Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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ONLINE APPENDIX

ASSOCIATION OF REFERENCE PRICING WITH DRUG SELECTION AND SPENDING IN THE UNITED STATES

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Descriptive Statistics

Appendix Table 1 presents descriptive characteristics on the endpoint variables and the study treatment and comparison populations, using the prescription (individual drug claim) as the unit of analysis.

Appendix Table 2 gives the names of the highest and lowest priced drugs in the drug classes with the highest volume of RETA prescription claims in the year prior to the reference pricing implementation (the 2012 fiscal year).

Statistical Analysis

To evaluate the association of the RETA reference pricing program with our endpoints of interest, we estimate the following difference-in-differences regressions. Separate regressions are estimated for each endpoint.

$$y_{itk} = \alpha + \beta_1 RETA_i + \delta_{DD} RETA_i \times post_t + \gamma gender_i + \boldsymbol{year}_t + \boldsymbol{month}_t + \boldsymbol{class}_k + \varepsilon_{itk}. \quad (1)$$

In this expression, y_{itk} represents each of the three endpoints (dependent variables) examined:

1. A binary indicator equal to one if the prescription fill is for the low-priced drug in its therapeutic class.
2. The log-transformed 30-day equivalent price (allowed charge) of the drug. The price is calculated as the sum of employer spending and patient copays. It is converted to a 30-day

equivalent by dividing by the days supply to get price per day and then multiplying by 30. We add one to this price and then take the natural logarithm.

3. The log-transformed 30-day equivalent patient cost-sharing. This is calculated from the patient's copayment ($10 per prescription plus any additional payment that results from the reference pricing program). The patient out-of-pocket price is converted to a 30-day equivalent and we use the log(x + 1) transformation.

In the regression equations we include indicator variables for the RETA population $RETA_i$. The δ_{DD} coefficient on the interaction between the RETA population indicator and the post-implementation period indicator gives the difference-in-differences estimate of the association between the program and each endpoint. We include a bivariate variable for patient gender. We include year and month fixed effects to control for across-year and within-year trends. The year fixed effects are collinear with the post-implementation period indicator and we thus do not include the $post_t$ main effect.

In our main specification, we include drug class fixed effects to control for differences across therapeutic drug classes. In our robustness tests, we also control for several additional factors. First, we interact year and month to control for time trends rather than merely within year and within month trends. Second, we interact the drug class fixed effects with the year fixed effects to control for time-varying changes within each drug class (e.g. introduction of generics). Our preferred specification does not include these interaction terms, but their addition does not meaningfully change the results. We do not include the full set of interaction terms in the main result to make the regressions more interpretable in the main text.

In each specification, we use robust standard errors clustered at the drug class level.

Alternative Specifications: Results

Appendix Table 3 presents the results for the probability of having a low-priced fill. The first column includes just the RETA treatment variable, the year fixed effects, and the $RETA_i \times post_t$ interaction term. We iteratively add controls for patient gender and month (column 2), drug class fixed effects (column 3), fixed effects for year by month interactions (column 4), and fixed effects for year by drug class interactions (column 5). Adding controls for patient gender and month has little effect on the results, while adding the drug class fixed effect reduces the measured impact of reference pricing by approximately one percentage point. Our preferred specification is in column 3, where the reference pricing program increased the use of low-priced drugs by 6.95 percentage points.

Appendix Table 4 presents analogous results using the prescription's 30-day price as the endpoint variable. As with Appendix Table 3, we find little effect as additional controls are added to the model. Our preferred specification is column 3, which indicates that the reference pricing program was associated with a decrease in the average price per prescription of 13.87%.

Appendix Table 5 uses the 30-day equivalent patient out-of-pocket co-payment as the endpoint variable. Adding the full set of controls reduces the increase in patient cost-sharing from 6.28% in the most parsimonious model in column 1 to 5.16% in the preferred specification in column 3.

Parallel Trends

To test for parallel trends, we use an event study approach to estimate trends in the monthly difference in use of low-cost drugs and prices between the RETA and Union trusts. To do so, we estimate the following multivariable linear regression:

$$y_{itk} = \alpha + \sum_{m=1}^{M} \delta_m RETA_i + \beta class_k + X_{it} + \varepsilon_{itk}. \qquad (2)$$

In this expression, y_{itk} measures each of our key dependent variables. The δ_m coefficients measure the difference in each outcome between the RETA and Union trusts during month m. We control for the same market and patient characteristics as in the main analysis.

Appendix Figure 1 presents the event study results for monthly trends in the difference between use of low-priced drugs between the RETA and Union trusts. The black line represents the monthly coefficient and the dashed lines represent 95% confidence intervals, which are derived from robust standard errors clustered at the patient level. In the period before the implementation of the reference pricing program, the RETA population consistently used a smaller share of low-priced drugs than the Union population. There was a slight decrease in this difference in the months prior to the implementation of the program, which we interpret as an anticipatory effect. Following the implementation of the program, the difference between the RETA and Union populations reversed. Starting in July 2013, the RETA population consistently used a higher share of low-priced drugs than did the Union population.

Appendix Figure 2 presents trends in the monthly difference in drug prices for the RETA and Union populations. Similar to the previous chart, in the months prior to the program, the RETA population consumed drugs that were 20% more expensive than the Union population. There is a small reduction in this difference prior to the implementation of the program, but

following the introduction of reference pricing in July 2013, the RETA population consumed drugs that were 15% less expensive than did the Union population.

For both charts, the lack of any meaningful change in the difference between the RETA and Union populations supports the parallel trends assumption that is necessary for difference-in-differences research designs.

Residual Plots

Appendix Figures 3 and 4 plot the residuals for alternative specifications of the price regression. For both plots, we use a randomly selected 1% sample of both the treatment and control populations. The regression model used for Figure 3 only includes year and month fixed effects and shows clear evidence of heteroskedasticity. The regression model used for Figure 4 includes the full set of controls. There is no evidence of heteroskedasticity. The absence of heteroskedasticity supports using the full set of controls in our main specification.

Supplementary Appendix Table S1: Descriptive statistics

	RETA Trust					Union Trust				
Fiscal Year *(July-June)*	2010	2011	2012	2013	2014*	2010	2011	2012	2013	2014*
Share of fills for low-priced drugs										
mean	60.2%	60.6%	61.8%	70.5%	70.6%	64.4%	64.2%	65.4%	66.5%	66.6%
Standard deviation	49.0%	48.9%	48.6%	45.6%	45.5%	47.9%	47.9%	47.6%	47.2%	47.2%
Price per 30-day equivalent fill										
mean	$68.6	$70.4	$66.5	$50.9	$50.4	$66.6	$66.5	$59.3	$55.5	$54.3
Standard deviation	$117.0	$133.3	$137.2	$106.0	$108.6	$130.9	$97.7	$95.4	$109.7	$105.2
Patient cost-sharing per 30-day equivalent fill										
mean	$16.9	$17.2	$16.1	$19.6	$18.2	$13.4	$14.4	$14.0	$13.3	$12.3
Standard deviation	$20.5	$24.1	$23.6	$42.7	$43.1	$19.9	$14.8	$15.0	$15.3	$14.2
Share of fills (males)										
mean	38.5%	39.0%	39.5%	39.9%	37.4%	52.1%	52.3%	52.6%	52.7%	52.8%
Standard deviation	48.7%	48.8%	48.9%	49.0%	48.4%	50.0%	49.9%	49.9%	49.9%	49.9%
Number of fills	158,174	149,244	121,518	105,968	38,552	124,123	119,789	117,166	125,839	62,368
Enrollment	24,970	23,995	21,166	18,061	15,537	35,003	33,226	27,070	25,929	27,145
Total Pharmaceutical Spending (millions)	$12.4	$11.6	$8.9	$5.9	$2.2	$13.6	$14.1	$12.2	$11.6	$5.8

* July-December only

Supplementary Appendix Table S2: Highest and Lowest Priced Drugs in RETA's Most Commonly Prescribed Drug Classes

Drug Class	Highest Price Drug	Lowest Price Drug
HMG CoA Reductase Inhibitors	LOVASTATIN TAB SR 24HR 60 MG	LOVASTATIN TAB 10 MG
Thyroid Hormones	LIOTHYRONINE SODIUM POWDER	THYROID TAB 15 MG (1/4 GRAIN)
Selective Serotonin Reuptake Inhibitors (SSRIs)	FLUVOXAMINE MALEATE CAP SR 24HR 100 MG	FLUOXETINE HCL CAP 20 MG
ACE Inhibitors	PERINDOPRIL ERBUMINE TAB 8 MG	CAPTOPRIL TAB 25 MG
Beta Blockers Cardio-Selective	NEBIVOLOL HCL TAB 10 MG (BASE EQUIVALENT)	METOPROLOL TARTRATE TAB 25 MG
Proton Pump Inhibitors	ESOMEPRAZOLE MAGNESIUM FOR DELAYED RELEASE SUSP PACKET 10 MG	PANTOPRAZOLE SODIUM EC TAB 40 MG (BASE EQUIV)
Biguanides	METFORMIN HCL TAB SR 24HR MODIFIED RELEASE 1000 MG	METFORMIN HCL TAB 500 MG
Hydrocodone Combinations	HYDROCODONE-ACETAMINOPHEN TAB 5-300 MG	HYDROCODONE-ACETAMINOPHEN TAB 7.5-750 MG
Nonsteroidal Anti-inflammatory Agents (NSAIDs)	MEFENAMIC ACID CAP 250 MG	MELOXICAM TAB 15 MG
Calcium Channel Blockers	DILTIAZEM HCL COATED BEADS CAP SR 24HR 360 MG	DILTIAZEM HCL TAB 30 MG
Angiotensin II Receptor Antagonists	CANDESARTAN CILEXETIL TAB 8 MG	LOSARTAN POTASSIUM TAB 25 MG
Benzodiazepines	ALPRAZOLAM TAB SR 24HR 2 MG	CHLORDIAZEPOXIDE HCL CAP 10 MG
Anticonvulsants - Misc.	LAMOTRIGINE TAB SR 24HR 50 MG	CARBAMAZEPINE CHEW TAB 100 MG
Nasal Steroids	BECLOMETHASONE DIPROPIONATE MONOHYD NASAL SUSP 42 MCG/SPRAY	FLUTICASONE PROPIONATE NASAL SUSP 50 MCG/ACT
Thiazides and Thiazide-Like Diuretics	CHLOROTHIAZIDE SUSP 250 MG/5ML	INDAPAMIDE TAB 1.25 MG
Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)	DULOXETINE HCL ENTERIC COATED PELLETS CAP 20 MG	VENLAFAXINE HCL TAB 75 MG
Beta Adrenergics	LEVALBUTEROL HCL SOLN NEBU 0.63 MG/3ML (BASE EQUIV)	ALBUTEROL SULFATE TAB 2 MG
Non-Benzodiazepine - GABA-Receptor Modulators	ESZOPICLONE TAB 1 MG	ZOLPIDEM TARTRATE TAB 5 MG
Human Insulin	INSULIN REGULAR (HUMAN) INJ 500 UNIT/ML	INSULIN REGULAR (HUMAN) INJ 100 UNIT/ML
Angiotensin II Receptor Antag & Thiazide/Thiazide-Like	OLMESARTAN MEDOXOMIL-HYDROCHLOROTHIAZIDE TAB 40-12.5 MG	LOSARTAN POTASSIUM & HYDROCHLOROTHIAZIDE TAB 50-12.5 MG
Antidepressants - Misc.	BUPROPION HCL TAB SR 24HR 450 MG	BUPROPION HCL TAB 100 MG
Estrogens	ESTRADIOL GEL 0.06% (0.52 MG/0.87 GM METERED-DOSE PUMP)	ESTRADIOL TAB 0.5 MG
Central Muscle Relaxants	CYCLOBENZAPRINE HCL CAP SR 24HR 15 MG	BACLOFEN TAB 10 MG
Sulfonylureas	CHLORPROPAMIDE TAB 250 MG	GLIPIZIDE TAB 5 MG
Opioid Agonists	HYDROMORPHONE HCL TAB SR 24HR 32 MG	METHADONE HCL TAB 5 MG
Fibric Acid Derivatives	FENOFIBRATE MICRONIZED CAP 130 MG	FENOFIBRATE TAB 54 MG
Leukotriene Receptor Antagonists	MONTELUKAST SODIUM ORAL GRANULES PACKET 4 MG (BASE EQUIV)	MONTELUKAST SODIUM CHEW TAB 4 MG (BASE EQUIV)
ACE Inhibitors & Thiazide/Thiazide-Like	QUINAPRIL-HYDROCHLOROTHIAZIDE TAB 20-12.5 MG	LISINOPRIL & HYDROCHLOROTHIAZIDE TAB 10-12.5 MG
Adrenergic Combinations	FLUTICASONE-SALMETEROL INHAL AEROSOL 115-21 MCG/ACT	IPRATROPIUM-ALBUTEROL NEBU SOLN 0.5-2.5(3) MG/3ML
Selective Serotonin Agonists 5-HT(1)	SUMATRIPTAN SUCCINATE NEEDLE-FREE INJ DEVICE 6 MG/0.5ML	SUMATRIPTAN SUCCINATE TAB 50 MG

Supplementary Appendix Table S3: Association between Reference Pricing and Probability Patient Uses the Low-Priced Drug within its Therapeutic Class

	(1)	(2)	(3)	(4)	(5)
Dependent Variable	Low-priced fill	Low-priced fill	Low-priced fill	Low-priced fill	Low-priced fill
RETA X post	0.0784***	0.0784***	0.0695***	0.0695***	0.0633***
	(0.0499 - 0.107)	(0.0498 - 0.107)	(0.0403 - 0.0987)	(0.0403 - 0.0987)	(0.0337 - 0.0929)
RETA	-0.0384	-0.0416	-0.0247**	-0.0247**	-0.0224**
	(-0.0932 - 0.0164)	(-0.0939 - 0.0107)	(-0.0437 - -0.00568)	(-0.0437 - -0.00563)	(-0.0421 - -0.00263)
FY2010	-0.0135	-0.0137	-0.0130*	-0.0124	-0.0451***
	(-0.0301 - 0.00318)	(-0.0303 - 0.00297)	(-0.0284 - 0.00233)	(-0.0282 - 0.00332)	(-0.0461 - -0.0441)
FY2011	-0.0119**	-0.0120**	-0.00915**	-0.0131***	-0.0183***
	(-0.0210 - -0.00280)	(-0.0211 - -0.00289)	(-0.0161 - -0.00218)	(-0.0228 - -0.00331)	(-0.0190 - -0.0176)
FY2013	0.00941*	0.00940*	0.00795**	0.00760*	0.110***
	(-0.00115 - 0.0200)	(-0.00110 - 0.0199)	(0.00132 - 0.0146)	(-0.00117 - 0.0164)	(0.0964 - 0.125)
FY2014	0.0108	0.0132	0.0133**	0.0138**	0.131***
	(-0.00538 - 0.0269)	(-0.00496 - 0.0313)	(0.00139 - 0.0253)	(0.000200 - 0.0274)	(0.119 - 0.144)
Controls		+gender, month	+drug class	+yearXmonth	+drug classXyear
Observations	1,122,741	1,122,741	1,122,741	1,122,741	1,122,741
R-squared	0.005	0.005	0.254	0.254	0.262
Mean	0.618	0.618	0.618	0.618	0.618

Supplementary Appendix Table S4: Association between Reference Pricing and Drug Price per Prescription

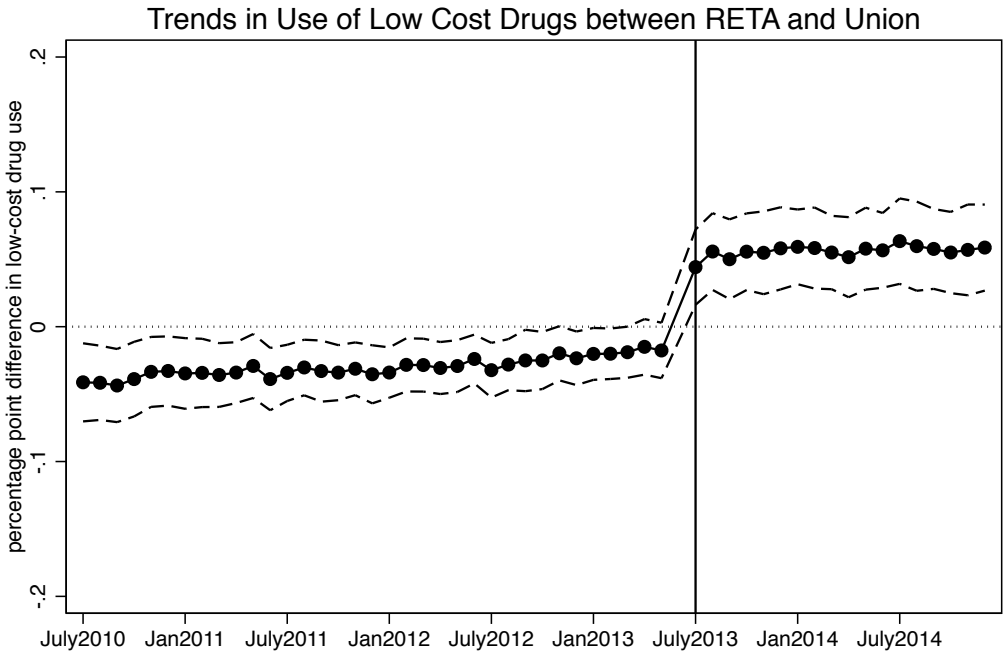
	(1)	(2)	(3)	(4)	(5)
Dependent Variable	ln(30 day price + 1)	ln(30 day price + 1)	ln(30 day price + 1)	ln(30 day price + 1)	ln(30 day price + 1)
RETA X post	-14.01%**	-14.05%**	-13.87%**	-13.73%**	-11.04%**
	(-23.76 - -3.001)	(-23.83 - -3.013)	(-23.77 - -2.687)	(-23.63 - -2.554)	(-19.97 - -1.117)
RETA	-1.156%	-0.308%	9.863%	9.758%	8.628%
	(-18.80 - 20.32)	(-17.80 - 20.91)	(-2.498 - 23.79)	(-2.586 - 23.67)	(-3.564 - 22.36)
FY2010	11.38%**	11.44%**	8.304%*	4.102%	18.43%***
	(2.243 - 21.34)	(2.280 - 21.42)	(-0.826 - 18.27)	(-4.730 - 13.75)	(17.79 - 19.07)
FY2011	14.09%***	14.06%***	12.19%***	13.32%***	14.76%***
	(7.101 - 21.53)	(7.070 - 21.51)	(5.085 - 19.78)	(6.578 - 20.49)	(14.31 - 15.20)
FY2013	-14.10%***	-14.08%***	-12.19%***	-5.900%	-36.34%***
	(-19.85 - -7.938)	(-19.81 - -7.946)	(-17.92 - -6.072)	(-12.58 - 1.285)	(-39.72 - -32.76)
FY2014	-19.69%***	-20.89%***	-18.68%***	-22.24%***	-39.90%***
	(-25.88 - -12.98)	(-27.48 - -13.70)	(-25.93 - -10.72)	(-29.19 - -14.60)	(-42.63 - -37.05)
Controls		+gender, month	+drug class	+yearXmonth	+drug classXyear
Observations	1,122,741	1,122,741	1,122,741	1,122,741	1,122,741
R-squared	0.017	0.018	0.509	0.510	0.535
Mean	66.48	66.48	66.48	66.48	66.48

Supplementary Appendix Table S5: Association between Reference Pricing and Patient Cost-Sharing per Prescription

	(1)	(2)	(3)	(4)	(5)
Dependent Variable	ln(30 day OOP + 1)	ln(30 day OOP + 1)	ln(30 day OOP + 1)	ln(30 day OOP + 1)	ln(30 day OOP + 1)
RETAXpost	6.282%**	6.215%**	5.165%**	5.223%**	6.918%***
	(1.082 - 11.75)	(1.018 - 11.68)	(0.173 - 10.40)	(0.234 - 10.46)	(2.678 - 11.33)
treatment	19.35%**	19.33%**	30.45%***	30.39%***	29.76%***
	(1.059 - 40.94)	(1.083 - 40.88)	(14.82 - 48.21)	(14.77 - 48.14)	(13.94 - 47.78)
FY2010	4.544%*	4.547%*	2.879%	0.933%	-5.800%***
	(-0.395 - 9.727)	(-0.392 - 9.730)	(-2.194 - 8.215)	(-4.632 - 6.824)	(-6.459 - -5.135)
FY2011	6.516%***	6.470%***	5.363%***	8.045%***	-1.548%***
	(3.434 - 9.689)	(3.388 - 9.644)	(2.312 - 8.504)	(4.185 - 12.05)	(-2.003 - -1.090)
FY2013	-6.452%***	-6.399%***	-4.884%***	-0.0252%	-11.01%***
	(-9.443 - -3.361)	(-9.379 - -3.321)	(-8.111 - -1.545)	(-4.451 - 4.606)	(-13.18 - -8.791)
FY2014	-12.56%***	-14.13%***	-12.23%***	-15.05%***	-15.87%***
	(-15.82 - -9.166)	(-17.58 - -10.53)	(-16.54 - -7.694)	(-19.19 - -10.69)	(-18.40 - -13.27)
Controls		+gender, month	+drug class	+yearXmonth	+drug classXyear
Observations	1,122,741	1,122,741	1,122,741	1,122,741	1,122,741
R-squared	0.020	0.021	0.363	0.363	0.379
Mean	16.15	16.15	16.15	16.15	16.15

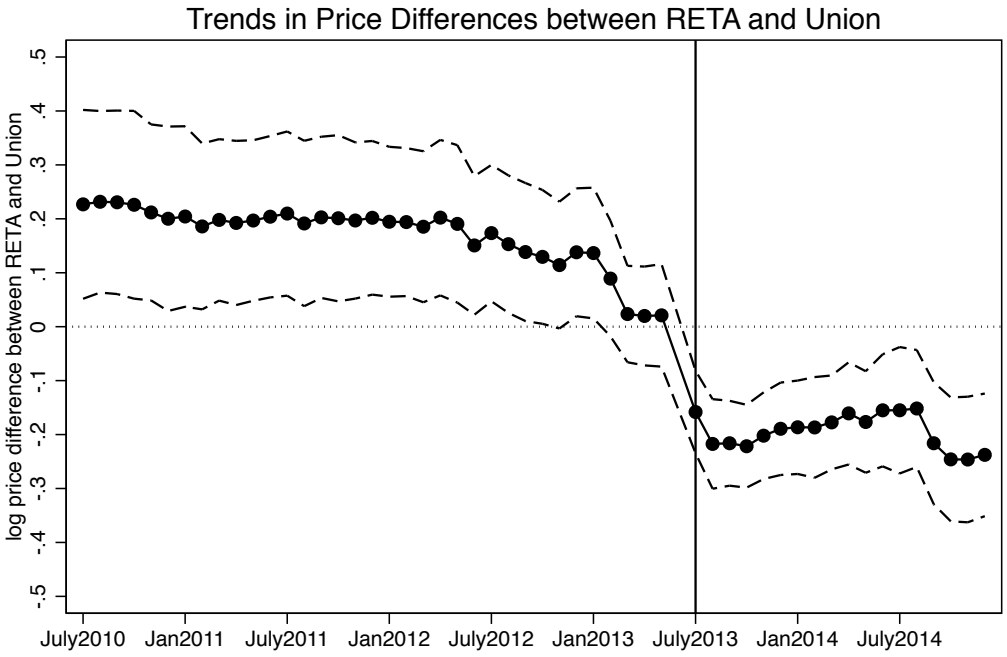
Note: OOP refers to out of pocket cost sharing. Some patients have zero cost sharing responsibilities on a prescription. Because the natural logarithm of zero is undefined, we add $1 to every prescription price to be able to take the natural logarithm (log), which permits interpretation of coefficients in percentage terms. Our results are robust to the addition of different constants to patient cost-sharing.

Supplementary Appendix Figure 1: Monthly Difference in Use of Low-Priced Drugs



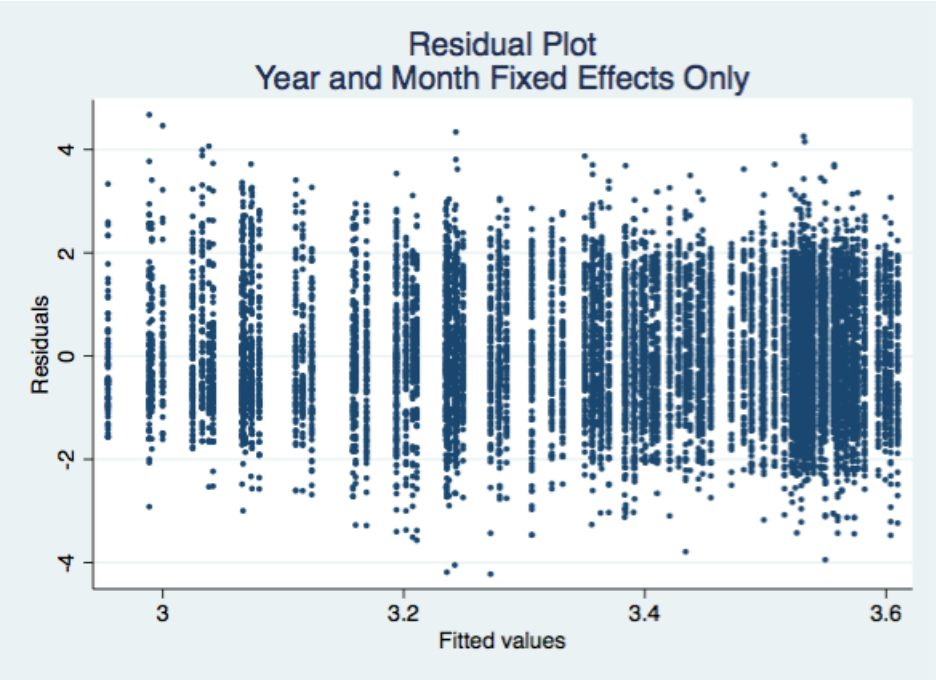
Solid vertical line: Reference pricing start

Supplementary Appendix Figure 2: Monthly Difference in Prices for Filled Drugs



Solid vertical line: Reference pricing start

Supplementary Appendix Figure 3: Residual Plots - Year and Month Fixed Effects Only



Supplementary Appendix Figure 4: Residual Plots -Full Controls