimated individual choice probabilities, $\hat{s}_{ij}$, with the following:

$$\hat{s}_{ij} = \frac{exp(\hat{\delta}_j + \hat{\alpha}\, I_i(p_{ij}))}{1 + \sum_k exp(\hat{\delta}_k + \hat{\alpha}\, I_i(p_{ik}))} \tag{5}$$

To get the market share for product j we can simply sum up all the choice probabilities for each product as such:

$$\hat{s}_j = \sum_{i=1}^{N_j} \hat{s}_{ij} = \sum_{i=1}^{N_j} \frac{exp(\hat{\delta}_j + \hat{\alpha}\, I_i(p_{ij}))}{1 + \sum_k exp(\hat{\delta}_k + \hat{\alpha}\, I_i(p_{ik}))} \tag{6}$$

With estimated markets, $\hat{s}_j$, I can compare it against the observed market share to examine how well the model fits the data. An important note, in the way the model is constructed, market shares can be understood as the proportion of claims made for a product j. This assumes that individuals do not have a choice over the quantity of product they will be receiving. This is an assumption I am willing to make, as the pharmacist will only dispense the amount specified on the prescription.[11]

To calculate demand elasticities, I follow closely the derivation from Rasmusen (2007). I would require $\frac{\partial s_j}{\partial p_k}$ for products k. Let's simplify the market share by using the following substitution:

$$M_{ij} \equiv exp(\hat{\delta}_j + \hat{\alpha}\, I_i(p_{ij}))$$

Therefore, equation (6) becomes:

$$\hat{s}_j = \sum_{i=1}^{N_j} \frac{M_{ij}}{1 + \sum_k M_{ik}}$$

[11] Additionally, this assumes no diversion made on the pharmacist's behalf, which might be problematic given the previous work done by Janssen and Zhang (2023).

Now taking the partial derivative with respect to product k, we have:

$$\frac{\partial \hat{s}_j}{\partial p_k} = \sum_{i=1}^{N_j} \frac{\partial \hat{s}_{ij}}{\partial p_k}$$

where,

$$\frac{\partial \hat{s}_{ij}}{\partial p_k} = \frac{\partial}{\partial p_k}\left(\frac{M_{ij}}{1+\sum_k M_{ik}}\right)$$

By product rule we have,

$$\frac{\partial \hat{s}_{ij}}{\partial p_k} = \left[\left(\frac{\partial M_{ij}}{\partial p_k}\right)\left(\frac{1}{1+\sum_k M_{ik}}\right) + M_{ij}\left(\frac{-1}{(1+\sum_k M_{ik})^2}\right)\left(\frac{\partial M_{ik}}{\partial p_k}\right)\right]\left(\frac{\partial I_i}{\partial p_k}\right)$$

Let's first consider the case of $j \neq k$ where $\frac{\partial M_j}{\partial p_k} = 0$ and $\frac{\partial M_k}{\partial p_k} = \hat{\alpha} M_k$. Additionally, I will assume that $\frac{\partial I_i}{\partial p_k}$ is simply the coinsurance for individual i, c_i. Then,

$$\begin{aligned}
\frac{\partial \hat{s}_{ij}}{\partial p_k} &= \left(\frac{-M_{ij}}{(1+\sum_k M_{ik})^2}\right)(\hat{\alpha} c_i M_{ik}) \\
&= -\hat{\alpha} c_i \left(\frac{M_{ij}}{1+\sum_k M_{ik}}\right)\left(\frac{M_{ik}}{1+\sum_k M_{ik}}\right) \\
&= -\hat{\alpha} c_i \hat{s}_{ij} \hat{s}_{ik} \\
\frac{\partial \hat{s}_j}{\partial p_k} &= \sum_{i=1}^{N_j} \frac{\partial \hat{s}_{ij}}{\partial p_k} = -\sum_{i=1}^{N_j} \hat{\alpha} c_i \hat{s}_{ij} \hat{s}_{ik} = -\hat{\alpha} \sum_{i=1}^{N_j} c_i \hat{s}_{ij} \hat{s}_{ik}
\end{aligned}$$

Now suppose that $j = k$. Then we have

$$\begin{aligned}
\frac{\partial \hat{s}_{ij}}{\partial p_k} &= \left[\left(\frac{\hat{\alpha} M_{ij}}{1+\sum_k M_{ik}}\right) - \left(\frac{M_{ij}}{(1+\sum_k M_{ik})^2}\right)(\hat{\alpha} M_{ij})\right] c_i \\
&= \hat{\alpha} c_i \left[\left(\frac{M_{ij}}{1+\sum_k M_{ik}}\right) - \left(\frac{M_{ij}}{(1+\sum_k M_{ik})}\right)^2\right] \\
&= \hat{\alpha} c_i (\hat{s}_{ij} - \hat{s}_{ij}^2) = \hat{\alpha} c_i \hat{s}_{ij}(1-\hat{s}_{ij}) \\
\frac{\partial \hat{s}_j}{\partial p_k} &= \sum_{i=1}^{N_j} \frac{\partial \hat{s}_{ij}}{\partial p_k} = \hat{\alpha} \sum_{i=1}^{N_j} c_i \hat{s}_{ij}(1-\hat{s}_{ij})
\end{aligned}$$

Now we can form the demand elasticity formula as the following piece wise function, where the percentage in the market share of product j when the price of product k increases:

$$\varepsilon_{jk}^{D} \equiv \frac{\%\Delta s_j}{\%\Delta p_k} = \frac{\partial s_j}{\partial p_k} \cdot \frac{p_k}{s_j} = \begin{cases} \hat{\alpha} \sum_{i=1}^{N_j} c_i \hat{s}_{ij}(1 - \hat{s}_{ij}) & if\ j = k \\ -\hat{\alpha} \sum_{i=1}^{N_j} c_i \hat{s}_{ij} \hat{s}_{ik} & otherwise. \end{cases} \tag{7}$$

4.3 Counterfactual Analysis for Abuse-Deterrent Drug Introductions

To examine how substitution patterns are affected by abuse-deterrent drug introductions, we would have to set up a counterfactual analysis. Specifically, I will be re-calculating equation (6) by imposing $k \neq Hysingla\ ER$. In other words, I will be assuming that Hysingla ER has zero utility for all individuals as if the product has not been introduced to the market. Afterward, I will calculate its effect based on dispensing by multiplying the counterfactual market shares with their respective aggregate levels of dispensing.

4.4 Cosine Similarity of Drug Labels

For the text analysis portion, I will examine which drug labels are most similar to each other. This will prove useful in validating the demand estimation as I believe cross-price elasticities should be correlated with the similarity of product labels. That is, products with similar labeling would have higher cross-price elasticities with each other, i.e. they are stronger substitutes.

To do this, I will be using cosine similarity to estimate the similarity of drug labels. I will use equation (8) between all combinations of products to construct an adjacency matrix which will then be compared to the matrix of elasticities:

$$cos(\theta) = \frac{\mathbf{A} \cdot \mathbf{B}}{||\mathbf{A}|| \cdot ||\mathbf{B}||} = \frac{\sum_{i=1}^{n} A_i B_i}{\sqrt{\sum_{i=1}^{n} A_i^2} \sqrt{\sum_{i=1}^{n} B_i^2}} \tag{8}$$

Where $\mathbf{A}$ and $\mathbf{B}$ are vectors of equal length n that describe two different texts that will be

compared for similarity. However, a method to represent a chunk of text as a vector must first be implemented. This process is called vectorization and there are many methods to choose from. I decided to use Term Frequency-Inverse Document Frequency (TF-IDF) Vectorization as my vectorizer, which is represented in equation (9):

$$w_{i,j} = tf_{i,j} \cdot log\left(\frac{N}{df_i}\right) \tag{9}$$

where $w_{i,j}$ is the value contained in the i^{th} element of the j^{th} document vector. For term i in a document j, $tf_{i,j}$ is the number of occurrences of term i in document j, $df_{i,j}$ is the number of documents containing term i, and N is the number of documents. The term summarizing term frequency is the $tf_{i,j}$ term, as it assigns a higher value to $w_{i,j}$ when the i^{th} term occurs in higher frequency within each document. The $log\left(\frac{N}{df_i}\right)$ defines the Inverse Document Frequency component, as it assigns a higher value to $w_{i,j}$ when the i^{th} term occurs less frequently across documents. This form of vectorization is quite useful in this application as drug labels contain many standardized sections that are very similar across drug labels. This tends to estimate low variation in drug labels if we were to only use Term Frequency. By adding Inverse Document Frequency, it provides more variation by assigning more weight to terms that occur less often across drug labels, picking up on more subtle differences.

4.4.1 Validation Check

After the cross-price elasticities from the structural demand model and the cosine similarities between drug labels have been estimated, I will be able to see whether there are any relations between them. To do so, I will be employing simple Ordinary Least Squares (OLS), as follows:

$$\varepsilon_{jk}^{D} = \rho cos(\theta_{jk}) + \eta_{jk},$$

where ε_{jk}^{D} is the estimated cross-price elasticity between product j and k, $cos(\theta_{jk})$ is the

cosine similarity between product j and k, and ρ the coefficient expressing the relationship between elasticities and cosine similarities. I will be using a one-sided hypothesis test, if the null hypothesis is rejected, that $H_0 : \rho \leq 0$, then it somewhat validates the structural model in a suggestive sense. As it would mean that higher cosine similarity is associated with higher cross-price elasticities between any two products on average. However, if the null is not rejected it also doesn't necessarily invalidate the model completely. It may be the case that drug labels are not representative of substitution patterns at all. It must also be noted that depending on the vectorizer used, the results here will most likely vary largely. Nevertheless, the inclusion of this specification is more so included for its relative novelty.

5 Results

First, let's consider the first-step estimation from the structural model and see how demand elasticity varies over time for the whole market. The α estimator being the same for all i, j means that we can interpret α as the mean response of demand to the average price increase for all schedule II prescription drugs. Having set no boundary restriction, I have allowed some of the α coefficients to be positive. After running the estimation again with boundary conditions on

Year	$\hat{\alpha}$	Year	$\hat{\alpha}$
2012	0.117831	2018	-0.065510
2013	-0.079810	2019	-0.136877
2014	-0.465751	2020	0.311885
2015	-0.672952	2021	0.096166
2016	-0.041407	2022	0.516330
2017	0.103225		

Table 1: α estimates from the first-step estimation. Note that standard errors are not reported as I could not finish bootstrapping standard errors. These results were computed with the boundary conditions (-100,100).

α making it strictly positive, the coefficient corners at zero for the positive α years. Therefore, reporting the unbounded estimations may be more appropriate to communicate the limitations

of this model. Disregarding the problematic years, it seems that the market experienced higher levels of elasticity in 2014 and 2015 relative to 2018 and 2019. This could be caused by the various drug introduction laid out previously, Targiniq ER in 2014, Hysingla ER, and MorphaBond ER in 2015.

The problematic α estimates may be caused by how the data was processed. As mentioned previously, I took large liberties in what observations I dropped. It seems clear to me at this point that state boundaries do not properly define market segmentation in the prescription opioid market. Over the years online prescription purchases have become more popular as it provides convenience and cheaper costs (Long et al., 2022), this coupled with the Covid-19 pandemic has further pushed individuals to online purchases during and post-lockdown. All these reasons could justify why the α estimates for 2020 onward are positive.

Online pharmacy purchases allow individuals to acquire drugs from outside their state which will bias my results as I have restricted the data to pharmacy claims made at drug providers in New Hampshire. Additionally, there has been speculation and research on the drug diversion potential of online pharmacies (Long et al., 2022). If it is the case that online pharmacies are more susceptible to diversion, there may be fewer cases of diversion at retail pharmacies as abusers are diverting to online pharmacies. Unfortunately, it is not possible with the current data to distinguish between online drug providers and other types of drug providers as the provider names are not provided with the public use data.

Figure 1 best illustrates that in the earlier periods of the data, from 2012-2016, we see higher levels of own-price elasticities across all products compared to future years. The majority of abuse-deterrent formulations were introduced between 2014-2016.[12] It seems that periods in which there are higher levels of own-price elasticity coincide with periods where abuse-deterrent formulations are introduced. However, I notice that products that are claimed more often than others tend to have higher price elasticities, which could be attributed to endogeneity problems. The drugs with noticeably higher levels of dispensing compared to others are

[12]Targiniq ER in 2014, Hysingla ER in the beginning of 2015, and MorphaBond ER in 2015.

Adderall, Oxycodone Hydrochloride and Dextroamphetamine saccharate, amphetamine aspartate monohydrate, dextroamphetamine sulfate, amphetamine sulfate[13].

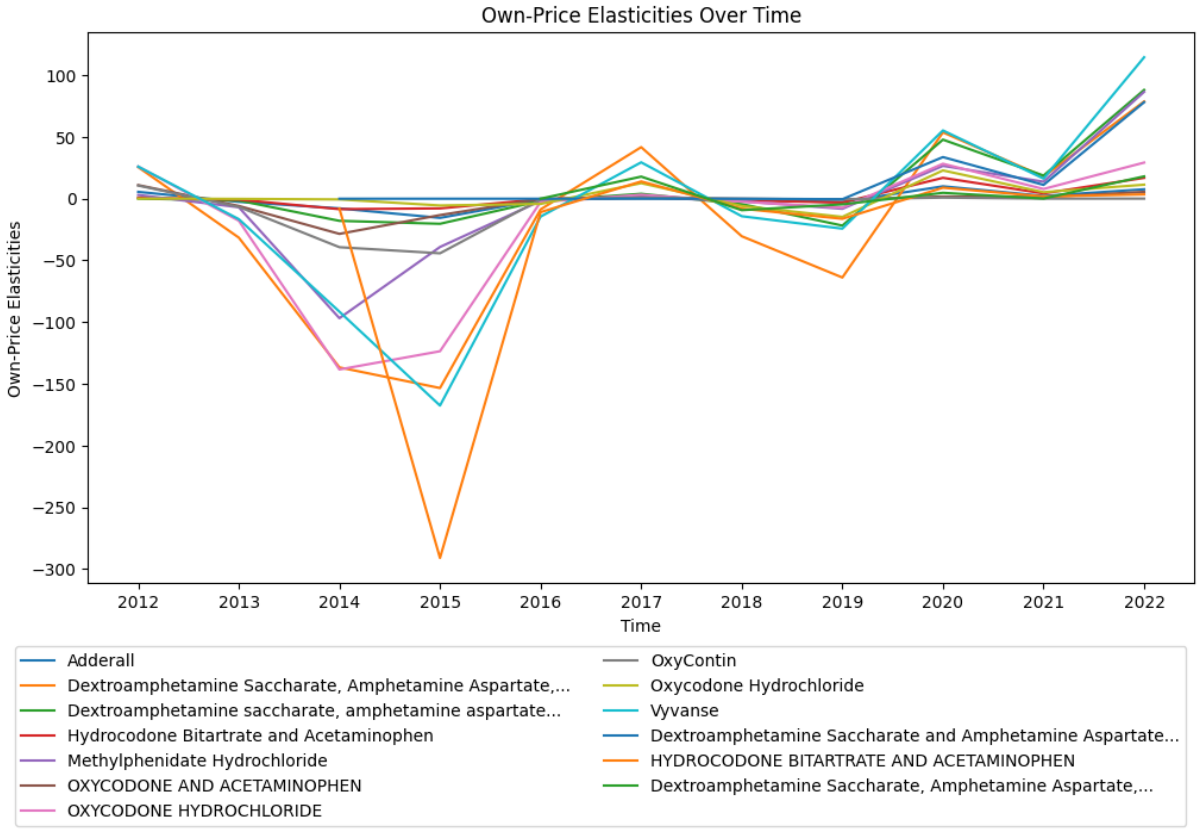

Figure 1: This plot contains only the drugs with the highest variation in own-price elasticity. I specifically filtered out those with magnitude less than 10 as well as drug products that had fewer than 10 claims made for it in each year. This contains a mix of drugs that span the whole time period and those that do not, although this may be hard to see from the plot. Product names that are all capitalized mean that it is a generic version of the branded drug.

Another issue related to the data is that the abuse-deterrent formulations of interest stated earlier in the introduction are not present in the data in its current filtered state. It appears that the majority of pharmacy claims are made outside the state of New Hampshire and claims made outside of New Hampshire report more missing values. This is simply a feature of the public use data which cannot be avoided. This would explain why certain products are much less represented in the data, as certain products are often sourced out of state for a number of

[13] A stimulant that is used to treat ADHD.

reasons. The main reason being legal reasons, as certain products are not allowed in certain states which also would explain why MorphaBond ER is not seen in the data at all.

However, we do observe the introduction of Hysingla ER at the beginning of 2015. I observe its share for the years 2016 and 2019.[14] In *Figure 2*, I have only included the drugs with the highest observed cross-price elasticity with Hysingla ER. Aside from the inclusion of the stimulant (Dextroamphetamine ...), these results seem to suggest that in that Hysingla ER, a branded version of Hydrocodone Bitartrate, price changes affect the demand for the generic version of Hydrocodone Bitartrate and Acetaminophen the most compared to other opioids. This would imply that Hysingla ER being introduced into the market, took market share mostly from the generic version of itself and the other drug products in the *Figure 2*. The degree of this effect is illustrated in *Table 2*. The generic versions included in *Table 2* typically do not have any abuse-deterrent formulations.

From *Table 2*, I have only included the top 5 pain relief drugs in terms of their cross-price elasticity with Hysingla ER. The counterfactual case was constructed by setting the individual choice probability for Hysingla ER to zero. The table was constructed by simply taking the percentage change between estimated market shares between the base scenario, where Hysingla ER was introduced, and the counterfactual scenario, where Hysingla ER was hypothetically not introduced. Within a year, the introduction of Hysingla ER could potentially have diverted the consumption of 80,000 from other pain relief products, the majority of whom do not have abuse-deterrent properties.

However, these results should be taken with a grain of salt, as standard errors have not been reported. The majority of pharmacy claims are made out of state which calls into question the external validity of this model to the whole opioid prescription market in the United States. As previously stated, it may be the case that abusers are making claims out of state as it may be easier to acquire prescription drugs unethically that way. These results can only speak to the local market for prescription opioids in New Hampshire by residents of New Hampshire.

[14] 2017 and 2018 were not included as there were too few claims observed for Hysingla ER.

Hysingla ER Introduction Counterfactual

Product Name	Brand/Generic	%ΔDispensing	ΔDispensed
Oxycodone Hydrochloride	generic	0.116%	32,509 tablets
Oxycodone Hydrochloride	brand	0.117%	12,900 tablets
Hydrocodone Bitartrate and Acetaminophen	generic	0.114%	19,414 tablets
Methylphenidate Hydrochloride	brand	0.125%	7,896 tablets
OxyContin	brand	0.122%	10,534 tablets
		Total:	83,253 tablets

Table 2: Counterfactual Case: If Hysingla ER's was not introduced in 2015. Note: %ΔDispensing is the percentage change in market share between the base and counterfactual scenario, ΔDispensing is the change in total dispensing between the base and counterfactual scenario. This only applies to changes in market share for drug providers in New Hampshire.

Finally, let's look at the elasticities between stimulants and pain relief medications. Due to how cross-price elasticities are computed, we will see no negative cross-price elasticities, hence, no complementary goods. This is due to the model restrictions which place stimulants and opioids within the same choice set. However, we can infer that small cross-price elasticities may be due to the fact that those products may be complementary to each other. *Table 3* seems to follow the conventional belief that stimulants should be substituted more with other stimulants versus opioids, with the exception of Oxycodone Hydrochloride. The table uses Adderall as the stimulant to compare to, as it was a popular drug of abuse during the time and was dispensed in large quantities.

I do not have results regarding the relationship between cross price elasticities and cosine similarities as I was unable to compute cross-price elasticities for all controlled substances. If I were to continue with the current set of products with computed elasticities, it will result in small sample bias. Given that standard errors have not been computed for the elasticities, it would make the OLS standard errors downward biased and thus, not statistically meaningful as I do not know the degree to that bias but I believe it is substantial.

Product Name	Brand/Generic	Drug Type	$\varepsilon^{D}_{j,Adderall}$
Dextroamphetamine Saccharate, Amphetamine Aspartate, Dextroamphetamine Sulfate and Amphetamine Sulfate	brand	Stimulant	1.67
Oxycodone Hydrochloride	generic	Opioid	0.89
Vyvanse	brand	Stimulant	0.82
Methylphenidate Hydrochloride	brand	Stimulant	0.33
OxyContin	brand	Opioid	0.31
Oxycodone and Acetaminophen	generic	Opioid	0.28
Hydromorphone Hydrochloride	brand	Opioid	0.11
Oxycodone and Acetaminophen	brand	Opioid	0.04

Table 3: These are cross price elasticities from 2013 for products with the highest levels of dispensing. $\varepsilon^{D}_{j,Adderall}$ is the cross-price elasticity with respect to Adderall. No standard errors as they have not been computed yet.

6 Conclusion

The preliminary findings so far seem quite promising in uncovering substitution effects related to abuse-deterrent drug introductions. From the counterfactual analysis, I can tentatively state that the introduction of Hysingla ER in the beginning of 2015 did have an impact on the prescription drug market local to New Hampshire. This drug introduction potentially diverted 80,000 tablets prescribed to residents of New Hampshire filing claims in New Hampshire. There were approximately 7,772 individuals with an average of 80 tablets per claim[15] which theoretically, diverted 1,000 individual claims away from other potentially more abusive substances. However, this result examines the effect on a small subset of the New Hampshire population as well as an even smaller subset of abuse potential substances. Further developments must be made to understand the long-term impacts of abuse-deterrent drug introductions, let alone understand its true impact on New Hampshire's prescription drug market as a whole.

Further work must be done to compute standard errors for the structural parameters and also address potential endogeneity problems related to price. Extensions to this model that consid-

[15]These numbers correspond to individual claims made for the drugs examined in Table 2

ers long-term effects must inevitably confront the interstate nature of this market which would require data much like the NH CHIS data but for every state. Although I have discussed various avenues for drug diversion, the model fails to disentangle medical demand from diversion demand directly. Therefore, we cannot assume that the estimated substitution patterns are caused by medical, diversion demand responses, or a combination of the two. Another extension to the model included in the Appendix is the second step to the demand estimation that would potentially bring in more interactions between product and individual characteristics.

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Appendix

All coding files used in the making of this paper can be found here.

Second-Step Demand Estimation

After obtaining $\hat{\delta}$ from the first-step estimation, I will use it in the following OLS specification:

$$\hat{\delta}_j = X_j\hat{\beta} + \xi_{ij}$$

where X_j is a $R \times J$ matrix. X_j will contain J products and R interactions between product and individual characteristics other than insurance coverage. Given the claims data, product characteristics would include active substances and their concentrations[16], method of dosage, generic/brand indicators, and abuse-deterrent indications[17]. Given the claims data, individual characteristics like age and gender, and county of residence. There has been well known that young men in more rural counties have shown the highest levels of abuse from Evans et al. (2019), which validates the inclusion of these individual characteristics.

[16]Note that this will create a high dimensional matrix if only active substance and their concentrations were included only. If this were used I would need to find methods of reducing the dimensions by a method like Principal Component Analysis.

[17]there are various types of abuse-deterrent strategies which could potentially cause differences in abuse-potential depending on the abuse-deterrent formulation type, see O'Malley (2015). Additionally, to incorporate this I would need to find more data on the abuse-deterrent formulation for this.

Text Analysis Plots

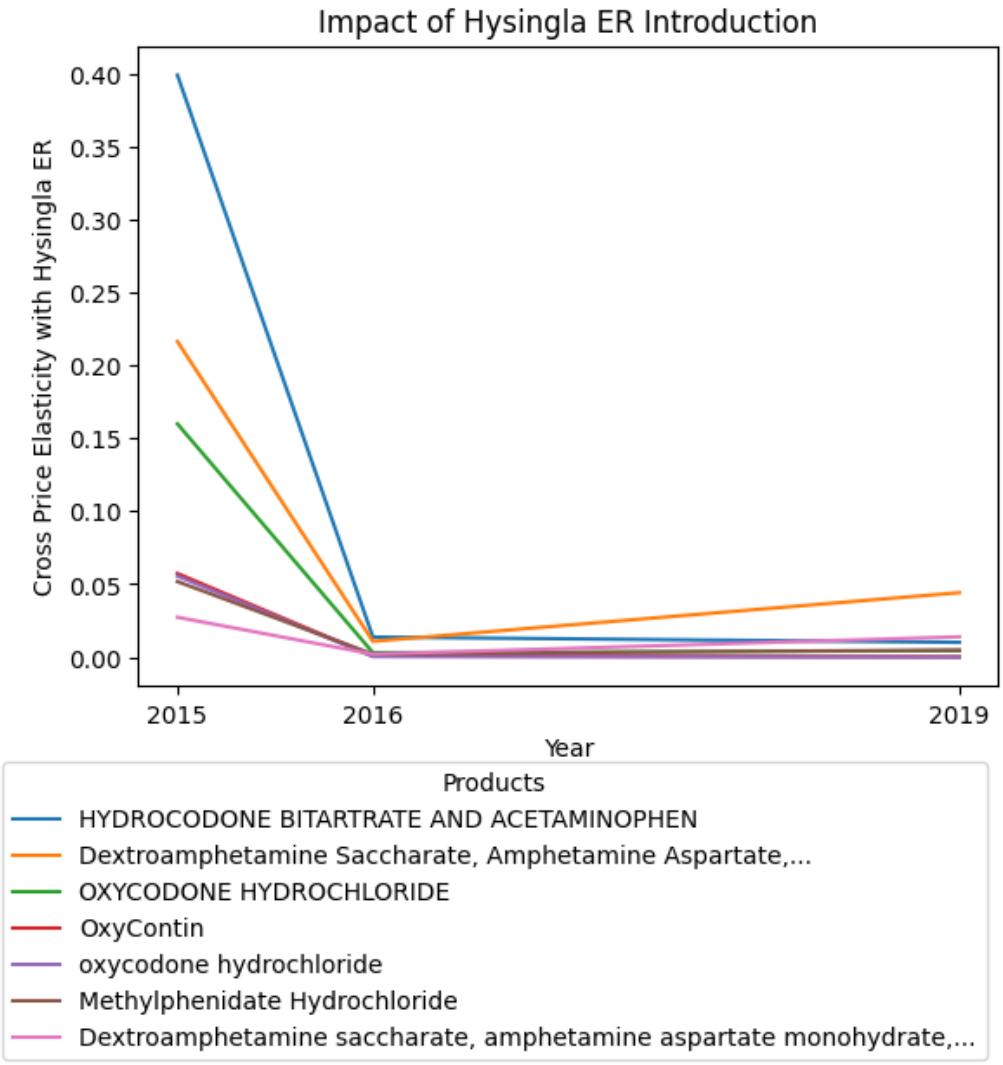

Figure 2: time plot containing the cross price elasticity of Hysingla ER to other drug products. The products included are those with higher levels of cross-price elasticity. Product names that are all capitalized mean that it is a generic version of the branded drug.

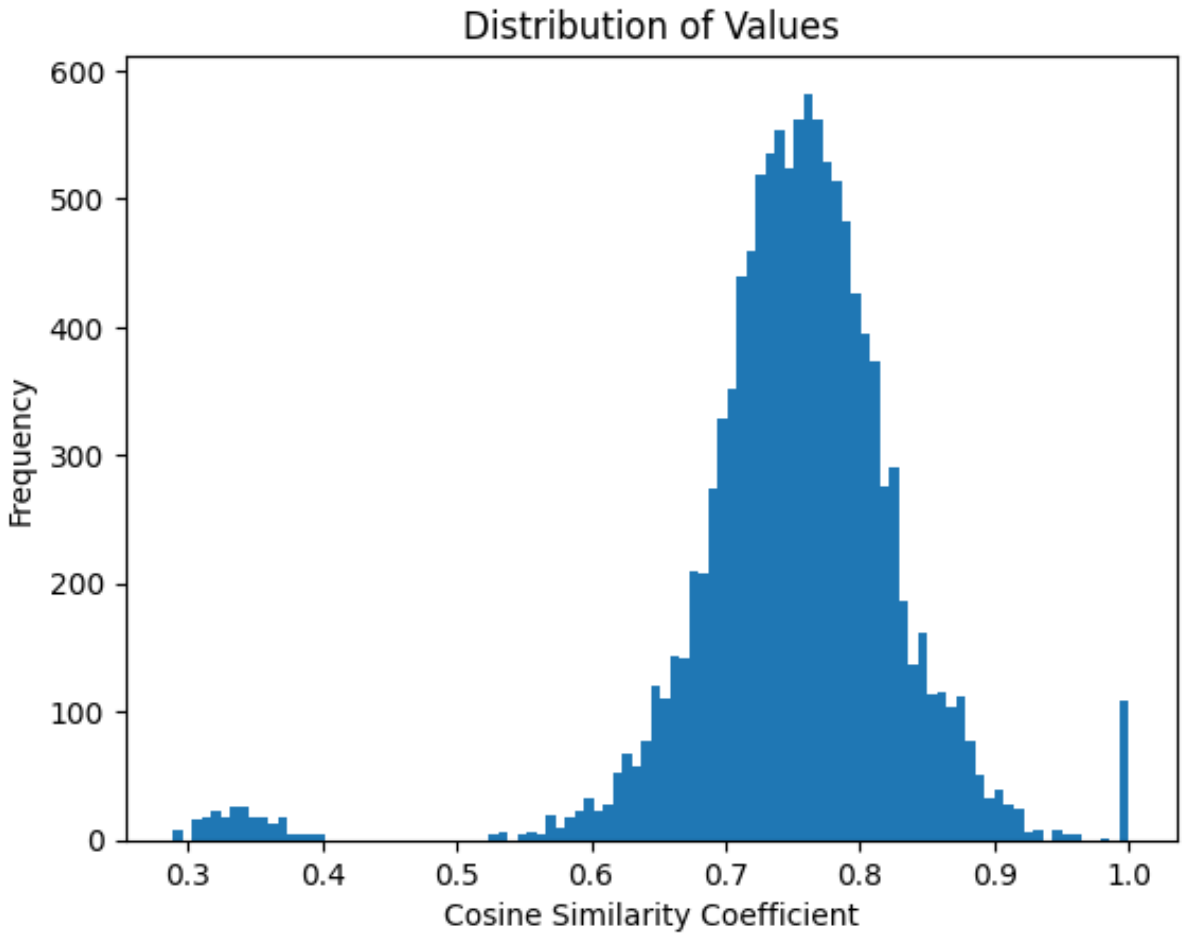

Figure 3: This plot shows the distribution of cosine similarity values between all drug labels for drugs that are considered a controlled substance, i.e. has a DEA schedule.

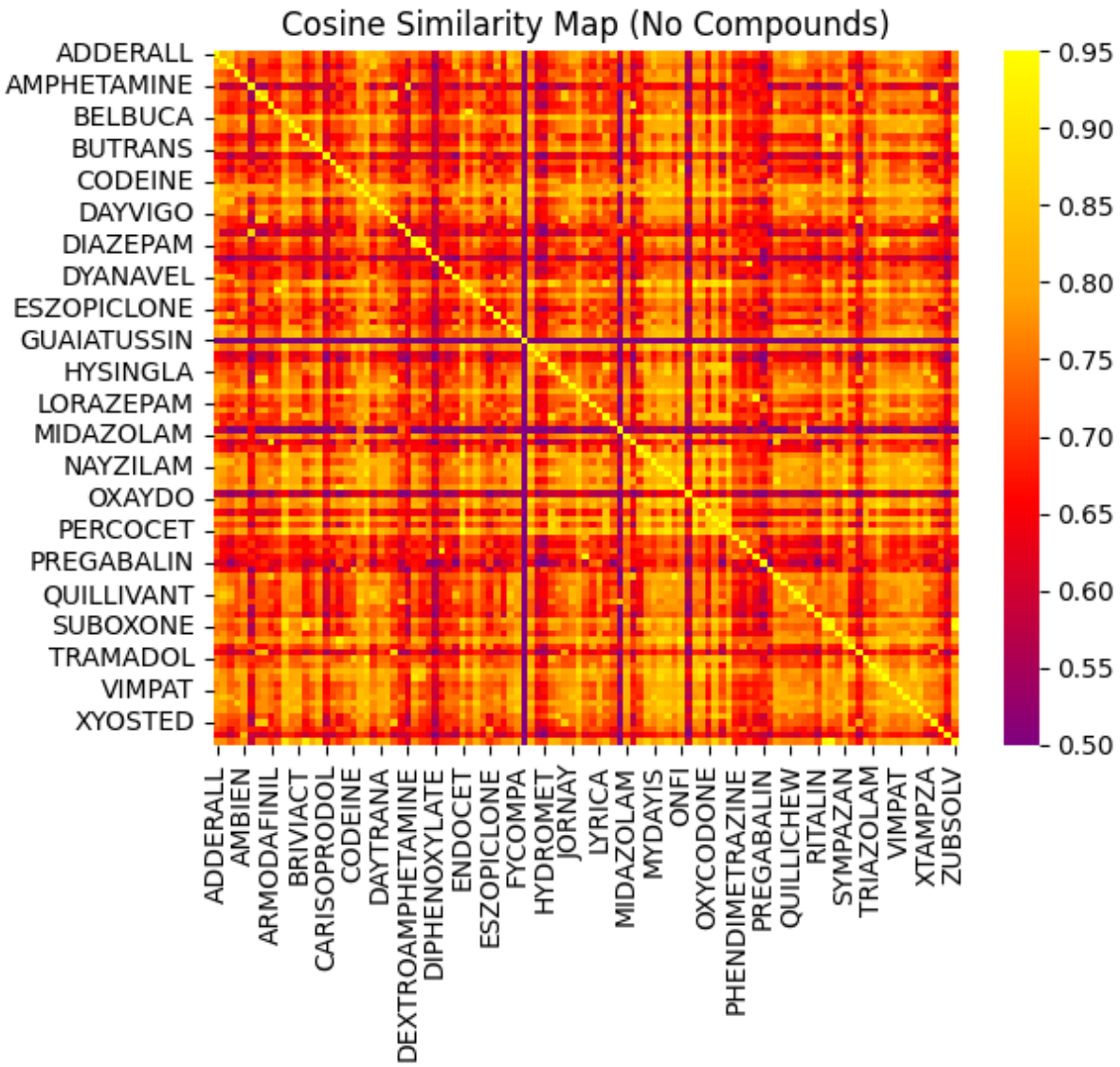

Figure 4: This is an adjacency table transformed into a heat map to illustrate the variation in cosine similiarity for all controlled substances in the US by drug label. In the Appendix there is another plot that shows the distribution of cosine similarities. Note that the axis labels here are relatively uninformative as there are more drug labels than the axis label suggest. To see the full table of results see the file at this github link here.