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# Does Misery Love Company?
## Evidence from Pharmaceutical Markets before and after the Orphan Drug Act

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Abstract

With substantial fixed costs of drug development, more common conditions can support more products. If additional pharmaceutical products are beneficial, they will attract greater consumption and promote greater longevity. We ask how market size – measured by condition prevalence – affects consumption and longevity. We document in condition cross sections that both the tendency to use a drug and longevity are higher for individuals with more prevalent conditions. We also make use of the 1983 Orphan Drug Act (ODA), which promotes development of drugs targeting individuals with rare conditions, to document increases in drug consumption and longevity surrounding the ODA for persons with rare conditions relative to others.

When production entails fixed or sunk costs, the number of available products can increase in the size of the market. Additional products increase welfare because if products are differentiated, then additional products confer benefits by allowing more types of consumers options that better suit their needs. In this way, consumers benefit each other via a mechanism one might term "preference externalities." Of course, whether products are differentiated or not, additional products can place downward pressure on prices.[1]

Although the relationship between market size and consumption and, by extension, welfare operating through product variety follows from theory in straightforward way, evidence on it is scarce.[2] Yet, the conditions giving rise to this phenomenon can appear whenever fixed costs are large relative to market size. Nowhere is this more likely to be true than in pharmaceutical markets. According to the pharmaceutical industry, the average cost of bringing one new medicine to market is $500 million.[3] The number of drugs available per condition bears out the claim that drug development costs are large relative to market size for many conditions. The median number of drugs labeled to treat a four-digit ICD9 condition is 2.[4] These facts lead us to ask whether individuals are better off in their capacity as drug consumers if their condition is more common. More succinctly, we ask whether "misery loves company."

[1] These are the mechanisms outlined in seminal papers by Spence (1976a,b) and Dixit and Stiglitz (1977). See Mankiw and Whinston (1986) for a paper emphasizing possible inefficiencies of entry.
[2] See Waldfogel (1999, 2001) and George and Waldfogel (2000).
[3] Of every 5,000 medicines tested, on average, only 5 are tested in clinical trials and only 1 of those is approved for patient use. Revenues from successful medicines must cover the costs of the "dry holes." *Why do prescription drugs cost so much?*, Pharmaceutical Research and Manufacturers of America, http://www.phrma.org/publications/publications/brochure/questions/whycostmuch.phtml.
[4] Source: Drug Indications Master Table of First DataBank's National Drug Data File.

Despite the novelty of the academic question of the welfare of small consumer groups in markets, concern about this issue is not new to policy makers. The possibility that small populations would see no medications developed for their conditions led the US Congress to pass the 1983 Orphan Drug Act (ODA), giving firms special incentives to develop drugs for diseases afflicting fewer than 200,000 Americans.[5] The ODA contains provisions that reduce the cost, and raise the appropriability, of research on rare diseases. First, under the act drugs approved as orphan drugs (for conditions affecting fewer than 200,000 persons), drug makers get seven years of exclusive marketing upon FDA approval. According to the FDA, this is the "most sought incentive." For seven years following FDA approval, the FDA cannot approve another drug for the same indication without the sponsor's consent. Second, drug makers qualify for a tax credit for clinical research expense of up to 50 percent of clinical testing expense (see http://www.fda.gov/orphan/taxcred.htm). In addition the FDA provides grant support for investigation of rare disease treatments (see http://www.fda.gov/orphan/grants/info.htm). Together, these provisions a) increase effective market size, and b) reduced fixed (sunk) costs. In doing so, the Act provides a natural experiment for measuring the impact of increased market size, relative to fixed costs, on product development, consumption, and welfare.

The ODA has had a large effect on drug development. Between 1974-83 and 1984-97, there was a twelvefold increase in the average annual number of orphan drugs brought to market. During the same period, the number of drugs (new molecular entities) approved by the FDA approximately doubled. According to the FDA, the "ODA has been very successful - more than 200 drugs and biological products for rare diseases have

[5] See http://www.fda.gov/orphan/oda.htm.

been brought to market since 1983. In contrast, the decade prior to 1983 saw fewer than ten such products come to market."[6]

In light of the apparent effect of the ODA on drug development, we examine its effect on two measures related to welfare, consumption and mortality. First, we ask whether there is evidence, in the pharmaceutical context, that misery loves company. We compare across conditions with different levels of prevalence ("market size"), asking whether people with more prevalent conditions are more likely to consume drugs for these conditions and are likely to live longer. Results from this approach are highly suggestive: more prevalent conditions have substantially more products available, and we document both that larger affected populations are much more likely to take a drug and that mortality rates are lower for persons with more common conditions. A shortcoming of this approach, however, is the possibility of unobserved heterogeneity leading both to large markets and many drugs. Putting this differently, the cross sectional measurement strategy may not provide a clean source of exogenous variation in market size.

Conveniently, the passage of the Orphan Drug Act provides a source of exogenous variation in market size, relative to fixed costs, for drugs targeting small populations. This motivates our second measurement approach for documenting the effect of market size on drug consumption and, by extension, welfare. We document growth in consumption and increases in longevity for individuals with less common conditions, relative to those with more common conditions.

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[6] Source: http://www.fda.gov/orphan/History.htm.

The paper proceeds in four sections. Section 1 provides background by outlining the mechanism for preference externalities. We also review relevant literature. Section 2 describes the data used in this study. Section 3 presents our empirical strategy and results. We find clear cross sectional evidence that misery loves company, both before and after the Orphan Drug Law. The Law weakens the link between market size and welfare: Individuals with rare conditions experience larger increases in the tendency to consume a medication and larger decreases in mortality rates. In the conclusion we consider our results in both narrow and broad contexts.

## I. Market Size, Entry, and Welfare: Why Would Misery Love Company?

### *1. The Product Selection Problem*

This paper is mainly concerned with the positive question of how market size affects drug development, consumption, and other measures of welfare. Still, it is helpful to locate this problem in its normative context, which we briefly do below.

When production carries fixed costs and products are imperfect substitutes, markets can fail to achieve optimal outcomes.[7] First, if sellers cannot appropriate the entire consumer valuation of their product, some products with consumer valuation in excess of their production cost will not be provided. That is, inefficient underprovision is possible. At the same time, because products are substitutes, the private benefit of entry can exceed the social benefit if some of a product's business is diverted from other products. For illustration, consider an additional identical product. It imposes its fixed

[7] These problems are the subject of important theoretical papers by Spence (1976a,b) and Dixit and Stiglitz (1977).

cost on society, but adds no consumer benefit (except, possibly, reduced prices). It is possible, as a result, for markets to support inefficient overprovision of products with sufficient total demand to cover the costs of multiple products. Spence terms the process by which the market determines what to produce, "the product selection problem."

Some products that the market selects not to produce are candidates for the "inefficient underprovision" designation. Indeed, one can view the ODA as an attempt to remedy inefficient underprovision. In this case, the reason the allocation may be inefficient is presumably inability to price discriminate.

We envision firms introducing competing products as long as it is profitable to do so. Competing products are imperfect substitutes for one another. Different products in a category work best for different sorts of patients, so that additional products in a category may draw additional persons to consumption, thereby increasing welfare. A sufficient, although not necessary, condition for additional products to increase welfare is that additional products raise the tendency for patients to consume a drug in the category corresponding to their condition. We assume that drug development carries only fixed (sunk) costs. There is an intuitive relationship between the tendency to consume and welfare. The presence of more products creates greater potential for consumers to find a product closer to their ideal. Unless pricing extracts all surplus, consumer welfare is greater.[8]

[8] We recognize that a higher tendency to consume in a cross section does not necessarily reflect higher welfare. Welfare is not higher if 80 percent of people are barely willing to consume than if 79 percent of persons consume and derive substantial surplus. On the other hand, if the arrival of a new product (without withdrawal of existing products) raises the tendency to consume, then by revealed preference welfare is higher. We will treat consumption tendencies as suggestive evidence about welfare in the paper, paying particular attention to results from longitudinal measurement approaches.

The "business stealing vs. market expansion" distinction provides a helpful framework for viewing the relationship between consumption and welfare (see Mankiw and Whinston, 1986). If a new drug is substantially differentiated, it may draw new customers into the market rather than simply diverting business from existing products. In this case, the share of affected people consuming a drug will increase with entry. On the other hand, an undifferentiated product may draw all of its business from existing products and will therefore not increase the tendency to consume. Of course, additional products can put downward pressure on prices, and this pressure is presumably more acute as the products are less differentiated.[9]

In this scheme it is easy to see how misery loves company. An increase in market size raises the amount of revenue available to a product category, possibly justifying an additional product. An additional product may attract a new customer (valuing the product above its price), whose use of the product generates some combination of consumer surplus and greater longevity. Furthermore, additional products may reduce the price paid by all customers.

The passage of the ODA increases the effective size of the market, relative to fixed costs, for drugs targeting uncommon conditions. This may give rise to more products in those categories, as well as a greater tendency to consume. Because rare conditions are targeted by few products, especially prior to the ODA, new products spurred by the ODA are likely to be strongly differentiated products; that is, their entry provides *some* product, as opposed to *no* product.

[9] This is the mechanism documented indirectly, based on the relationship between market size and entry, by Bresnahan and Reiss (1990, 1991).

The foregoing suggests the following questions. Do larger markets attract more products? Is there a greater tendency to consume in markets with more products and/or lower prices? Do additional products promote longevity? We now turn to the empirical analysis of these questions.

## III. Data

The basic data for this study consist of two condition-level cross sections containing information on prevalence (the size of the affected population), consumption (the share of persons with a condition taking a drug to treat the condition), and mortality (mean age at death). The first cross-section covers the years 1980-81, before the ODA, and the second refers to 1997-98, substantially after the ODA.

### *1. Physician Survey Data on Drug Consumption and Condition Prevalence*

Our primary data on the tendency to take a drug and prevalence are drawn from a physician survey, the National Ambulatory Medical Care Survey (NAMCS). We supplement these with household-level data available only for the post-ODA period, described below. The NAMCS surveys offer information on patients' visits to a national sample of office-based physicians. The universe consists of office visits to nonfederally employed physicians classified by the American Medical Association (AMA) or the American Osteopathic Association (AOA) as "office-based, patient care" (excluding specialties of anesthesiology, pathology, and radiology), from 112 Primary Sampling Units (PSUs) in the United States.

Each NAMCS office visit record reports the physician's diagnoses, any drugs ordered, administered, or provided, and a sampling weight. We measure condition i's prevalence in a year by the number of visits in which diagnosis i (4-digit International Classification of Diseases (ICD9) code) is recorded. In particular, we define:

$N\_VISIT\_PRE_i$ = the estimated annual number of office-based physician visits in which ICD9 diagnosis i was recorded in the pre-ODA period (1980-1981); and

$N\_VISIT\_POST_i$ = the estimated annual number of office-based physician visits in which ICD9 diagnosis i was recorded in the post-ODA period (1997-1998).

Thus, the NAMCS-based prevalence measure is based only on physician visits. The advantage of this sampling condition is that physician diagnoses are more likely than self-diagnoses to be correct. At the same time, this sampling has the possible disadvantage of excluding persons who are ill but do not seek medical care.

We measure drug consumption tendencies from prescription information in the NAMCS. Our measure is whether patients diagnosed with a condition have one or more drugs prescribed for them. The "consumption" measure is therefore based not literally on consumption but rather whether the doctor believes beneficial drugs exist for the individual's circumstance. In particular, the fraction of visits with primary diagnosis i in which one or more drugs were prescribed as follows:

$RX\%\_PRE_i$ = visits in which any medications were prescribed as a fraction of total visits in which ICD9 diagnosis i was recorded in the pre-ODA period (1980-1981); and

$RX\%\_POST_i$ = visits in which any medications were prescribed as a fraction of total visits in which ICD9 diagnosis i was recorded in the post-ODA period (1997-1998).

Table 1 provides summary statistics on prevalence and consumption measures from the NAMCS survey.[10] Population estimates based on the samples indicate 628 million physician visits in the 1980-81 period and 982 million in the 1997-98 period. The earlier sample includes 2454 conditions, while the later sample includes 1996. The number of physician visits per condition varies widely, with roughly 50 million for the most frequently-cited condition, compared with a few thousand for the least common. Drugs are prescribed at about three quarters of visits in both periods.

The relationship between disease prevalence and probability of prescription drug use can also be examined, at least during the post-ODA period, using a household survey, i.e. the Medical Expenditure Panel Survey (MEPS). MEPS was conducted in each of the years 1996-1998 to provide nationally representative estimates of health care use, expenditures, sources of payment, and insurance coverage for the U.S. civilian non-institutionalized population. The MEPS Medical Conditions files provide information on household-reported medical conditions collected on a nationally representative sample of the civilian noninstitutionalized population of the United States. We describe the data in more detail in the appendix. It suffices here to say that these data differ from the physician survey by their inclusion of persons who report an illness but do not visit a

[10] Our sample includes diagnoses (ICD9 codes) corresponding to natural causes of death only, i.e. ICD9 codes 0000-7999. External causes of death (accidents, injuries, homicide, etc.) are excluded. When a patient visit record includes multiple diagnoses (up to three may be recorded), we include that record multiple times—once for each diagnosis recorded. When a drug is prescribed, we don't know which diagnosis it is prescribed for.

physician. Interestingly, a high fraction (37 percent) of persons reporting a condition but not seeing a physician report taking a prescription medication for the condition.

We can use the MEPS data to examine the relationship between condition prevalence and probability of Rx use, using two definitions of each:

PREV1: total number of people with condition;

PREV2: number of people with condition, who had one or more office-based visits for the condition in the past year;

Rx_PROB1: % of people with condition who used any drugs (unconditional probability of Rx use); and

Rx_PROB2: % of people who visited doctor for the condition who used any drugs (probability of Rx use, conditional on doctor visit).

There are two possible reasons for excluding people with zero doctor visits from the calculations. First, people who have not seen the doctor about the condition may be more likely to misidentify the condition. (Physicians are far more qualified to offer diagnoses than patients.) Hence, excluding people with zero doctor visits may yield less noisy prevalence estimates. Second, excluding people with zero doctor visits may result in "severity-adjusted" prevalence estimates.

*2. Mortality and Prevalence Data from Vital Statistics*

Our data on mortality, as well as a second measure of prevalence, are drawn from Vital Statistics-Mortality Detail files. Two items that are recorded on death certificates are the *cause of death*, and the *age at death*. The most detailed classification of cause of

death published by the CDC has 282 distinct causes, and this is the classification we use. The number of (non-infant) deaths due to a condition is our second measure of prevalence. We employ the mean age at which (non-infant) deaths due to a condition as an indicator of the welfare of people with the condition. The sample is a universe of roughly 2 million US deaths per year.

## IV. Empirical Strategy and Results

### *1. Empirical Strategy*

Our goal in this paper is to measure the effect of market size on consumer welfare in drug markets, and we employ two empirical strategies. First, we exploit cross sectional comparisons across conditions with different levels of prevalence ("market size"), asking whether people with more prevalent conditions exhibit a greater tendency to consume prescribed medicines.[11] The inherent difficulty with this approach, however, is the possibility of unobserved heterogeneity leading both to large markets and many drugs.

Fortunately, the passage of the Orphan Drug Act provides a source of exogenous variation in market size for drugs targeting small populations. Using panel data at two points in time, we can exploit this policy change to provide more compelling evidence of the effects of market size on consumption and mortality, than one might find using cross-

[11] Unfortunately, data on consumption of over-the-counter (nonprescription) medicines generally aren't available.

sectional comparisons across medical conditions alone. As a useful byproduct of this approach, we can also simply examine the effectiveness of the Orphan Drug Act.

*2. Prevalence and Consumption using Physician Survey Data*

Do persons with more common conditions have a greater tendency to take a drug? First, we estimate the cross-condition relationships between the tendency to take a drug and condition prevalence, via the following equations:

$$RX\%\_PRE_i = \alpha_0 + \beta_0 \ln (N\_VISIT\_PRE_i) + \varepsilon_{i0} \quad (1)$$

$$RX\%\_POST_i = \alpha_1 + \beta_1 \ln (N\_VISIT\_POST_i) + \varepsilon_{i1} \quad (2)$$

where eq. (1) characterizes the pre-ODA period and eq. (2) characterizes this relationship in the post-ODA period. We recognize that these are very parsimonious specifications of what are, essentially, demand equations. It would be natural to also include a drug price as an explanatory variable. We experimented with a number of price measures and found little sensitivity of consumption to prices, perhaps owing to the role of insurance in financing prescription drug expenditures.

The estimates are reported in table 2. The equations were estimated by weighted least squares, with the number of visits as the weight. Consistent with our expectations, probability of drug use is higher for more prevalent diseases both before and after enactment of the ODA. We hypothesize that ODA enactment weakened this relationship, i.e. that $0 < \beta_1 < \beta_0$. One way to test this is to compute an estimate of ($\beta_1$ - $\beta_0$), and test whether is it significantly less than zero. The prevalence-consumption profile was significantly flatter in 1997-98 than it had been in 1980-81. In this sense misery loves company in the cross sections, especially prior to the ODA. To get a feel

for the magnitude of the estimated effects, consider the following quantiles of the distribution of diseases in 1980-81, by prevalence, in table 3. The 75th percentile disease is 13.8 times as prevalent as the 25th percentile disease. The log-difference in prevalence is 2.63 (= ln(129,427/9,367)). The estimates imply that in 1980-81, the probability of drug use was .147 (= $\beta_0$ * 2.63) lower for the 25th percentile disease than it was for the 75th percentile disease.

It is possible that the cross sectional relationship between consumption and prevalence arises because of unobserved heterogeneity. Some factor determining consumption may be correlated with prevalence for reasons outside our explanation.[12] Because we have consumption data at two points in time, we can eliminate the fixed unobservable by differencing. We can then test whether the change in consumption is larger for the ODA-targeted conditions than for more common conditions. A major obstacle to implementing this approach arises because we cannot clearly classify conditions as ODA-targeted. First, it is not clear how to map our prevalence measure(s) into the ODA cutoff of 200,000. Second, the language of the law appears to allow some flexibility in the location of the ODA cutoff. It seems reasonable nonetheless to expect greater increases in consumption for less common conditions, and we test this as follows:

$$(RX\%\_POST_i - RX\%\_PRE_i) = \alpha_\Delta + \beta_\Delta \ln (N\_VISIT\_PRE_i) + \varepsilon_{i\Delta} \qquad (3)$$

We hypothesize that $\beta_\Delta < 0$, i.e. that (initially) low-prevalence diseases tended to exhibit greater increases in the probability of drug utilization than high-prevalence diseases.[13]

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[12] For example, the measure of prevalence used in these regressions, doctor visits where a condition is diagnosed, may be driven by the known availability of particular medications (e.g. Viagra). Other measurement approaches we employ, including both longitudinal data and mortality-based prevalence measures, avoid these problems. Death is not endogenous in the same way as doctor visits.

[13] Relative prevalence of diseases is quite stable over time: $N\_VISIT\_POST_i$ is roughly proportional to $N\_VISIT\_PRE_i$. If $N\_VISIT\_POST_i$ were *exactly* proportional to $N\_VISIT\_PRE_i$, then the point estimate

The estimate of $\beta_\Delta$, shown in the last column of Table 2, is negative and highly significant, which is consistent with the hypothesis that the ODA reduced the extent to which misery loves company.

We can revisit the cross sectional relationship between prevalence and consumption using MEPS-based household data for 1996-98. These data allow us to calculate two measures of prevalence (the number reporting, and the number visiting a doctor for, a condition) and the two associated measures of drug use (percent of persons with a prescription among all with the condition and among those visiting the doctor). These data cover 751 conditions.

Table 4 summarizes this evidence, dividing conditions into three groups based on prevalence. The top ("unconditional") panel describes all persons reporting conditions and shows that the tendency to consume a prescription drug is higher for persons with more common conditions. The difference between the consumption tendency for high and low prevalence groups is not statistically significant, however (p-val=0.218). The pattern is stronger, and statistically significant among those visiting a doctor, reported in the bottom panel.

We also examine this evidence with regressions of the form[14]:

$$Rx\_PROB_i = \alpha + \beta \ln(PREV_i) + \varepsilon_i$$

where $Rx\_PROB_i$ = the (unconditional or conditional) probability of drug use for condition i, and $PREV_i$ = the total number of people with the condition, or the number of people who have seen a doctor about it. The results are shown in table 5. The correlation

of $\beta_\Delta$ would be identical to the point estimate of $(\beta_1 - \beta_0)$. However since $\beta_\Delta$ is a "matched-pairs" estimator, it is likely to be more efficient (have a smaller standard error) than $\beta_\Delta$.

[14] The weight is the denominator of the dependent variable.

between unconditional probability of drug use and prevalence is negative, but not significant at the 5% level. In contrast, the correlation between conditional probability of drug use and log number of people visiting the doctor is positive and highly significant ($t = 10.6$). Moreover, the point estimate of the conditional probability $\beta$ from the household survey data (.061) is fairly similar to the conditional-probability estimates ($\beta_0$ and $\beta_1$) from the physician survey data (0.056 and 0.048, respectively).

In principle, there might be "reverse causality": the number of people visiting the doctor might depend positively on the (expected) probability of receiving a drug. We try to address this possibility in two different ways. First, we examine, in eq. (3), the relationship between conditional Rx probability and total number of people with the condition (including those not consulting a physician). The point estimate falls by about 25%, but the relationship remains highly significant ($t = 8.6$). Second, we examine the correlation across conditions between the conditional Rx probability and the probability of physician visit. That correlation is far from statistically significant: people are not more likely to visit doctors for conditions that doctors are more likely to prescribe for.

*3. Mortality and Prevalence*

Although product consumption is the usual economic measure underlying welfare inferences, the medical context provides other intuitive measures of welfare. We can use the mortality data to examine the relationship between prevalence and mean age at death. To do this we examine the relationship between prevalence (here measured, for consistency with the mortality dependent variable, by the number of deaths attributed to the condition) and age at death, by ranking conditions by number of deaths, dividing

conditions into groups based on this rank, and computing the mean value of age at death for each group of conditions. In this analysis, because we have ample data (about 2 million observations per year), we divided the conditions into five, rather than three, groups, i.e. we divided the conditions into quintiles.

First, we performed this calculation using data from the 1980 Mortality Detail file. Then, we performed a similar calculation using data from the 1995 Mortality Detail file. The results are shown in Figures 1 and 2 as well as table 6. Figure 1 shows mean age at death, by mortality quintile and year. In both years, mean age at death is strictly increasing with respect to frequency quintile: people tend to die younger from less common diseases. In 1980, mean age at death in the lowest quintile was 23.2 years lower than mean age at death in the highest quintile. As with the consumption results, there is a possibility of unobserved heterogeneity in these results: individuals may die older from more prevalent diseases for reasons apart from our explanation.

We can use the two time observations, as above, to see how the change in mean age at death varies with prevalence. Figure 2, and the last columns of table 6, show this. From 1980 to 1995, the entire schedule shifted up: mean age at death increased in every quintile. However, as emphasized by Figure 2, the shift was much greater in the lowest two quintiles than it was for the top three quintiles. Mean age at death increased by a minimum of 6.9 years in the bottom 2 quintiles, three times as much as the maximum increase in the top three quintiles. Comparing the highest to the lowest quintile, the differential in the age at death shrank by 5.8 years between 1980 and 1995, with an associated t-statistic of 11.2.[15]

[15] Table 5 is calculated based on contemporaneous prevalence. Mean age at death in 1980 is based on 1980 prevalence, while the column describing mean age at death in 1995 is based on 1995 prevalence, so that

We can also examine the impact of the ODA using these data in a regression context. We do this by running the regression[16]:

$$mean\_age_{it} = \beta_0 + \beta_1 \delta^{95} + \beta_2 \ln(prevalence\_1980) * \delta^{95} + \mu_i + \varepsilon_{it},$$

where:

mean_age$_{it}$ is the mean age at death for condition i at time t (t=1980, 1995),
$\delta^{95}$ is a dummy for the post-ODA period,
ln(prevalence_1980)*$\delta^{95}$ is the pre-ODA prevalence interacted with the post-ODA dummy,
$\mu_i$ is a condition fixed effect,
and $\varepsilon_{it}$ is an error.

In this specification, $\beta_1$ shows the baseline change in longevity between 1980 and 1995, and $\beta_2$ shows how the baseline change varies with the prevalence of the condition in 1980. If rare condition longevity increases more quickly following the ODA, then $\beta_2$ will be negative. The errors are not independent across observations. We address this by clustering by condition-by-year.

Column (1) of table 7 reports estimates, and the estimate of $\beta_2$ is negative but insignificant. Columns (2) and (3) replace ln(prevalence_1980) with a series of quintile dummies interacted with post-ODA dummies. The most common quintile (#1) is excluded. The columns differ only in how standard errors are clustered (by quintile x year in (2) and by condition x year in (3)). Longevity increases significantly faster in the quintiles for rarest conditions. The final two columns repeat the exercise in columns (2) and (3), aggregating the top two quintiles together. While longevity increased by about 2

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conditions are not constrained to remain in the same quintiles across time. However, the prevalence correlation across the years is about 0.95, so that inferences we draw in the text about how the change on longevity varies with prevalence are not sensitive to whether we look at changes based on 1980 or contemporaneous prevalence.

[16] Observations are weighted by the number of deaths.

years for persons with common conditions, longevity increased about twice as much for persons with less common conditions.

*2. Discussion: the ODA's Effects and Context*

The effects of the ODA are visible in a variety of ways in our results. Prior to the ODA, drug availability – and ensuing welfare – were quite sensitive to market size. Misery really loved company. We see this primarily in the contrast between the pre and post-ODA estimates of the relationship between consumption and prevalence. The ODA increased the incentive for firms to develop drugs for small populations, relative to the incentive for larger populations. As a result, there was sharper growth in the drug consumption tendency in low-prevalence conditions than in more common conditions. Similarly, there was a large decrease in mortality for low-prevalence conditions relative to higher-prevalence conditions. The ODA decreases the extent to which misery loves company. It is not clear whether these effects are efficient, although if the Act simply allows more complete appropriation of drug benefits, then there would be no reason to suspect inefficiency.

Most observers of the ODA applaud this policy precisely for its effect of reducing the dependence of welfare on market size. Intuitively, in the context of disease, it is not hard to understand the popularity of this policy. Yet, the conditions facing would-be consumers of drugs for unpopular conditions are not unique to pharmaceutical markets. These conditions arise, generically, whenever there are large fixed costs and preferences differ across consumers.

The process by which markets select which products to make causes markets deliver more welfare to persons with common preferences than to persons with uncommon ones. As Spence (1977) has emphasized, there is no reason to expect the market to select the right mix of products in contexts of this sort. As we consider the sense of the ODA, we might also ask whether other policies aimed at raising the welfare of small consumer groups are also justified.

Some people believe that investment is not too sensitive to incentives (e.g. patent enforcement, price controls). They doubt that weakening patent protection or imposing price controls would significantly reduce investment in new drug development. Our evidence supports the hypothesis that at least one type of incentive (the extent of the market) has an important effect on the amount of investment. It may shed light on the effect of changes in other incentives on investment. For example, a government-mandated 25% price reduction may have a similar effect on investment as a ("market-mandated") 25% reduction in prevalence.[17]

## V. Conclusion

The results show two things. First, the results show that in this market, as in some others, supply-side nonconvexities give rise to an important relationship between market size and consumption and, arguably, welfare. In this context, misery loves company. This has broad implications. The prevailing, and generally implicit, view is that market allocation, unlike allocation through collective choice, gives each consumer whatever she wants, regardless of her fellow consumers' preferences. Given the large drug

[17] See Lichtenberg, *Cipro and the Risks of Violating Pharmaceutical Patents*.for further discussion of how incentives to develop drugs affect investment and welfare.

development costs, however, consumers see drugs developed for their conditions only as they make up large potential markets. Our results are, frankly, not surprising; but they do provide some evidence about how the mix of differentiated products selected in a market depends on the distribution of product-preferring types in the market.

Second, our results show that the Orphan Drug Law "works," in the sense that it has induced increased development of drugs targeted at small populations[18] and that these populations are now more likely to take drugs. The policy is lauded, and other policies of this type (equalizing utility across large and small populations) exist. Perhaps most notably, the US Postal Service has an explicit policy of charging the same rates for postage regardless of letter origin or destination within the US. If mail pricing were left entirely to the market, postage rates would presumably be lower for letters sent to and from densely populated areas. Under government provision, by contrast, administered rates are the same for consumers with substantially different costs of service, in densely and sparsely populated areas.

It is becoming increasingly clear that in large-fixed cost contexts where preferences differ across individuals, markets deliver fewer products and perhaps less satisfaction to small groups. In the pharmaceutical market this is deemed a bad feature of market outcomes; and policies have been devised to remedy the situation. Yet, there is no clear distinction between the economic circumstance of pharmaceutical markets and other large-fixed-cost markets. How widely such a policy rationale should be applied is an important remaining question for policymakers.

[18] Lichtenberg (2001), "The effect of new drugs on mortality from rare diseases and HIV," provides time-series evidence.

Appendix – MEPS data description

The files contain variables describing medical conditions reported by respondents in several sections of the MEPS questionnaire, including the Condition Enumeration Section, Health Status Section, and all questionnaire sections collecting information about health provider visits, prescription medications, and disability days. Each record represents one household-reported medical condition reported regardless of whether or not the condition was associated with a medical provider event (e.g., prescribed medicine event or office-based visit). Since each record represents a single condition reported by household respondents, some household respondents may have multiple medical conditions and thus will be represented in multiple records on this file. Other household respondents may have reported no medical conditions and thus will have no records on this file.

**Classification of medical conditions.** The medical conditions reported by the respondent were recorded by the interviewer as verbatim text, which were then coded to fully-specified 1996 ICD-9-CM medical condition codes, by professional coders. Although codes were verified and error rates did not exceed 2.5 percent for any coder, analysts should not presume this level of precision in the data; the ability of household respondents to report condition data that can be coded accurately should not be assumed (see Cox and Cohen, 1985; Cox and Iachan, 1987; Edwards, et al, 1994; and Johnson and Sanchez, 1993). In order to preserve respondent confidentiality, nearly all of the condition codes provided on this file (ICD9CODX) have been collapsed from fully-specified codes to 3-digit code categories. ICD-9-CM condition codes are also aggregated into clinically meaningful categories that group similar conditions (CCCODEX). CCCODEX was generated using Clinical Classification Software (formerly known as Clinical Classifications for Health Care Policy Research (CCHPR)), (Elixhauser, et al., 1998), which aggregates conditions and V-codes into 260 mutually exclusive categories, most of which are clinically homogeneous. Table _ provides weighted and unweighted frequencies for CCCODEX.

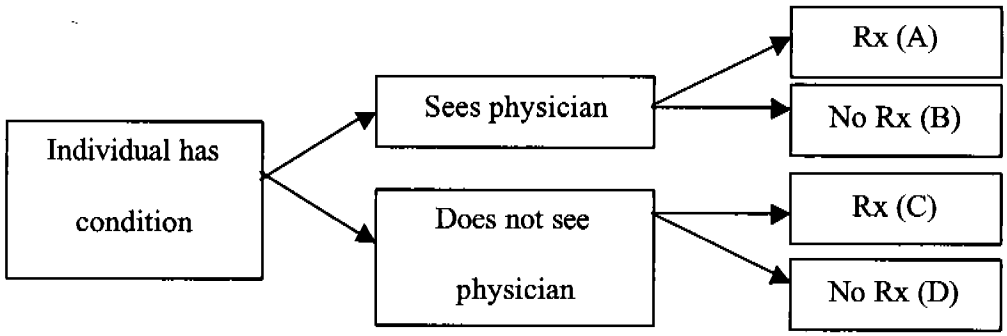
Each record in the Medical Conditions file contains the following variables:

- Medical condition codes (ICD9CODX, CCCODEX)
- RXNUM: the number of prescribed medicines associated with the condition
- OBNUM: the number of office-based events associated with the condition
- A person-level weight (for calculation of population estimates)

We also calculated (at the micro level) the following:

ANY_RX = 1 if RXNUM > 0
= 0 if RXNUM = 0
ANY_OB = 1 if OBNUM > 0
= 0 if OBNUM = 0

An office-based visit (physician consultation) is usually required for an individual to receive prescribed medicines. Consider the following schematic:




An individual with a condition either sees a physician or does not see a physician about the condition. *In practice, about half of medical conditions have no office-based visits associated with them in a given year.* Moreover, the larger the number of people who report having a medical condition, the lower the fraction of people who see a physician about it. One possible interpretation of this is that highly prevalent conditions tend to be less severe (impose fewer limitations on activities) than less prevalent conditions.

One might expect to observe virtually no Rx utilization for a condition by those people who have not seen a doctor about the condition during the year. This is not the case, however: 37% of people with no office-based visits used one or more prescription drugs. (C / (C + D) = 37%) 61% of people with one or more office-based visits used one or more prescription drugs. (A / (A + B) = 61%)

**References**


Berry, Steven T. and Joel Waldfogel. "Free Entry and Social Inefficiency in Radio Broadcasting." *RAND Journal of Economics*. 1999.

Bresnahan, Timothy F; Reiss, Peter C. "Entry and Competition in Concentrated Markets." *Journal of Political Economy*. Vol. 99 (5). p 977-1009. October 1991.

Bresnahan, Timothy F; Reiss, Peter C. "Entry in Monopoly Markets." *The Review of Economic Studies*. Vol. 57 (4). p 531-53. October 1990.

Dixit, Avinash K; Stiglitz, Joseph E. "Monopolistic Competition and Optimum Product Diversity." *American Economic Review*. Vol. 67 (3). p 297-308. June 1977.

George, Lisa and Joel Waldfogel. "Who Benefits Whom in Daily Newspaper Markets?", NBER Working Paper 7944, October 2000

Lichtenberg, Frank. "Cipro and the Risks of Violating Pharmaceutical Patents." National Center for Policy Analysis, Brief Analysis No. 380, November 2001, http://www.ncpa.org/pub/ba/ba380/ba380.pdf

Lichtenberg, Frank. "The effect of new drugs on mortality from rare diseases and HIV". NBER Working Paper No. 8677, December 2001.

Mankiw, N Gregory; Whinston, Michael D. Free Entry and Social Inefficiency. *Rand Journal of Economics. Vol. 17 (1). p 48-58. Spring 1986.*

Pharmaceutical Research and Manufacturers of America, .*Why do prescription drugs cost so much?*, http://www.phrma.org/publications/publications/brochure/questions/whycostmuch.phtml

Spence, Michael. "Product Selection, Fixed Costs, and Monopolistic Competition." *The Review of Economic Studies*. Vol. 43 (2). p 217-35. June 1976.

Spence, Michael. "Product Differentiation and Welfare." *American Economic Review*. Vol. 66 (2). p 407-14. May 1976.

Waldfogel, Joel. "Preference Externalities: An Empirical Study of Who Benefits Whom in Differentiated Product Markets" NBER Working Paper 7391, October 1999

**Figure 1**

**Mean age at death, by year and quintile of mortality frequency distribution**

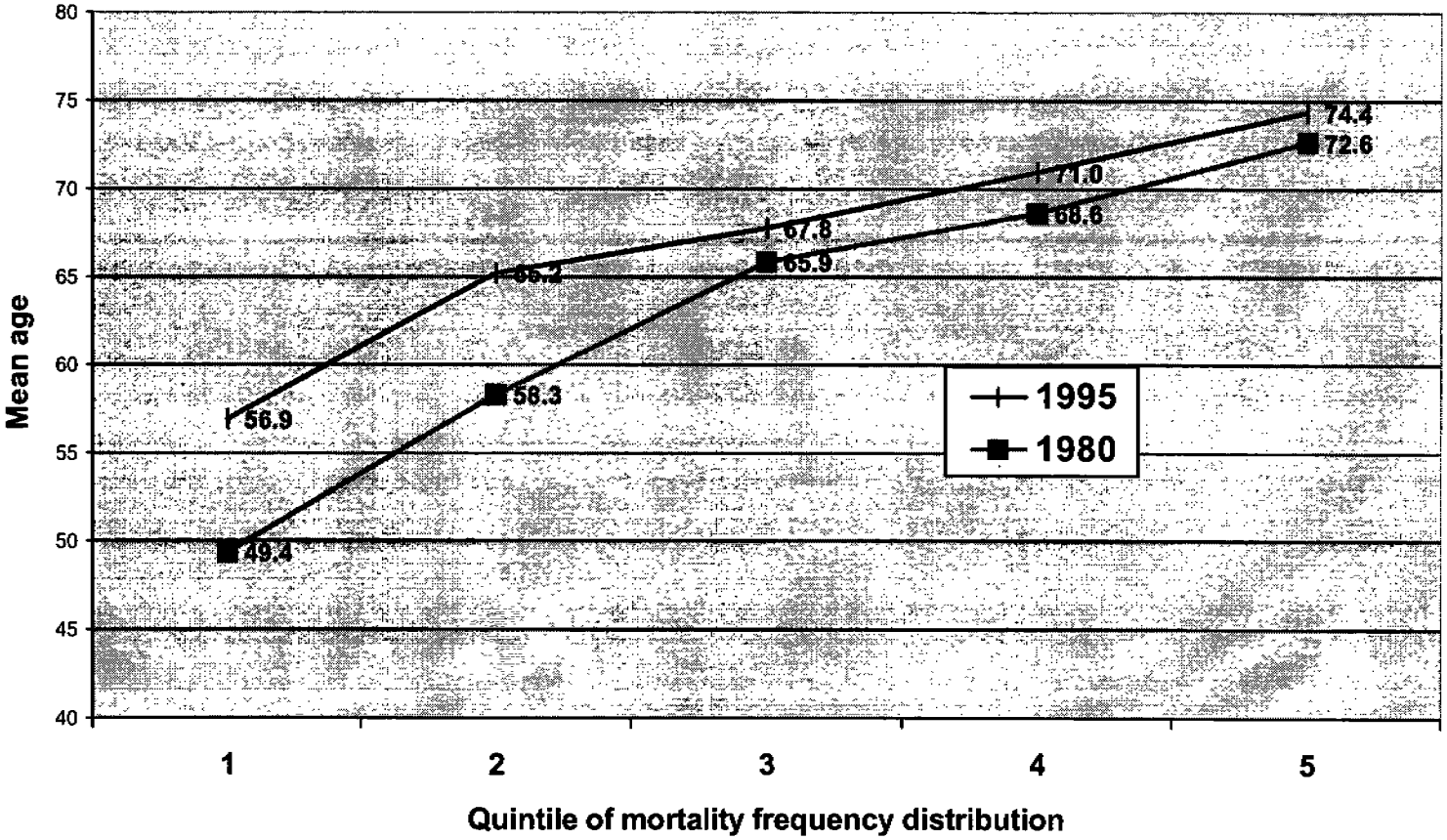


**Figure 2**
**1980-1995 increase in mean age at death,**
**by quintile of mortality frequency distribution**

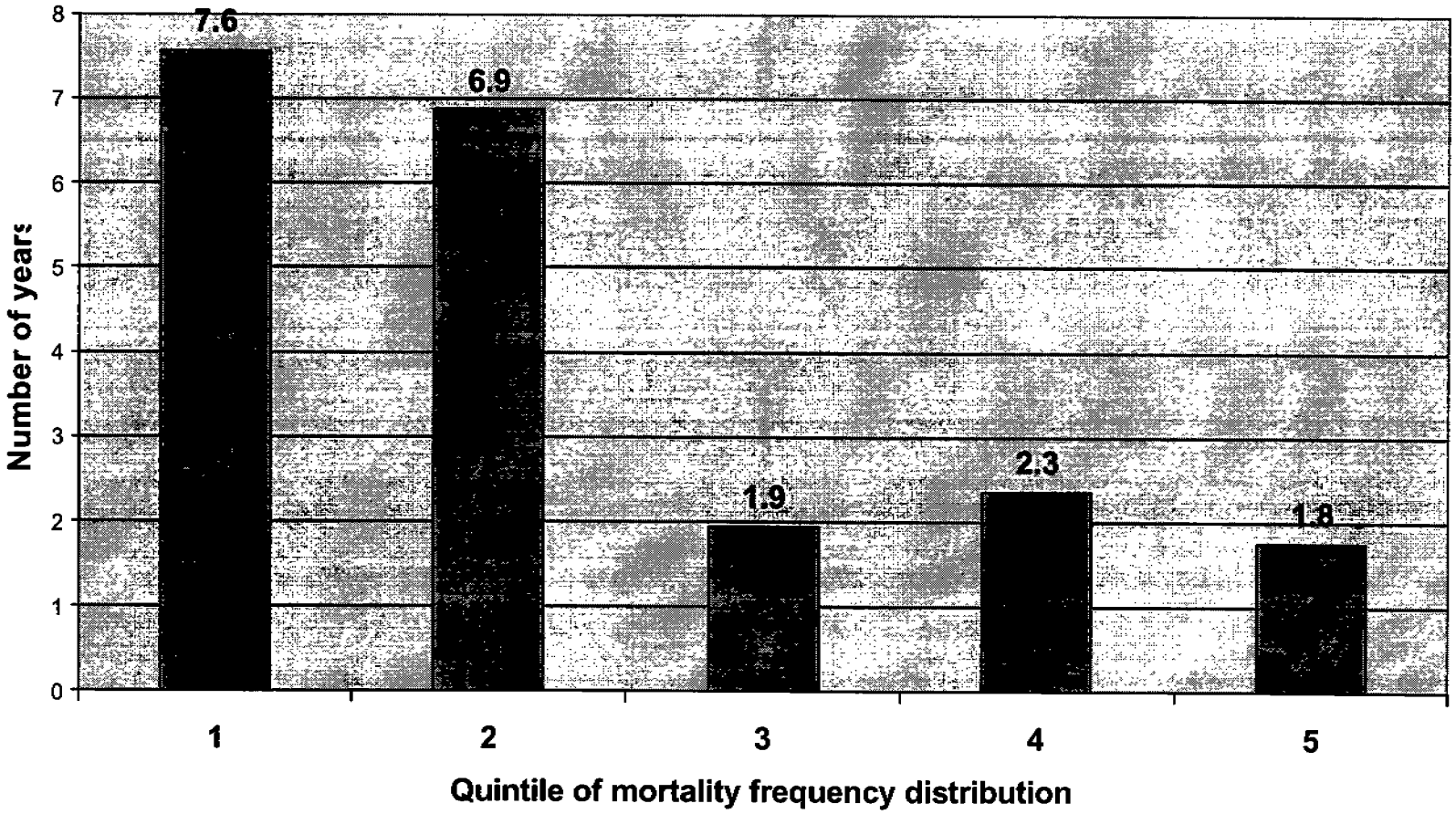


**Table 1: Physician Survey Summary Statistics**

| **Period** | **1980-1981** | **1997-1998** |
|---|---|---|
| Number of diseases | 2454 | 1996 |
| Total no. of physician visits | 627,701,627 | 981,751,220 |
| Mean no. of physician visits | 255,787 | 491,859 |
| Minimum no. of physician visits | 1,031 | 1,921 |
| Maximum no. of physician visits | 44,162,054 | 54,396,942 |
| Rx visits/total visits | 0.73 | 0.74 |

**Table 2: Relationship between Prevalence and Drug Use from Physician Survey**
**Regression Estimates**

| | $\beta_0$ | $\beta_1$ | $\beta_1 - \beta_0$ | $\beta_\Delta$ |
|---|---|---|---|---|
| estimate | 0.056 | 0.048 | -0.00835 | -0.01383 |
| std. error | 0.002442 | 0.002103 | 0.003222 | 0.00191 |
| t-statistic | 22.93 | 22.66 | 2.59 | 7.24 |
| p-value | <.0001 | <.0001 | 0.0096 | <.0001 |
| No. of obs. | 2454 | 1996 | | 1691 |

**Table 3:**
**Distribution of Prevalence by Condition, 1980-81 Physician Survey Data**

| | Frequency |
|---|---|
| 100% Max | 44,162,054 |
| 99% | 3,831,712 |
| 95% | 885,934 |
| 90% | 452,223 |
| 75% Q3 | 129,427 |
| 50% Median | 32,053 |
| 25% Q1 | 9,367 |
| 10% | 4,307 |
| 5% | 2,849 |
| 1% | 1,894 |
| 0% Min | 1,031 |

**Table 4: Prevalence and Drug Use Post ODA (Household Survey)**

**A. All individuals with the condition**

| Prevalence category | No. of conditions | mean no. of people with condition | Total no. of people with condition | % of people consuming any drugs for condition (weighted) |
|---|---|---|---|---|
| low | 250 | 18,214 | 4,553,366 | 40.4% |
| medium | 251 | 150,838 | 37,860,207 | 41.7% |
| high | 250 | 3,136,314 | 784,078,364 | 48.4% |
| prob. value | | | | 0.218 |

**B. Individuals who visited a doctor about the condition**

| Prevalence category | No. of conditions | mean no. of people with condition | Total no. of people with condition | % of people consuming any drugs for condition (weighted) |
|---|---|---|---|---|
| low | 250 | 9,263 | 2,315,709 | 46.8% |
| medium | 251 | 83,791 | 21,031,471 | 47.1% |
| high | 250 | 1,439,605 | 359,901,146 | 61.6% |
| prob. value | | | | 0.000 |

**Table 5: Drug Consumption and Prevalence – Regression Evidence from Household Survey**

| Equation | 1 | 2 | 3 |
|---|---|---|---|
| | unconditional probability of prescription drug use | probability of prescription drug use, conditional on doctor consultation | probability of prescription drug use, conditional on doctor consultation |
| dependent variable | $N_{1.}/N_{..}$ | $N_{11}/N_{.1}$ | $N_{11}/N_{.1}$ |
| weight | $N_{..}$ | $N_{.1}$ | $N_{..}$ |
| regressor | $\log(N_{..})$ | $\log(N_{.1})$ | $\log(N_{..})$ |
| estimate | -0.00992 | 0.06078 | 0.04317 |
| std. error | 0.00569 | 0.00572 | 0.00501 |
| t-statistic | 1.74 | 10.63 | 8.62 |
| prob.-value | 0.0817 | <.0001 | <.0001 |

Key:
$N_{rv}$ = number of people with rx status r and visit status v
r = 1 if person used prescribed medicines for condition
= 0 if person did not use prescribed medicines for condition
v = 1 if person visited physician for condition
= 0 if person did not visit physician for condition

unconditional probability of rx = $N_{1.}/N_{..}$
conditional probability of rx = $N_{11}/N_{.1}$

$N_{..} = N_{00} + N_{01} + N_{10} + N_{11}$

$N_{.1} = N_{01} + N_{11}$

Table 6: Disease Prevalence and Mean Age at Death

| | 1980 | | | 1995 | | | 1995 - 1980 | | |
|---|---|---|---|---|---|---|---|---|---|
| Prevalence quintile | No. of deaths | Mean age | std. err. | No. of deaths | Mean age | std. err. | Mean age | t-statistic | p-value |
| Lowest | 1,586 | 49.4 | 0.379 | 1,839 | 56.9 | 0.352 | 7.6 | 14.6 | <.0001 |
| 2 | 18,537 | 58.3 | 0.111 | 18,189 | 65.2 | 0.112 | 6.9 | | |
| 3 | 56,233 | 65.9 | 0.064 | 62,951 | 67.8 | 0.060 | 1.9 | | |
| 4 | 169,345 | 68.6 | 0.037 | 215,638 | 71.0 | 0.033 | 2.3 | | |
| Highest | 1,541,562 | 72.6 | 0.012 | 1,836,369 | 74.4 | 0.011 | 1.8 | 106.4 | <.0001 |
| | | | | | | | | | |
| Highest - lowest | | 23.2 | | | 17.4 | | -5.8 | 11.2 | <.0001 |

Table 7: Prevalence and the Change in Mortality 1980-1995

| | (1) | (2) | (3) | (4) | (5) |
|---|---|---|---|---|---|
| | Mean Age at Death | Mean Age at Death | Mean Age at Death | Mean Age at Death | Mean Age at Death |
| Post-ODA ('95) Dummy | 4.3470 | 2.4544 | 2.4544 | 2.4544 | 2.4544 |
| | (1.3374)** | (0.0581)** | (0.2267)** | (0.0581)** | (0.2267)** |
| Quartile 2 X Post-ODA | | 0.6283 | 0.6283 | 0.6283 | 0.6283 |
| | | (0.2319)** | (0.4096) | (0.2319)** | (0.4096) |
| Quartile 3 X Post-ODA | | 0.6773 | 0.6773 | 0.6773 | 0.6773 |
| | | (0.4647) | (0.9262) | (0.4647) | (0.9262) |
| Quartile 4 X Post-ODA | | 2.7322 | 2.7322 | | |
| | | (0.1278)** | (0.9371)** | | |
| Quartile 5 (rarest) X Post-ODA | | 1.0376 | 1.0376 | | |
| | | (0.2551)** | (0.8949) | | |
| Rarest 40% X Post-ODA | | | | 2.6040 | 2.6040 |
| | | | | (0.1927)** | (0.8724)** |
| Post-ODA X ln(1980 Prevalence) | -0.1675 | | | | |
| | (0.1348) | | | | |
| Constant (average of fixed effects) | 71.4706 | 71.4799 | 71.4799 | 71.4800 | 71.4800 |
| | (0.1418)** | (0.0294)** | (0.1461)** | (0.0294)** | (0.1461)** |
| Clustering on... | Condition x year | Quintile x year | Condition x year | Quintile x year | Condition x year |
| Observations | 3922238 | 3922248 | 3922248 | 3922248 | 3922248 |
| R-squared | 0.22 | 0.22 | 0.22 | 0.22 | 0.22 |

Notes: All regressions include condition fixed effects. Robust standard errors (clustering as indicated in table) in parentheses. * significant at 5%; ** significant at 1% .