Evaluating Pharmaceutical Policy Options.

Tamking Clement and Carrie Chair Lecture

Taipei, Taiwan.

Ariel Pakes, Harvard University

June, 2024

Recent U.S. policies.

- Allowing Direct to Consumer Advertising ("DTCA") of prescription pharmaceuticals (mostly TV and only allowed since 1997). Only two developed countries allow this (U.S. & New Zealand).
- Allowing Medicare (grew to 30% of prescription drug sales in the U.S. in 2017) to bargain prices. Currently ten products ($\approx$ \$48 billion in sales). However President Biden's state of the union address states:

  "*Now it's time to go further and give Medicare the power to negotiate lower prices for 500 drugs over the next decade*".
- Allowing importation of pharmaceuticals from Canada. Florida has been approved to do so (initially in a limited way). 7 others applying for permission ($\approx$ 20% of U.S. sales). U.S. sales are over 50% of global sales (62.5% of sales in OECD countries studied below).

The European Union's Policies.

• I will be focused primarily on U.S. policies, but will return to the interaction with European Union policies at the end of the talk. (Apologies for not knowing the policies in Taiwan).

• The European Parliament adopted a Pharmaceutical Reform on April 10, 2024. It still has to be passed by the governments of the member states. It has two main parts that I return to later:

- One part is directed at centralizing procurement among member states. Similar to Europes' acquisition of COVID vaccines: procurement for the member states was centralized in one body.
- The second part is designed to increase the incentives for pharmaceutical R&D. It largely consists of insuring minimum levels of regulatory protection for new pharmaceutical products.

Two papers in process on these changes.

• **DTCA.** Pierre Dubois and I analyze the impact of Direct to Consumer Advertising. This paper also introduces new methodology for studying the evolution of markets; here I summarize of the empirical findings.

• Kate Ho and I study the likely implications of

- Bargaining with Medicare and
- Importation of pharmaceuticals from Canada,

on *both pharma company profitability and on consumer welfare*. We then consider how the European proposal interacts with this.

• **Goal**. Provide a comparison of the private and public incentives for company funded R&D.

Background: Benefits from pharma R&D in the U.S.

- Buxbaum et. al. (2020) report that between 1990 and 2015
  - life expectancy in the U.S. increased 1.32 years per decade, and
  - attribute about 35% of this, or .46 years, to pharmaceuticals.

- I do not have numbers on other developed countries, but they are likely similar.

- There were 48.9 million live births in the U.S. between 2005 and 2015. Valuing a life year at $100,000, this generates 2.25 trillion dollars in value.

- Taking the same period, we should:
  - Value the improvement in life expectancy of immigrants.
  - Value the decrease in morbidity in the population.

- Valuing the improvement in life expectancy of immigrants:
  - net immigration is $\approx$ 1.04 million per year;
  - at 1/10th of the decadal life year increment for every year in the U.S.

  This adds $\approx$ .57 trillion.

- Valuing the decrease morbidity.
  - Only have a study of the over 65 population ($\approx$ 16% of pop).
  - Chernew et al (2023); disability free life expectancy increased by 1.125 years per decade with $\approx$ 1/2 due to treatment improvements & "most of the treatment improvements are pharmaceutical";

  This adds $\approx$ .25 trillion (50,000$ per morbidity free year), and this does not count decreases in morbidity for the under 65 population.

• **Conclude:** The welfare benefit of pharma research to the U.S. population per decade was considerably more than 3 trillion dollars (using conservative valuations of years and morbidity; see Neumann et al, 2014).

Relationship to U.S. Costs (sum private and public).

• U.S. resident companies spent 747 billion dollars on pharma research in the U.S. between 2011-2021.

- US. pharmaceutical firms funded 87% of these expenditures.
- Companies whose parents were foreign funded 7%, other U.S. companies funded 3%, and 3% came from a mix of governments and other (primarily U.S.) institutions.

• "Funding from the NIH *contributed to* 354 of 356 drugs approved from 2010 to 2019 totaling $187 billion ..." (JAMA Health Forum. 2023 Apr)

Social Welfare and Social Costs in the U.S.

- So NIH grants are involved in some way in the development of most pharmaceuticals that receive FDA approval, but they spend much less than the pharmaceutical firms do on drug development.
- Even if we allocate all the NIH funds that "contributed to" new drugs to the R&D of drug development, the U.S. population's welfare benefit to cost ratio from pharma research is well above four.

• Of course there is

- a difference between average and marginal welfare benefits, and
- it has been difficult to empirically establish the connection between company funded pharma research and its benefits (explain).

• Still the numbers suggests that it would be socially beneficial to increase pharmaceutical research, not decrease it.

Policies, Incentives, and Company Profitability.

- As long as the vast majority of the funds for research keeps being supplied by firms, an increase in pharma research likely requires increased private incentives to do that research.

- Pharmaceutical companies supply their products to all countries. So when calculating returns we compute returns from world-wide sales.

- U.S. sales are over 50% of world wide sales. They are 62.5% of the sales of the OECD countries.

- Now a "back of the envelope" calculation of the impact of the proposed U.S. policies on the profitability of pharma companies.

- I come back to the proposed European policies and their interaction with the U.S. policies below.

- Calculating the impact of Medicare bargaining requires "bargained prices".
  - Medicare pricing would be similar to pricing procedures in other countries (a quasi-governmental institution would represent the buyer).
  - Canada has the second highest pharma prices of OECD countries.
  - So moving to Canadian prices would incur the smallest loss in profits.
- If we also allowed importation from Canada at Canadian prices for the eight states who have applied for permission
  - assumed that demand was inelastic (else we would need to adjust benefits; see Alston and Harris, 2020) and
  - no other mitigating developments,

There would be a $\approx$ **16% fall** *in pharmaceutical revenue.*

• We have SEC reports on the 16 largest research based pharma firms (by capitalization). 10 are U.S. firms & 6 are European.

• The SEC reports provides net profits and net margins.

- Net profit is computed as pharmaceutical global revenue after rebates minus operating expenses, taxes, interests, and other expenses.
- Net margins = net profits/ global revenue after rebates.

• The weighted average of the net margin, the weights being net profit shares, is 32%.

• A 16% fall in U.S. revenue with no change in costs or demand would imply net margins fall from 32% to 25%[1].

[1] If the price decrease increased demand the benefits would have to be adjusted as well as the costs. The largest source of non-adherence to drug regimen is costs, and non-adherence leads to significantly higher death rates; see Alston and Harris, 2024.

This would cut margins in the pharmaceutical industry by $\approx$ 20%.

• Of course a cut in margins by 20% does not necessarily imply a cut in research expenditures of 20%.

• Still it is hard to believe a cut in the returns to research of this magnitude would not negatively impact research investments.

• All of this despite the fact that our welfare calculations suggest we want to increase pharmaceutical research, not decrease it.

• On the other hand, rejecting these policy options would

- increase the cost of pharmaceuticals to the American economy,
- likely hurting poor and elderly consumers disproportionately.

- If one believes both
  - in the contractarian view that certain basic goods, including a minimal amount of health care, are a right of consumers who abide by society's rules, and that this requires less costly access to the drugs that are subject to these policies, and
  - that pharmaceutical R&D is as welfare enhancing as it seems to be,

then we need to change how the pharmaceutical market works.

- There has been many proposals on ways to mitigate the tradeoff between incentives for R&D and the costs of pharmaceuticals to society. The U.S. mostly focuses on subsidies (to consumers and/or firms)[2].

- We want to draw attention to a characteristic of the market that, though often mentioned, is seldom discussed with detailed magnitudes.

[2] Improvements in FDA procedures have also a possibility

The global dimension of the pharmaceutical market.

• Pharmaceuticals, like climate change, are "international products": once a new drug is developed all countries can benefit from it.

• Yet unlike the attempts to mitigate the impacts of climate change there are no international agreements on either

- pharmaceutical pricing, or
- public funds that facilitate pharmaceutical research.

• **Price Comparisons.** RAND (2023) calculates that the share weighted indices of U.S. to foreign prices (using U.S. revenue shares as weights)

- 234% for Canadian prices,
- 280% for United Kingdom prices, and
- 308% for a share weighted average of 33 developed countries.

• These percentages have been growing (see Danzon, 2018), & the levels underestimate the relative price differences (as U.S. prices discount rebates but, due to a lack of data, other countries prices do not).

• Below we quantify the impact of these price differences on the distribution of the costs and benefits of pharma research among developed countries.

First consider International differences in other government policies.

• Currently there are at least two sources of differences in public policies that impact the international division of the costs and benefits from pharmaceutical research.

- Publicly funded research that contributes to the development of new pharmaceutical products.
- Differences in tax/subsidy regimes which impact both the allocation of ownership rights among subsidiaries and the location of production.

Implications from Non Price Policies

• We ignore the tax & subsidy issues but research indicates that they would increase the inequities in the international distribution of costs & benefits from pharma research primarily because of the allocation of licensing rights and production to low tax environments (Sester, 2023, Senate Finance Committee).

• OECD report (2021) on publicly funded health related research (which includes more than pharma) is

- .21% of GDP in the U.S.
- .07% of GDP in Europe (which includes the 21 members of the EU member states that are part of the OECD), and
- .04% of GDP. in the other OECD members countries.

• Finaly European (but not U.S.) laws forbid DTCA. I come back to the impact of this below.

• **Conclude.** The international differences in pharmaceutical prices that imply the costs of research are born disproportionately by the U.S. population are not mitigated, indeed are likely accentuated, by international differences in other government policies.

The Impact of Internationalizing Pharma Prices.

• We consider the impact of internationalizing drug prices for only those 21 countries with at least $45,000 in per capita GDP.

• We ask
  - if there is an international price for each drug that each of these countries abide by,
  - and we assume total revenue is the same as current total revenue (so incentives to perform R&D would be unchanged),

What would be the weighted average markup or markdown in each country's prices, where the weights are country specific revenue shares?

Price Index Results.

- I focus on the results for branded pharmaceuticals (exclude generics), as they should be most informative w.r.t. R&D incentives (if we include generics the results are similar though a little less dramatic).
- Every country except the U.S. has a price increase.
- U.S. consumers would pay only .46 cents for every dollar we now spend.
- The country with the lowest price increase would be Canada; index =1.28. I.e. Canadians would pay 28% more for their pharma purchases.
- Other European indices:
  - Germany 1.48
  - France 1.97
  - United Kingdom 2.00
  - Italy 2.63
  - Spain 2.87.

- **Conclude:** Internationalizing pharma prices would cut U.S. prices in half, but would cause sharp increases in European prices (50% to almost 300%).
- Obstacles and benefits to proceeding with international prices
  - Benefits would include not having to worry about either
    - the costs of quasi-governmental committees setting and monitoring prices in different countries and the consequent "free riding" that now exists,
    - "parallel trade" in pharmaceuticals; at least among the countries that agree to the single price policy,
  - Obstacles include
    - many countries might have to find alternative ways of providing their citizens the minimal level of health care that they require,
    - and we would need to formulate international prices, hopefully in a way that leads to optimal R&D incentives.

Two Parts Of The European Parliament's proposal.

- First part: concentrates purchases of pharmaceuticals for all Europe in one purchaser. This would effect
  - administrative procedures,
  - pricing, and
  - R&D incentives.

- Administratively: similar to international pricing (but just Europe); i.e.
  - it would eliminate free riding problems in setting drug prices and eliminate parallel trade (and the associated "monitoring" costs).
  - it may decrease the cost of negotiations (once for all Europe).

- The impact of R&D incentives depend on how the new arrangements affect pharmaceutical prices.

- The price effects of a single agency purchasing for all of Europe would
  - *Increase the bargaining power of European negotiators, which would lower European prices further & accentuate current international inequities.*
- In principle it could also facilitate setting single U.S./European prices. There would be one rather than many agents to bargain with.
- However for this to occur and result in higher European prices this would require the European agency be willing increase prices due to their incentive effects on R&D and
  - *Currently we do not know of any pricing institution that ties their pharmaceutical pricing policies to the incentives to perform pharmaceutical research.*

• The European Package also does have policies that are designed to increase R&D incentives. To do so they focus on various ways of extending exclusivity of pharmaceutical products. These could be helpful and include

- A minimum period of protection of 7.5 years (impact depends on time from application to approval).
- Two years of market exclusivity (regardless of the appearance of a bio-similar product).
- Other extensions if the drug meets an "unmet" medical need, is for an "orphan" disease, the research is done in Europe, or if permission is obtained for a second indication.

• *Notice, however, that there is no reference to pharmaceutical price disparities. Without a lessening of these disparities the political pressure on the U.S. government to decrease pharma prices is unlikely to abate, which likely will have dire consequences for pharma innovation.*

Direct to consumer advertising

- U.S. is the largest pharmaceutical market in both revenue (recently $\approx$ \$600B per annum) and promotional spending: $\approx$ \$ 7B on DTC (3/4 on TV), & $\approx$ \$20B on detailing (most on free samples).
- Analyze: treatments for Asthma, Cholesterol, Depression, & Ulcer: $\approx$ 25% of DTC, and 22% of all detailing.
- Is DTC socially useful? Arguments:
  - *Against*; (i) incentives for excessive use, & (ii) returns largely a result of business stealing (no net benefit to society).
  - *For* makes; (i) consumers aware that they can treat a condition before it becomes serious (particularly those that do not regularly see doctors; often the poor and under-educated), &/or adherence to regimen (Wosinska, 2005) & (ii) providers aware of treatment alternatives.
- As above we also want to keep track of DTC's effects on profits.

Framework for the Analysis.

• Start with empirical model; Only assume agents maximize discounted profits given their perceptions; but **do not** assume their perceptions are "correct" or are "equilibrium perceptions".

• Then compute an equilibrium that conditions on the same variables. The equilibrium imposes that the perceptions of discounted profits are correct; at least on average over time (an Experience Based Equilibrium, see Fershtman and Pakes, 2012).

• Compare the *in-sample* predictions of the equilibrium model to the: i) empirical model and (ii) to the data.

• Recompute equilibrium for counterfactual (no DTC). This is what we need the equilibrium model for. That is data alone can not make predictions for an environment which we have never seen.

Summary of Results: Demand & Business Stealing.

• Demand system. Allow many variables to enter (on average ≈ 100, includes molecule effects, ATC(4) effects, price effects, price interactions....). It is clear that

- even given the other variables advertising has a significant effect on demand, and
- that detailing and DTC are complements, that is an increase generates more demand if it is combined with an increase in the other.

• Define business stealing as the impact on profits of one firm shutting down its DTCA while the other firms do not. Then average over firms.

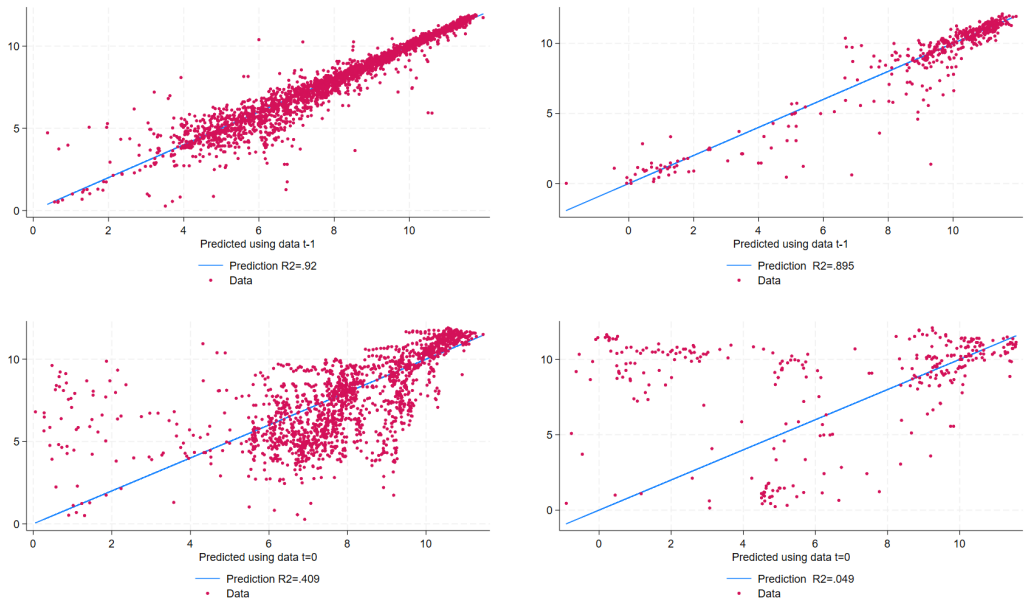
- Business stealing effects are huge when; we close down one products' DTC but let the other's continue (similar to other studies).
- One goal: compare this to equilibrium effects of shutting down DTC for everyone.

Variables that advertising responds to.

- Observables (i.e. in data).
  - The derivative of log profits w.r.t. advertising. The value function is an iterate of the profit function, but far too complex to compute. So using the impact of advertising on profits as a proxy is logical.
  - Time to loss of patent exclusivity. Advertising goes down as we approach the end of the patent life.
  - Advertising of competitors in the same therapeutic (ATC4) class has a negative impact. The profit function imposes a negative cross partial, so this accentuates the fact that competitors' advertising are strategic substitutes.

- Disturbances are highly serially correlated. $\Rightarrow$ the variables that the firm conditions on that we do not observe are highly serially correlated.

Results 3: Fit of the Empirical Model.

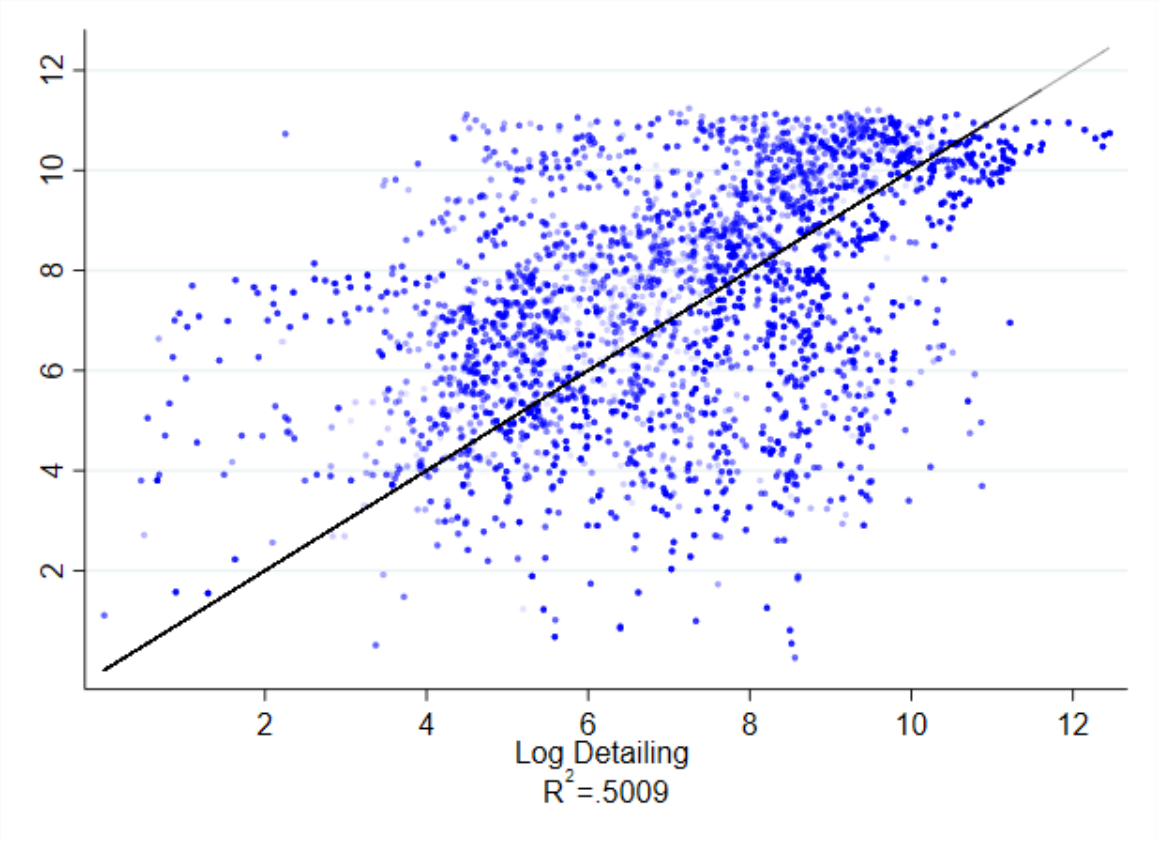


Note: Detailing on the left, DTC on the right. Using data t-1 for top graphs and only data at t=0 for bottom graphs.

EBE With Estimated Primitives.

- *Experience Based Equilibrium (Fershtman and Pakes, 2012):*
  1. As in empirical model: firms chose policies that maximize their perceptions of EDVs conditional on the variables they use to determine their advertising expenditures, and
  2. **New condition**: perceptions are consistent with outcomes at states visited repeatedly (on the "recurrent" class).
- *Equilibrium Analysis:*
  - Use estimated demand function, costs, and stochastic processes.
  - Develop computational algorithm to compute the fixed point for EBE policies (both DTC and detailing endogenous).
- **In sample fit.** Compare EBE policies to data.

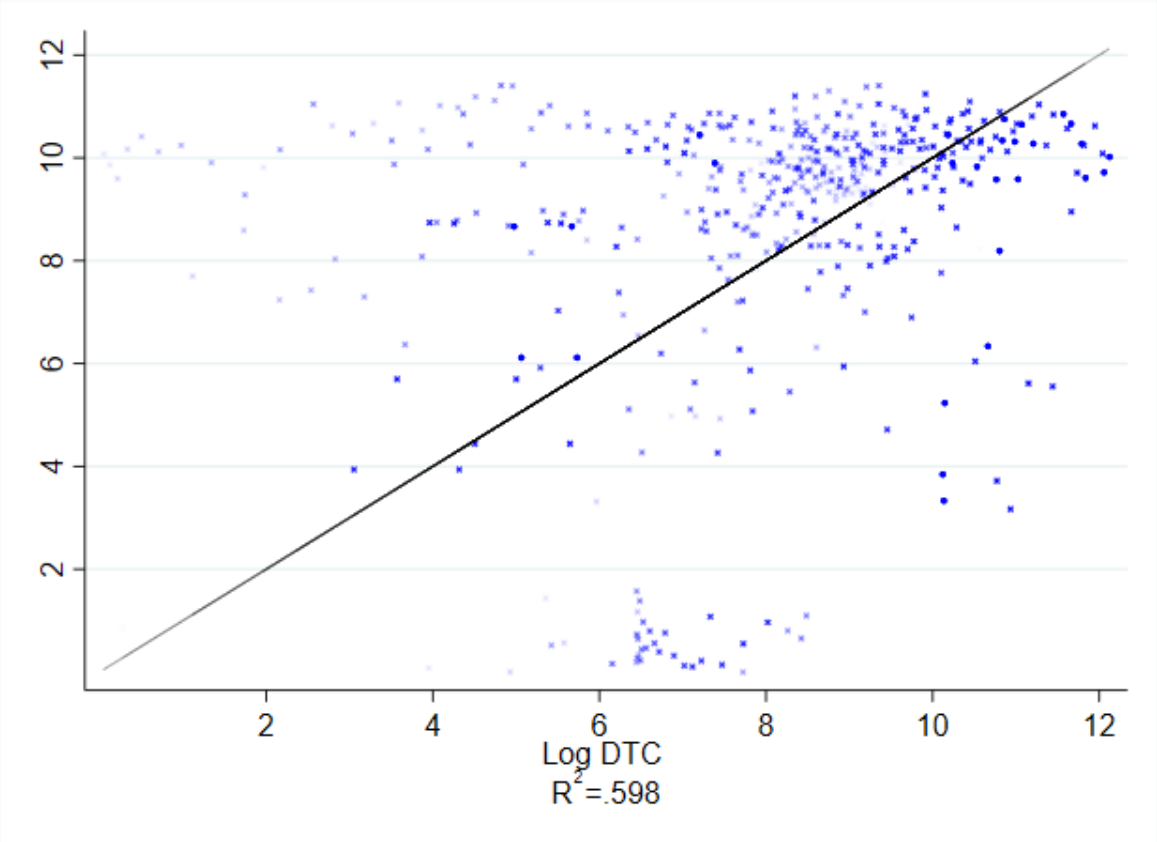
Results 4: Data against EBE for Detailing.



Note: Color intensity is decreasing with time since initial period of simulation.

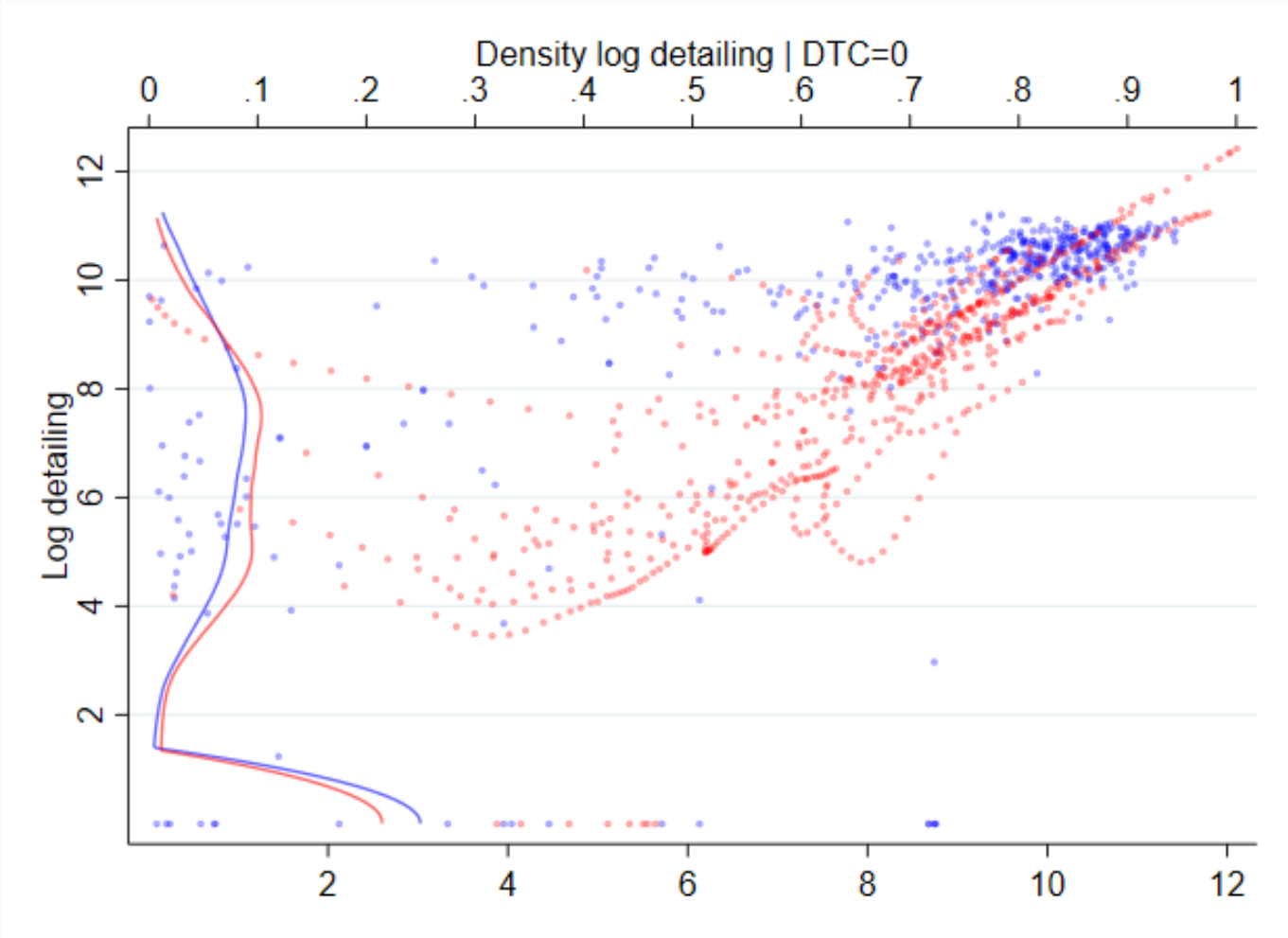
- The R^2 declines from $\approx .9$ in initial period, to $\approx .5$ in last (38^{th}) period.

Results 4: Data against EBE for DTC



- The R^2 declines from $\approx .9$ in initial period, to $\approx .6$ in last (38^{th}) period.

Results 4: Disturbances: Detailing vs DTC.



Note: Blue is data, red is EBE. Detailing on the vertical axis versus DTC on horizonal. The density distribution of Detailing when DTC is zero is plotted horizontally on the left vertical axis.

Counterfactuals: Preliminary Comments.

- We have just started work here, and are still doing robustness checks.

- When we compute counterfactuals with DTC=0 we assume an experience based equilibrium, the fit is about the same as in the actual data, and current prices.

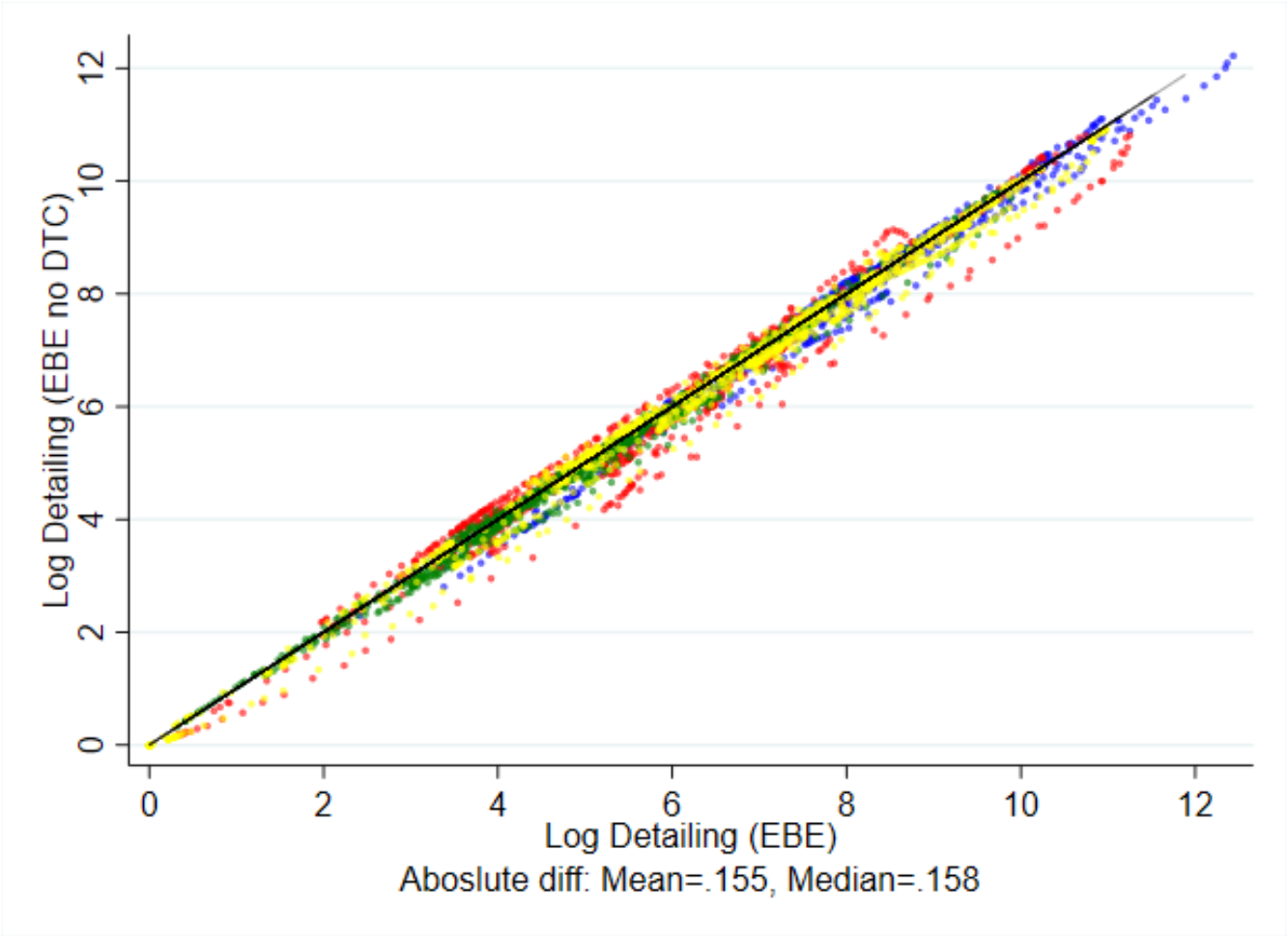
- Would like to do robustness w.r.t. allowing prices to change in the counterfactual environment. E.g. prices that maximize value given no DTC.

- We have only done this for banning DTCA.

- Will also compute for a regulation which bans advertising for a specific drug, but allows advertising the availability of treatments for a given disease by the FDA funded by a tax on sales of the relevant drugs.

Results 5: Detailing with and without DTC?

Equilibrium Detailing if DTC banned (y-axis) versus when DTC allowed.



Note: Blue for Anticholesterol, Red for Antiulcer, Green for Antidepressants, Black for Antiasthma.

Results 5: Profits & Inside share with no DTC.

Detailing, DTC, net profit (in 1000's quarterly); inside share

	Anticholesterol		Antiasthma		Antidepressants		Antiulcer	
All products	Total	% Δ	Total	% Δ	Total	% Δ	Total	% Δ
Detailing	225,805		125,089		25,358		76,758	
DTC	162,451		196,144		68,567		125,824	
Net profit	1,615,770		1,718,350		930,858		1,243,062	
Detailing (no DTC)	180,127	-20.2%	106,474	-14.8%	23,929	-5.6%	55,209	-28%
Net profit (no DTC)	1,378,562	-14.6%	1,519,602	-11.5%	922,682	-.8%	1,070,045	-13.9%
Inside goods	.467		.315		.623		.609	
Inside goods (no DTC)	.353		.296		.528		.49	

• Fall in detailing: reflects the positive cross partial between $a_d \& a_D$ in the demand function (tested extensively for this).

• The equilibrium profit fall is significant (except antidepressants), but far less than what the "business stealing" (40-60%)

• Per annum profit loss (millions 2014 dollars): Cholesterol $996, Asthma $795, Depression $33, Ulcer $692. Large except Depression.

• Big losers are the patented products which are likely also owned by firms that do R&D.

• A direct indicator of the impact on the fraction accessing the drugs to alleviate their conditions is the "inside good share" which falls noticeably for all but Asthma. Average over the 38 periods is:
Cholesterol: 11.4%; Asthma: 1.9%; Depression: 9.5%; Ulcers: 11.9%.

• Of course some of the fall in inside share may be a fall in those using it but not benefiting (the "excessive use" argument.). We note that there is evidence that too few Americans are taking these drugs.

• We are trying to access data on DTC's impact on take-up by income and education groups (Kilts marketing data plus BRFSS and/or NHIS).

• The loss in profit and the loss in the inside goods share indicate that if we do ban DTC we might want to mitigate the effects on:

1. Inside good share.
2. The incentives to do R&D.

• The counterfactual which prohibits DTC which mentions brand name but insures DTC that advertises the existence of drugs that attack particular diseases is designed to mitigate (1).

• **That is all we have for now. Thanx for coming.**