Supplemental Online Content

Desai SM, Chen AZ, Wang J, et al. Effects of real-time prescription benefit recommendations on patient out-of-pocket costs: a cluster randomized clinical trial. *JAMA Intern Med.* Published online September 12, 2022. doi:10.1001/jamainternmed.2022.3946

eMethods

eFigure 1. Example of screenshot of a RTPB recommendation

eFigure 2. Informational email sent to all outpatient physicians regarding RTPB recommendations

eFigure 3. Subgroup analyses by patient factors and specialty: Effects of RTPB recommendations on patient out-of-pocket costs

eTable 1. Number of practices, prescribers, and medication orders using pre-trial volumes in intervention and control practice profiles

eTable 2. Percent of orders by drug class for 15 most common drug classes

eTable 3. Types of alternatives and maximum out-of-pocket cost variation ("potential savings") by alternative type across orders

eTable 4. Proportion of orders with alternatives by medication (for 25 highest volume medications)

eTable 5. Comparison of all outpatient orders in NYU Langone system versus analytic sample during study period

eTable 6. Model specifications: Sequential inclusion of covariates

eTable 7. Most common medication classes with $0 out-of-pocket cost orders

eTable 8. Logistic regression model estimates for secondary outcomes: Odds ratios and marginal effects

eTable 9. Sensitivity analyses: Stratification by whether an order and its alternatives were in distinct medication classes

eTable 10. Ten most frequent drug classes by quartiles based on average drug class out-of-pocket cost

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

Table of Contents
eMethods

1. Randomization design and implementation....3
2. Intervention description....3
3. Data....5
4. Power analysis and implied intervention length....6
5. Regression specification....6
6. Sensitivity analyses: Methods....6
7. Subgroup analyses: Methods....7
8. Description of orders and types of alternatives....8
9. Comparison of all outpatient prescriptions versus prescriptions in analytic sample....9
10. Sensitivity analysis: Results....10
11. Subgroup analyses: Results....10
12. Changes from the pre-analysis plan....10
eFigure 1. Example of screenshot of a RTPB recommendation....12
eFigure 2. Informational email sent to all outpatient physicians regarding RTPB recommendations....13
eFigure 3. Subgroup analyses by patient factors and specialty: Effects of RTPB recommendations on patient out-of-pocket costs....14
eTable 1. Number of practices, prescribers, and medication orders using pre-trial volumes in intervention and control practice profiles....15
eTable 2. Percent of orders by drug class for 15 most common drug classes....16
eTable 3. Types of alternatives and maximum out-of-pocket cost variation ("potential savings") by alternative type across orders....17
eTable 4. Proportion of orders with alternatives by medication (for 25 highest volume medications)....18
eTable 5. Comparison of all outpatient orders in NYU Langone system versus analytic sample during study period....19
eTable 6. Model specifications: Sequential inclusion of covariates....20
eTable 7. Most common medication classes with $0 out-of-pocket cost orders....21
eTable 8. Logistic regression model estimates for secondary outcomes: Odds ratios and marginal effects....22
eTable 9. Sensitivity analyses: Stratification by whether an order and its alternatives were in distinct medication classes....23
eTable 10. Ten most frequent drug classes by quartiles based on average drug class out-of-pocket cost....24

eMethods

1. Randomization design and implementation

We randomized the implementation of the RTPB recommendations across NYU's Faculty Group Practice and Family Health Centers. Family Health Centers are federally qualified health centers integrated with NYU Langone Health.

We performed a stratified, cluster randomization. We randomized practice profiles to receive RTPB recommendations. Practice profiles are the lowest level at which the RTPB recommendations could be turned on. Within NYU Langone Health, a single clinical site can comprise multiple practices (internally referred to as "departments"), where prescribers within a single practice are in the same specialty group. Within a single clinical site, practices can be assigned to multiple practice profiles. And practices within a single practice profile can be located in different clinical site locations. Each practice is assigned to a practice profile by the system's IT team, and the practice profile is used to control a multitude of EHR-related settings, including the RTPB recommendations.

We used a stratified randomization technique, stratifying at the specialty level since the volume, average price, and opportunity for savings through prescribing of lower-cost drugs may vary across specialties. We grouped subspecialties together to ensure sufficient sample size within a given specialty.

Some physicians may practice across multiple practices or departments. We did not anticipate concerns about contamination, because the intervention is at the order-level, and the same drug can have different out-of-pocket costs depending on a patient's benefit design and deductible.

On November 9th, 2021, stratified randomization of practice profiles was performed with a 1:1 allocation ratio by a data analyst at NYU Langone Health (who was not involved in any other aspect of the study) using R. Balance between the treatment and control groups was examined by specialty on the number of prescribers, the number of practices, and the number of drug orders using pilot data from before the commencement of the trial (eTable 1). No re-randomization procedure was prespecified. Data was blinded with respect to intervention and control assignment until after the trial period.

2. Intervention description

The intervention comprised Surescripts RTPB recommendations for medication order alternatives with lower out-of-pocket costs relative to the ordered drug in NYU Langone Health outpatient setting. The RTPB system was integrated into the system's Epic electronic health record system, such that the recommendations are shown at the point of e-prescribing. Prescribers can select one of the alternatives or continue with the initiated order. As an example, eFigure 1 is a screenshot of the RTPB recommendation for an anonymous patient. The recommendation displays the total fill and out-of-pocket cost per day for the initiated order as well as all recommended alternatives. Because in some cases, recommendations are for a longer days supply to take advantage of quantity discounts, the total fill cost for a recommended alternative could be higher than the initiated order.

Out-of-pocket cost estimates for the initiated order and all alternatives were patient-specific and "real-time" in that they took into account patients' benefit design, formulary restrictions, and patient's cost-sharing requirements inclusive of all copays, coinsurance, and deductibles. The NYU Langone's e-prescribing system reverts orders to generics unless the prescriber specifies that the order be "dispensed as written". Therefore, any out-of-pocket cost estimates would be based on the generic version. Therefore, we were not concerned that the out-of-pocket cost estimates would overestimate out-of-pocket costs for the branded drugs when the pharmacist could dispense the generic.

The potential alternatives that could be recommended for each medication are determined by each prescription benefit manager and provided to Surescripts. Therefore, the types of alternatives that are displayed could vary across patients and insurers.

The RTPB system recommended three kinds of alternatives: 1) a different medication that was determined to be clinically-substitutable with the initiated medication order, 2) a mail-order prescription, and 3) a longer days supply.

For the first month of the intervention, prescribers had the option to turn off all recommendations by checking the box in the screenshot. If this box was checked, the physician would no longer see any recommendations, and there was no way for the prescriber to turn recommendations back on. However, in February 2021, a setting was made available by Epic to remove this option such that prescribers can no longer opt-out of recommendations. This change was implemented immediately and all prescribers that had turned off the recommendations had them turned on again.

RTPB recommendations were made only when several conditions were met:

1. The patient's identifying and insurance information could be linked between the EHR and the Surescripts database. This was necessary for the system to yield out-of-pocket estimates. Patient linkage was based on a five-point matching algorithm, and if this linkage was not successful, the system could not generate out-of-pocket cost estimates or make lower-cost recommendations. In addition to this linkage, the patient's prescription benefit manager (PBM) had to be entered into the EHR for the system to yield out-of-pocket cost estimates, which are specific to each patient's benefit design.
2. Among patients whose information could be linked to the Surescripts database, potential alternatives had to be available according to the RTPB system for the medication order being initiated.
3. Among orders with alternatives, we required that the alternatives must offer some minimum degree of savings to yield a RTPB recommendation. In particular, recommendations were made for orders if the order being initiated had a total fill cost of at least $5.00 and if there was at least one alternative offering savings of at least $0.10 per day in out-of-pocket costs ($3.00 savings for a 30-day supply). These thresholds were determined after discussions with operational leadership and consultations with Epic and Surescripts about recommended thresholds. The goal was to balance the volume of notifications with providing opportunities to save.

The intervention was originally planned to begin on November 18, 2020. However, due to an IT glitch, the intervention was not turned on for the randomized practices. Therefore, the intervention start date was delayed to January 13, 2021 as soon as the glitch was rectified.

Prior to implementation, a written orientation and guide to the RTPB recommendations were sent to all NYU Langone outpatient physicians in a weekly email series on Epic updates (eFigure 2). The email informed physicians that RTPB recommendations would be introduced and described potential benefits of RTPB recommendations. The email did not provide information about which practices were assigned to the intervention or control groups. One member of the study team practices in the outpatient setting at NYU Langone. The clinical site of this member was one of our pilot locations and therefore, excluded from the analysis.

Prior to the trial, the RTPB recommendation system was piloted in two clinical sites. For the purposes of the pilot, we did not set any threshold requiring alternatives to offer any minimum degree of savings to generate a recommendation. The purpose of the pilot was to ensure that the system was in fact working and to examine the nature of the data capture. We also conducted informal, unstructured interviews with several physicians at one of the pilot sites to ensure they were seeing the recommendations. In part based on feedback from these interviews stating that there were a high volume of orders with recommendations offering trivial savings, we imposed a threshold to require savings of at least $0.10 per day to provide a recommendation.

3. Data

We drew data on all outpatient medication orders at NYU Langone Health during the trial period from the Epic EHR database which also contained relevant information from the Surescripts RTPB system for cases when the patient link between the EHR and Surescripts database was successful. For each order, we could observe the medication, medication class, days supply, and pharmacy type (retail, mail, or specialty), and the out-of-pocket cost (per day and for the fill). For each order, we could also see this information for all potential alternative orders.

Importantly, one feature of our data is that we could observe information on all alternatives regardless of whether the alternatives were higher or lower cost than the initiated or the ordered medication and regardless of whether the alternatives were recommended in the RTPB system. This feature of our data allowed us to identify orders that would have had recommendations in the control group as well as the treatment group. It also allowed us to identify our sample without conditioning on the ordered drug's out-of-pocket cost and facilitated sub-analyses based on the opportunity for savings.

For each medication order, we also had patient and provider characteristics. Patient characteristics included sex, age which we divided into categories (18-40, 40-65, >65), and insurance type (which we divided into Medicare, Medicaid, private, and other). We observed the specialty of the practice profile from which the order was placed as well as whether the order was placed from a federally-qualified health center.

4. Power analysis and implied intervention length

Using pilot data, we determined that the mean out-of-pocket cost adjusted for a 30-day fill was $50.1 and intraclass correlation between practices was 0.02. We powered for an effect size of a 10% reduction in out-of-pocket costs with 5% significance level and 80% power, our power calculation suggested a minimum required sample size of 28,221 orders with alternatives. According to our pilot data, we estimated that 190 orders with potential alternatives (necessary to render an RTPB recommendation) would be placed each business day within the NYU system. This suggested we needed to run our intervention for at least 150 working days.

5. Regression specification

To estimate the impacts of RTPB recommendations on our outcomes, we estimated the following model:

$$Outcome_{\text{idjsp}} = \beta_0 + \beta_1 treat_{\text{p}} + \gamma X_{\text{ij}} + \alpha_{\text{s}} + \alpha_{\text{d}} + \varepsilon_{\text{idjps}}$$

where $Outcome_{\text{ijpd}}$ is the outcome for order i for medication in drug class d for patient j prescribed by practice in profile p with physician in specialty s, $treat_{\text{p}}$ denotes whether that prescription was ordered in a practice randomized to the treatment, X_{j} is a vector of patient-level factors (age, sex, whether the patient is insured by Medicaid, Medicare, or a commercial insurer), $\propto_{\text{s}}$ is a vector of specialty fixed effects, $\propto_{\text{s}}$ is a vector of drug class fixed effects and $\varepsilon_{\text{ijps}}$ is an individual error term. We clustered standard errors by practice profile which is the level of randomization.

The original pre-analysis plan did not specify the inclusion of drug class fixed effects. We included medication fixed effects due to the significant variability in costs and coverage between drug classes. The inclusion of fixed effects yields within-drug class estimates of the effects of the intervention. Nonetheless, we also include results from the original specification, which do not change drastically following the inclusion of drug class fixed effects (eTable 6).

6. Sensitivity analyses: Methods

We conducted several sensitivity analyses.

Alternate specifications

First, we tested the robustness of our results to alternative specifications. We estimated two-part models for out-of-pocket costs and logit models for our binary outcomes, mail-order prescription and 90-days supply.

Role of switching to different medication classes

We conducted sensitivity analyses to investigate the degree to which the RTPB intervention could be prompting prescribers to switch medication classes. Whether the intervention led to medication class switches has implications for the validity of our model specification which includes medication class fixed effects. Medication class fixed effects are important in our

design, because they account for overall differences in out-of-pocket costs due to differing specialty mix in our intervention and control groups stemming from our clustered randomization of practices (and differing volumes across practices). With medication fixed effects, we are essentially estimating the intervention's effects "within" medication class. On the other hand, if the RTPB recommendations were leading to prescribers switching to drugs in other medication classes, inclusion of medication class fixed effects could cause attenuation bias.

First, we counted the proportion of orders for which any medication option (all alternatives or the ordered medication) are in a different medication class. Only 12.7% of orders in the analytic sample had medications in different classes defined as alternatives, suggesting potential effects of switching classes is limited. We then stratified orders based on whether any alternatives were in a different medication class, and we estimated the main model. Effects of similar magnitude would also indicate that switching medication classes did not overwhelmingly drive the main effects.

7. Subgroup analyses: Methods

Stratified analyses by opportunity for savings

We conducted subgroup analyses to examine heterogeneity in the intervention's effects by the "opportunity for savings" or the difference in out-of-pocket cost between alternatives available for a given medication order. For the stratification, we used data on out-of-pocket cost for each ordered drug and all associated alternatives. Among all options for an ordered drug (all alternatives and the ordered drug), we defined the difference between the minimum and maximum out-of-pocket cost (for a 30-day supply) as the "opportunity for savings". We stratified the sample into quartiles based on the "opportunity for savings". We estimated the main model on each stratification and reported estimates and confidence intervals for each.

Drug costs

We also examined heterogeneity across higher and lower cost drug classes. We first calculated the average drug cost for each drug class. Using control group data, we computed the average out-of-pocket cost among orders in each drug class. (We excluded the intervention group from this average, because the intervention could impact the out-of-pocket cost.) We divided the drug classes into quartiles and stratified our sample based on these quartiles. Because quartiles were determined at the drug-class level, rather than the order level, the number of orders may not be balanced across strata. We estimated the main model on each stratification and reported estimates and confidence intervals for each.

Median household income

We sought to test for heterogeneity across income groups. We merged zip-code level median household income from the Census to patient zip code in our data. We stratified the sample using quartiles, and estimated our main model on each stratification.

Privately insured versus Medicare patients

We separately analyzed the intervention's effects for Medicare and privately insured patients, using medical insurance type information available in the EHR database. We excluded patients insured by Medicaid and other insurers, given the small number of observations for these patients.

Age and gender

Effects could vary by patient demographic characteristics such as age and gender. For example, younger patients may be more price sensitive compared to older patients in which case we may estimate larger effects of the intervention for younger patients. On the other hand, if older patients on Medicare Part D face higher cost-sharing overall, they may be more likely to be prescribed lower cost drugs. To investigate this, we separately analyzed effects by patient age category (<18, 18-40, 40-65, >65). Similarly, we stratified analyses by sex.

Specialty

Some specialties may be more conducive to RTPB recommendations than others, due to the number of alternatives available for common medications and the price variation between different options. We stratified orders from the 5 most common specialties in our data, which are primary care, cardiology, neurology, surgery, and endocrinology.

Patient medication use

Responsiveness to RTPB recommendations could differ based on the volume of patient medication use, though the direction is unclear. On the one hand, patients taking many medications may be more sensitive because they face higher overall drug out-of-pocket costs. On the other hand, patients with high volumes of medication use may be less sensitive if they are above their deductible or expect to be above their deductible. Patients with a longer medication history may also be less likely to switch if they have more experience with medications and have already used and ruled out alternative treatments.

We investigated heterogeneity in the intervention's effects by patient medication volume. Using data on all prescriptions placed at NYU Langone during the trial period, we calculated the number of prescriptions per patient over the course of the study period. We divided all patients in the full sample into terciles, and merged patients' terciles to orders in the analytic sample. We stratified main analyses based on these terciles.

8. Description of orders and types of alternatives

We characterized the types of alternatives associated with orders in our sample. For each order, we used information on all associated alternatives unconditional on the out-of-pocket costs (i.e., we could observe alternatives with out-of-pocket costs higher than the ordered drug), though we could not observe the specific alternatives that were recommended by the RTPB system.

We also investigated the potential savings offered by each type of alternative. For each order, we calculated the "potential savings" as the maximum out-of-pocket cost difference between options

(all alternatives and the ordered drug). We reported the average potential savings by type of alternative. We characterized the types of alternatives and potential savings in the sample overall and by drug class out-of-pocket cost (using the quartiles used in the drug class cost stratified analysis).

There were three types of alternatives: mail-order prescription instead of retail pharmacy, a different days supply, or a different medication. These were not mutually exclusive. In other words, an order could be for a mail-order pharmacy, a different days supply, and/or a different medication. In fact, most orders had several types of alternatives. Most orders (86%) had at least one alternative with a mail-order prescription, while about half of orders had at least one alternative with different days supply and half with a different clinically-appropriate medication (eTable 3, Panel A). For 22% of orders, the only type of alternative was a mail-order prescription, and for 10% of orders, the only type of alternative was a different medication type. In the highest cost drug classes, a greater proportion of orders (84%) had alternatives with a different medication.

Potential savings were largest when a different medication was available and smallest for a mail-order prescription (eTable 3, Panel B). On average, potential savings for a 30-day fill for orders with an alternative medication was $102.30. And potential savings when an alternative had a mail-order prescription was $43.20. Using orders where only the medication or pharmacy differed, switching medications led to an average potential savings of $8.70 while switching to mail-order led to average potential savings of $234.60. This difference in potential savings by type of alternative was amplified in the highest cost drug classes.

We also examined medication-level variation in whether an order was considered to have any alternative. We examined the share of orders with any alternative among the 25 most ordered medications at NYU Langone among randomized practices and patients in the analytic sample (patients with information matching the Surescripts database and above aged 18). We observe variation for most medications in whether an order has alternatives, suggesting that there is discretion on the part of PBMs in whether a drug is considered to have an alternative (eTable 4).

9. Comparison of all outpatient prescriptions versus prescriptions in analytic sample

eTable 5 presents characteristics of all outpatient prescriptions ordered at NYU Langone Health during the trial period versus orders in the analytic sample. Patient demographic characteristics were similar in both groups, though the percentage of orders for patients over 65 was greater in the analytic sample (59.4% versus 37.0%), largely representing the exclusion of children (defined as individuals with age < 18) from the analysis and the underrepresentation of orders for Medicaid enrollees. Only 0.2% of orders in the analytic sample were for Medicaid enrollees compared to 18.2% of all orders at Langone. This is likely driven by the fact that Medicaid enrollees face very low to no cost-sharing for medications, making RTPB recommendations less applicable. The share of prescriptions for privately insured patients was similar (42.4% of all orders and 39.0% of the analytic sample). The percentage of orders placed from NYU Langone Federally Qualified Health Centers which predominantly serve Medicaid patients was lower in the analytic sample (2.0%) compared to all orders (11.6%).

Among outpatient prescriptions placed at NYU Langone Health that could be linked to the Surescripts RTPB database, we compared our primary and secondary outcomes. Out-of-pocket costs were higher than the overall average for prescriptions in our analytic sample ($51.3 in analytic sample versus $30.6 overall a 30-day adjusted fill). Moreover, 8.2% and 8.8% of prescriptions were mail-order overall versus in the analytic sample. A larger proportion of orders in the analytic sample were for 90-days supply (44.8% versus 27.3%).

10. Sensitivity analysis: Results

Alternate specifications

Estimates from the two-part model are in Table 3. In the intervention group, 97.4% of orders had some out-of-pocket cost compared to 98.6% in the control group. After controlling for patient factors, drug class, and specialty, we estimated that the intervention led to a 1.0 percentage point (95% CI: -0.6pp to -1.5pp) decrease in the likelihood of an order requiring cost-sharing. Conditional on having positive out-of-pocket costs, the average out-of-pocket cost adjusted for a 30-day fill was $42.0 in the intervention group versus $69.0 in the control group. The intervention led to an adjusted 7.9% (95% CI:-10.0% to -5.7%) decrease in out-of-pocket costs among these prescriptions. The most common medication classes with $0 out-of-pocket costs are reported in eTable 7.

Estimates from the logistic regression model are reported in eTable 8. Logistic model estimates indicate the intervention led to 1.3 (95% CI: 1.1 to 1.5) greater odds in mail-order prescriptions, which translates to a 1.9% marginal increase. Moreover, the intervention led to 1.1 (95% CI: 0.9 to 1.5) greater odds or a 2.0% marginal increase in 90-days supply orders.

Role of switching medication classes

We did not find evidence that many RTPB notifications recommended medications in different medication classes or that switching medication classes contributed disproportionately to the estimated effects. For only 12.7% of orders did the medication class differ between the order and any of the alternatives (or between any of the alternatives). In analyses stratified by whether a medication in a different class was considered an alternative, the intervention's effect estimates were similar for the two strata. Confidence intervals were overlapping suggesting the effects were not significantly different. Specifically, the intervention led to an adjusted 11.2% (95% CI: -13.6% to -8.7%) decrease in out-of-pocket costs for orders with alternatives in the same medication class compared to a -14.3% (95% CI: -20.3% to -7.9%) reduction for orders with alternatives in more than one medication class.

11. Subgroup analyses: Results

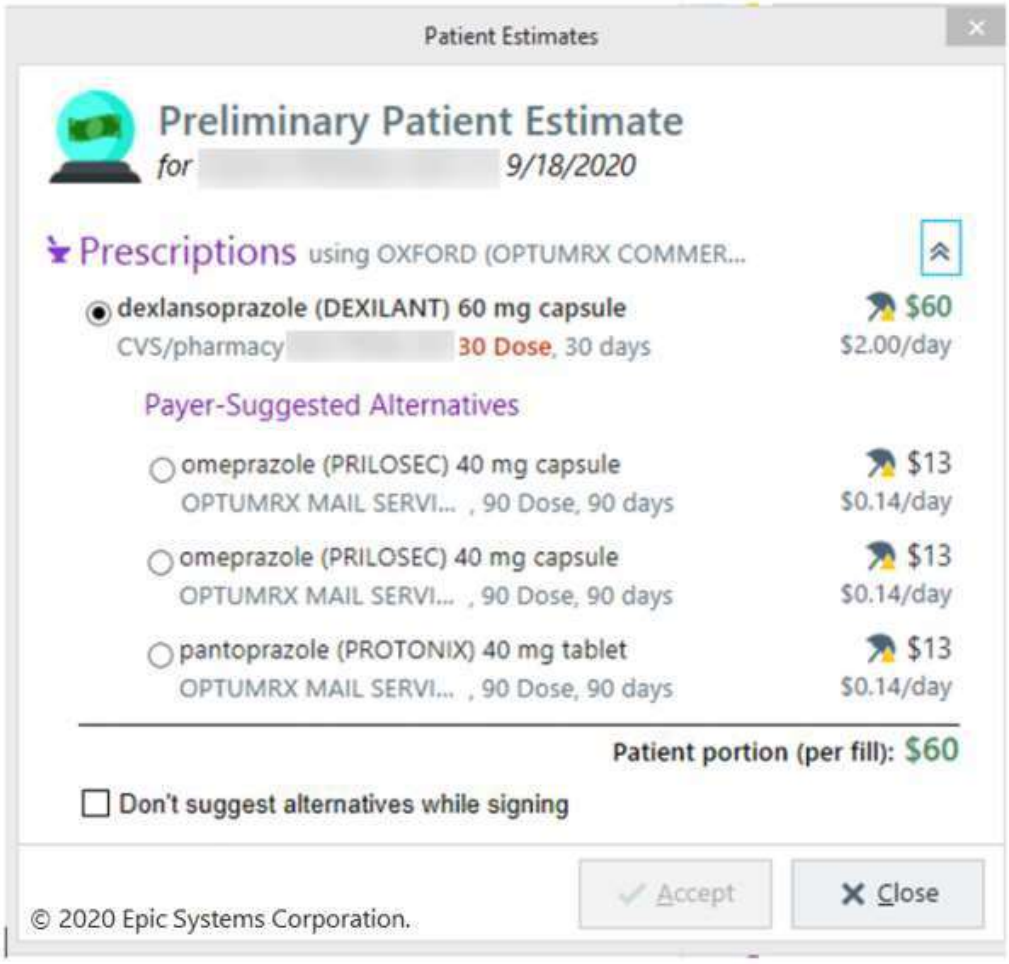
Effects of the intervention on out-of-pocket costs did not differ substantially by age or gender. Across most specialties, effects were similar, though the intervention did not appear to reduce out-of-pocket costs for orders placed by neurology practices. Effects also did not differ substantially based on patients' medication volume (eFigure 3).

12. Changes from the pre-analysis plan

This section describes changes that we made relative to our pre-analysis plan.

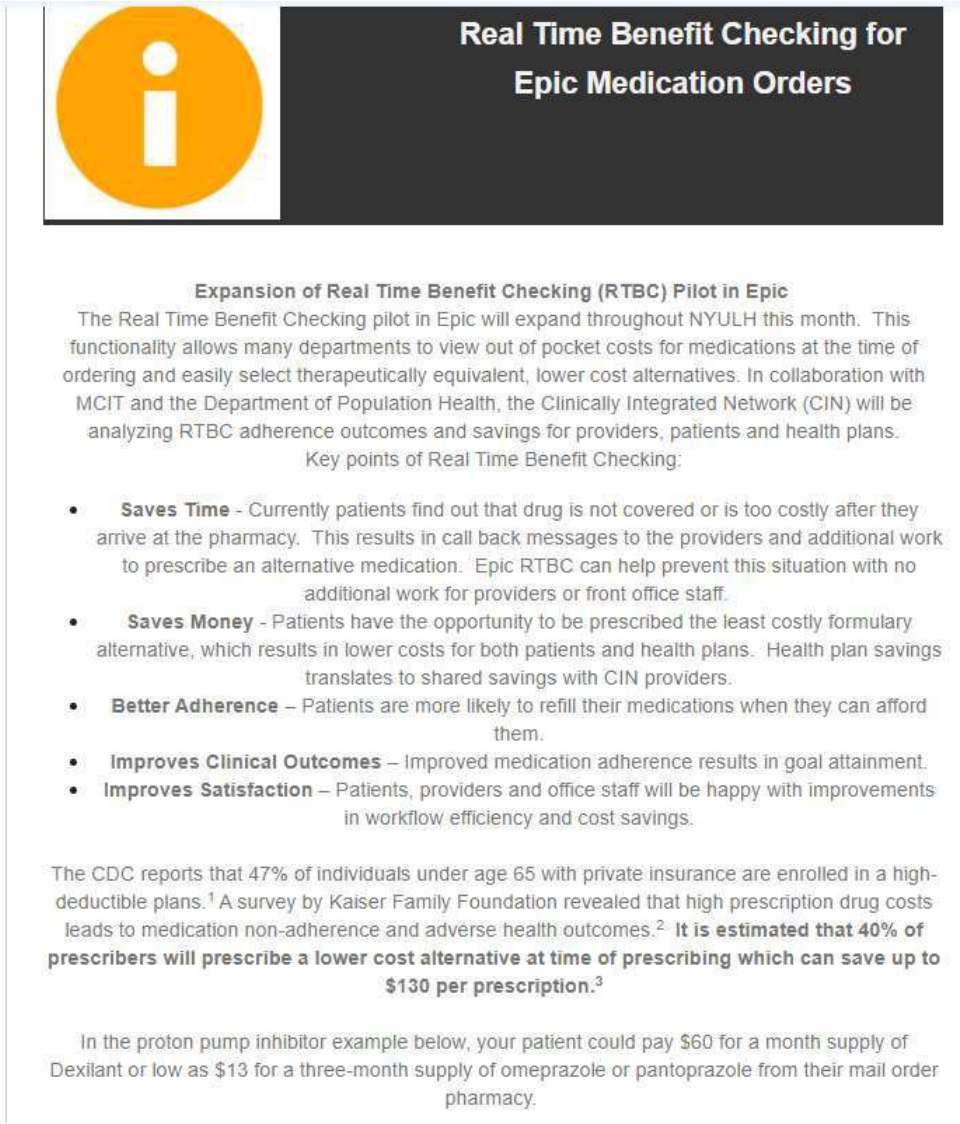
1. As described above, the intervention start date was delayed from November 18 to January 13 due to a technical IT issue that occurred. As a result of this technical issue, randomized providers were not receiving RTPB recommendations. The issue was corrected on January 13.
2. Instead of specifying the secondary outcome as the number of days supply, we specified it as whether the order was for a 90-day supply instead of a 30-day supply. This decision was made upon examination of the distribution of the outcome. Almost 90% of orders were for either 90- or 30-day supply.
3. In addition to patient covariates and specialty fixed effects in our originally planned analysis, we controlled for drug class in our main specification, given large differences in out-of-pocket costs that can exist between drug classes. In eTable 4, we report estimates of the originally-specified models, which are not substantively different from the main results.
4. We were not able to study the impacts of the intervention on overall payment inclusive of the patient and payer's payment, due to lack of the appropriate data. The vast majority (>90%) of orders in our data did not contain the total payment information, since most PBMs do not supply this information to Surescripts. Also, external data on prices for drugs that were specific to days supply and pharmacy type are not available.
5. We did not conduct stratified analyses for brand versus generic drugs or new versus continuing medications, because we did not have the data to accurately stratify the sample on these dimensions.
6. We did not contain sub-analyses for orders placed from federally qualified health centers, given the small number of orders in our analytic sample placed by providers in federally qualified health centers. These providers predominantly serve Medicaid patients, and Medicaid enrollees face little to no cost-sharing on drugs.
7. Because our data did not reliably capture individual orders for which a recommendation was shown and accepted, we could not calculate the acceptance rate for recommendations.
8. We also conducted several additional post-hoc analyses.
    a. We examined descriptive statistics with respect to the types of alternatives associated with medication orders, the potential savings, the medications and classes with no out-of-pocket costs, and the medication-specific, order-level variation in having any alternatives (eTables 3, 4, and 7).
    b. We investigated the degree to which the intervention led to switching medication classes (eTable 9).
    c. We conducted additional heterogeneity analyses on patient age, gender, and amount of medication use. We also stratified analyses for the 5 most common specialties in our data (eFigure 3).

eFigure 1. Example of screenshot of a RTPB recommendation



Note: Example screenshot drawn by NYU Langone Epic analyst for an anonymous patient. The first drug listed is the medication order that was being initially ordered: a 30-day supply of dexlansoprazole from CVS with patient cost of $60 or $2.00 per day. The following 3 medications are recommendations for lower-cost suggested alternatives. For example, the first recommendation is for a 90-day mail-order prescription of omeprazole for $13 or $0.14 per day. For this fill, selecting one of the recommendations would yield the patient savings of $47. And assuming the patient's cost-sharing stayed steady at $60 for the next 3 fills, over the course of 90-days the savings would accrue to $141.

eFigure 2. Informational email sent to all outpatient physicians regarding RTPB recommendations



Real Time Benefit Checking for Epic Medication Orders

Expansion of Real Time Benefit Checking (RTBC) Pilot in Epic

The Real Time Benefit Checking pilot in Epic will expand throughout NYULH this month. This functionality allows many departments to view out of pocket costs for medications at the time of ordering and easily select therapeutically equivalent, lower cost alternatives. In collaboration with MCIT and the Department of Population Health, the Clinically Integrated Network (CIN) will be analyzing RTBC adherence outcomes and savings for providers, patients and health plans.

Key points of Real Time Benefit Checking:

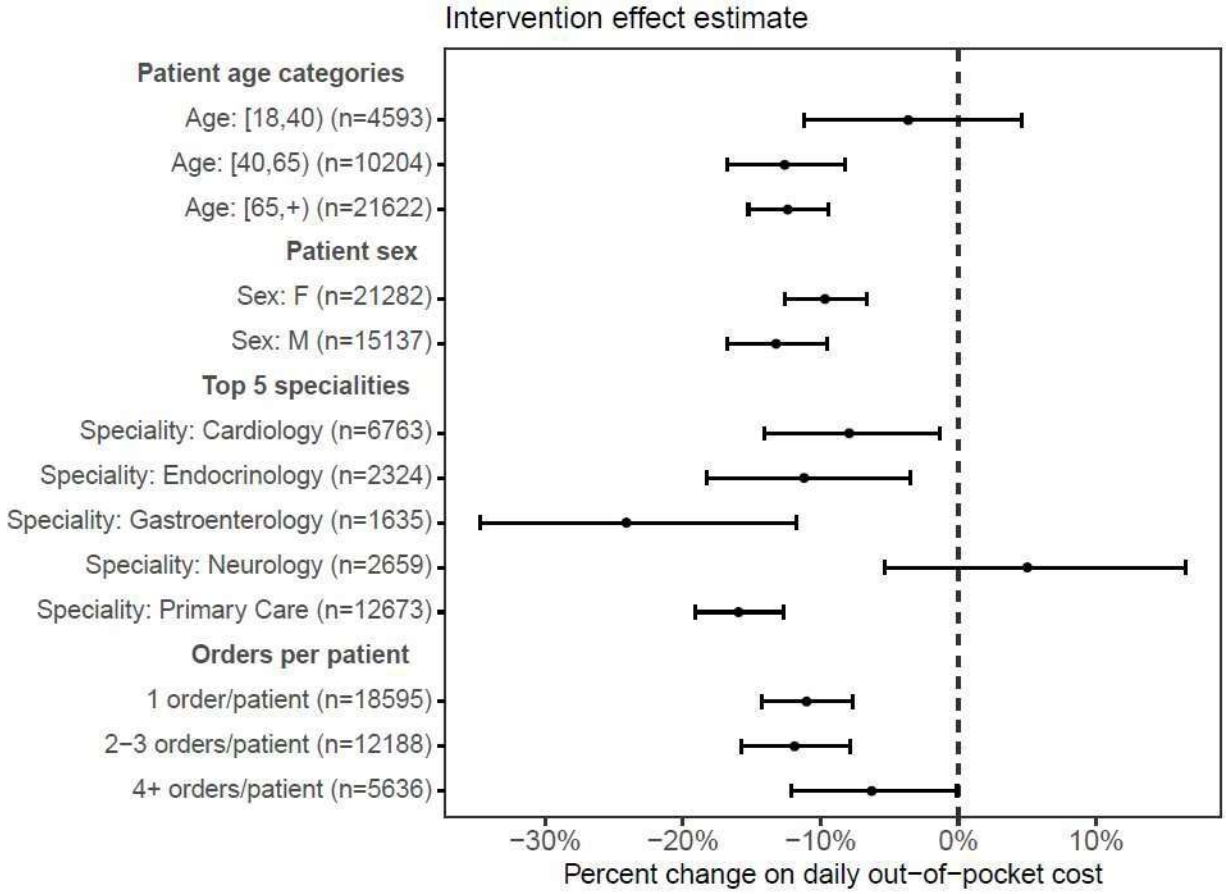
- **Saves Time** - Currently patients find out that drug is not covered or is too costly after they arrive at the pharmacy. This results in call back messages to the providers and additional work to prescribe an alternative medication. Epic RTBC can help prevent this situation with no additional work for providers or front office staff.
- **Saves Money** - Patients have the opportunity to be prescribed the least costly formulary alternative, which results in lower costs for both patients and health plans. Health plan savings translates to shared savings with CIN providers.
- **Better Adherence** – Patients are more likely to refill their medications when they can afford them.
- **Improves Clinical Outcomes** – Improved medication adherence results in goal attainment.
- **Improves Satisfaction** – Patients, providers and office staff will be happy with improvements in workflow efficiency and cost savings.

The CDC reports that 47% of individuals under age 65 with private insurance are enrolled in a high-deductible plans.[1] A survey by Kaiser Family Foundation revealed that high prescription drug costs leads to medication non-adherence and adverse health outcomes.[2] **It is estimated that 40% of prescribers will prescribe a lower cost alternative at time of prescribing which can save up to $130 per prescription.[3]**

In the proton pump inhibitor example below, your patient could pay $60 for a month supply of Dexilant or low as $13 for a three-month supply of omeprazole or pantoprazole from their mail order pharmacy.

Note: A screenshot of the email that was sent to all outpatient physicians at NYU Langone as part of a weekly series on Epic updates. The email mentioned that the RTPB recommendations would expand and focused on the potential benefits of these recommendations. Details of the trial or assignment to intervention or control were not included.

eFigure 3. Subgroup analyses by patient factors and specialty: Effects of RTPB recommendations on patient out-of-pocket costs



Note: Data are drawn from the electronic health record database and reflect the analytic sample. The sample size for each regression is next to the group label. All confidence intervals are calculated using heteroskedasticity-robust standard errors clustered at the level of randomization. Covariates include indicators for specialty, indicators for drug pharmaceutical class, categorical patient age bins ([18-40), [4-65), [65+)), patient sex, and patient insurance type (Medicare, Medicaid, private, or other). Where relevant, the stratification variable is excluded as a covariate in each subgroup analysis.

eTable 1. Number of practices, prescribers, and medication orders using pre-trial volumes in intervention and control practice profiles

	Practice Profiles		Clinical sites		Prescribers		Medication order volume (2-week period)	
	Ctr	Int	Ctr	Int	Ctr	Int	Ctr	Int
Cardiology	9	9	27	122	127	462	6423	36405
Dermatology	3	3	4	19	9	98	1038	5230
Endocrinology	7	6	29	40	103	88	10377	14121
Gastroenterology	7	7	38	15	131	54	11491	3062
Hematology and Oncology	5	6	33	21	207	127	4720	4109
Infection Disease	5	4	6	11	13	30	716	1225
Mental Health	6	7	15	11	24	109	1428	12610
Nephrology	3	4	3	22	5	50	868	3370
Neurology	11	11	16	45	112	152	7640	8104
Obstetrics & Gynecology	7	7	38	32	97	142	5068	9396
Ophthalmology	1	2	10	2	58	4	2930	775
Other	13	14	52	41	118	153	2948	3895
Otolaryngology	2	1	25	1	96	3	4864	62
Pain Management	2	3	5	7	23	12	812	924
Pediatrics	3	4	35	17	118	89	5383	16593
Podiatry	2	3	2	18	5	43	757	2295
Primary Care	10	10	91	108	667	542	148697	80129
Pulmonology	5	5	12	21	32	105	2474	6509
Rheumatology	5	5	24	10	94	27	14310	932
Surgery	21	21	90	88	414	354	8023	10478
Urology	2	3	12	9	61	19	3368	801

eTable 2. Percent of orders by drug class for 15 most common drug classes

	All	Intervention	Control	Standardized Mean Difference
ANTIHYPERLIPIDEMIC-HMGCOA REDUCTASE INHIB(STATINS)	7.40%	8.40%	5.90%	0.1
BETA-ADRENERGIC BLOCKING AGENTS	6.80%	8.30%	4.80%	0.1
THYROID HORMONES	6.80%	7.10%	6.20%	0.0
SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRIS)	4.50%	5.10%	3.70%	0.1
PROTON-PUMP INHIBITORS	4.20%	3.30%	5.50%	0.1
ANTIHYPERTENSIVES, ANGIOTENSIN RECEPTOR ANTAGONIST	3.10%	3.80%	2.10%	0.1
CALCIUM CHANNEL BLOCKING AGENTS	3.00%	3.50%	2.50%	0.1
NSAIDS, CYCLOOXYGENASE INHIBITOR - TYPE ANALGESICS	2.90%	2.50%	3.50%	0.1
ANTICONVULSANTS	2.80%	2.10%	3.90%	0.1
ADRENERGICS, AROMATIC, NON-CATECHOLAMINE	2.30%	2.90%	1.30%	0.1
ANTI-ANXIETY - BENZODIAZEPINES	2.20%	2.20%	2.20%	0.0
BETA-ADRENERGIC AGENTS, INHALED, SHORT ACTING	2.00%	2.50%	1.40%	0.1
LIPOTROPICS	1.90%	2.20%	1.40%	0.1
BENIGN PROSTATIC HYPERTROPHY/MICTURITION AGENTS	1.70%	1.10%	2.60%	0.1
THIAZIDE AND RELATED DIURETICS	1.60%	1.80%	1.30%	0.0
OTHER	46.80%	43.20%	51.90%	0.2

eTable 3. Types of alternatives and maximum out-of-pocket cost variation ("potential savings") by alternative type across orders

	Panel A: Frequency of orders by type of alternative				
		Average out-of-pocket cost in drug class for 30-day fill			
	All orders	<$19.8	$19.8-$47.7	$47.7-$106.5	>$106.5
Orders with at least one alternative of this type					
Mail-order	86%	94%	93%	86%	69%
Different days supply	46%	33%	55%	51%	44%
Different medication	50%	37%	33%	46%	84%
Orders with all alternatives are of this type					
Mail-order	22%	39%	25%	20%	5%
Different days supply	0.01%	0%	0%	0%	0%
Different medication	10%	4%	6%	10%	21%

	Panel B: Maximum potential savings from switching for 30-day fill, mean $				
		Average out-of-pocket cost in drug class for 30-day fill			
	All orders	<$19.8	$19.8-$47.7	$47.7-$106.5	>$106.5
At least one alternative of this type, $					
Mail-order	43.2	8.7	9.3	60.6	114.6
Different days supply	65.4	13.2	9.3	89.7	145.5
Different medication	102.3	15.6	15	27.3	214.5
All alternatives are of this type, $					
Mail-order	8.7	5.4	8.7	13.8	14.4
Different days supply	107.4	21.6	N/A	N/A	193.2
Different medication	234.6	23.1	18	30.6	430.8

eTable 4. Proportion of orders with alternatives by medication (for 25 highest volume medications)

Medication name	Number of orders during trial period	Proportion of orders with an alternative, %
OMEPRAZOLE 40 MG CAPSULE,DELAYED RELEASE	10840	14%
ATORVASTATIN 20 MG TABLET	10498	15%
AMLODIPINE 5 MG TABLET	10196	19%
METOPROLOL SUCCINATE ER 25 MG TABLET,EXTENDED RELEASE 24 HR	9345	13%
ATORVASTATIN 10 MG TABLET	9130	15%
ATORVASTATIN 40 MG TABLET	8917	14%
ERGOCALCIFEROL (VITAMIN D2) 1,250 MCG (50,000 UNIT) CAPSULE	8385	10%
ALBUTEROL SULFATE HFA 90 MCG/ACTUATION AEROSOL INHALER	7362	15%
NITROFURANTOIN MONOHYDRATE/MACROCRYSTALS 100 MG CAPSULE	7250	0%
METOPROLOL SUCCINATE ER 50 MG TABLET,EXTENDED RELEASE 24 HR	7134	31%
AMOXICILLIN 875 MG-POTASSIUM CLAVULANATE 125 MG TABLET	7033	0%
METFORMIN 500 MG TABLET	6728	11%
LOSARTAN 50 MG TABLET	6683	9%
ASPIRIN 81 MG TABLET,DELAYED RELEASE	6474	3%
FLUCONAZOLE 150 MG TABLET	6375	0%
MONTELUKAST 10 MG TABLET	6175	12%
TAMSULOSIN 0.4 MG CAPSULE	6129	16%
CIPROFLOXACIN 500 MG TABLET	6020	0%
NAPROXEN 500 MG TABLET	5994	5%
TRAMADOL 50 MG TABLET	5972	4%
LOSARTAN 100 MG TABLET	5921	9%
AMLODIPINE 10 MG TABLET	5871	17%
METFORMIN ER 500 MG TABLET,EXTENDED RELEASE 24 HR	5844	14%
ROSUVASTATIN 10 MG TABLET	5819	23%
DOXYCYCLINE HYCLATE 100 MG TABLET	5793	10%

eTable 5. Comparison of all outpatient orders in NYU Langone system versus analytic sample during study period

	All orders in NYU system	Analytic sample
N		
Orders	869406	36419
Patients	302518	25113
Prescribers	3298	2031
Practice Profiles	256	196
Patient-level characteristics:		
Female, %	59.3%	58.4%
Age category, %		
<18	5.3%	
18-40	17.6%	12.6%
40-65	40.0%	28.0%
>65	37.0%	59.4%
Insurance type, %		
Private	42.4%	39.0%
Medicaid	18.4%	0.2%
Medicare	35.1%	57.3%
Other	4.0%	3.5%
Median household income of zip code, $ mean (sd)	88,004 (35,281)	100,659 (35,794)
Specialty group, %		
Primary Care	40	34.8
Cardiology	12.3	18.6
Neurology	5.5	7.3
Surgery	5.2	3.8
Endocrinology	4.5	6.4
Other	32.5	29.1
Federally Qualified Health Center, %	11.60%	2.00%
Out-of-pocket cost (30-day adjusted), $	$30.60	$51.30
Mail-order pharmacy	8.2%	8.8%
90-day supply	27.3%	44.8%

Notes: This table compares outpatient prescriptions placed at NYU Langone Health during the study period to those in our analytic sample. Figure 1 in the manuscript reports exclusions that led to the analytic sample. Outcomes data was limited to orders for which patient and plan information could be linked to the Surescripts database. The percentage of orders with 90-days supply were limited to orders with either 90- or 30-days supply

eTable 6. Model specifications: Sequential inclusion of covariates

	(1) Estimate [95% CI]	(2) Estimate [95% CI]	(3) Estimate [95% CI]	(4) Estimate [95% CI]
Outcome:				
Out-of-pocket cost (log $)	-19.8% [-33.7%, -3.1%]	-7.4% [-13.7%, -0.6%]	-11.2% [-16.0%, -6.2%]	-11.2% [-15.7%, -6.4%]
Mail-order pharmacy	2.0 [0.3, 3.8]	1.8 [0.9, 2.8]	2.0 [0.9, 3.0]	1.9 [0.9, 3.0]
90-day supply	7.2 [-4.5, 20.3]	0.1 [-4.5, 5.0]	1.8 [-2.9, 6.6]	2.0 [-2.5, 6.7]
Specialty fixed effects		X	X	X
Drug therapeutic class fixed effects			X	X
Patient characteristics				X

Notes: Order-level outcomes of interest are the out-of-pocket (log-transformed), the probability of an order from a mail-order pharmacy, and the probability of a 90-days supply versus 30-days supply. The analysis on the probability of a 90-days supply medication order includes only orders with 30- or 90-days supply, which comprise 89.2% (n=32,485) of the full analytic sample. The out-of-pocket cost outcome is log-transformed, and the corresponding effect estimate has been transformed to indicate the percent change implied by the coefficient estimate. The unadjusted intervention effect (1) is estimated via linear regression of the outcome on an indicator for the intervention group with no other covariates. Model (2) additionally includes indicators for specialty of the practice from which the prescription was ordered. Model (3) adds drug class fixed effects. Model (4) adds patient factors which are: categorical age bins ([18, 40), [40,65), 65+)), sex, and insurance type (Medicare, Medicaid, private, other). Heteroskedasticity- robust standard errors clustered at the level of randomization, the practice profile, are reported.

eTable 7. Most common medication classes with $0 out-of-pocket cost orders

Medication class	Proportion of orders with zero out-of-pocket cost, %
ANTIHYPERLIPIDEMIC-HMGCOA REDUCTASE INHIB(STATINS)	12.3%
CONTRACEPTIVES,ORAL	7.6%
PROTON-PUMP INHIBITORS	5.5%
CALCIUM CHANNEL BLOCKING AGENTS	5.3%
BETA-ADRENERGIC BLOCKING AGENTS	4.7%
ANTICONVULSANTS	3.3%
ANTIHYPERTENSIVES, ANGIOTENSIN RECEPTOR ANTAGONIST	3.2%
PLATELET AGGREGATION INHIBITORS	2.9%
THYROID HORMONES	2.7%
ANTIHYPERGLYCEMIC, BIGUANIDE TYPE	2.7%
SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRIS)	2.6%
NSAIDS, CYCLOOXYGENASE INHIBITOR - TYPE ANALGESICS	2.3%
LOOP DIURETICS	1.9%
THIAZIDE AND RELATED DIURETICS	1.6%
ANTIVIRALS, HIV-SPEC, NUCLEOSIDE-NUCLEOTIDE ANALOG	1.5%
ANTI-ANXIETY - BENZODIAZEPINES	1.2%
OPIOID ANALGESICS	1.2%
ALPHA/BETA-ADRENERGIC BLOCKING AGENTS	1.1%
ANTIHYPERGLYCEMIC, INSULIN-RELEASE STIMULANT TYPE	1.1%
ANTINEOPLASTIC - AROMATASE INHIBITORS	1.1%
ANGIOTENSIN RECEPTOR ANTAG.-THIAZIDE DIURETIC COMB	1.1%
ANTIHYPERTENSIVES, ACE INHIBITORS	1.0%
LIPOTROPICS	1.0%
LAXATIVES AND CATHARTICS	1.0%
BETA-ADRENERGIC AGENTS, INHALED, SHORT ACTING	0.9%

Note: We identified all orders with $0 out-of-pocket costs and tabulated the frequency by medication class. The proportion is the number of orders in the respective drug class divided by the total number of orders with $0 out-of-pocket cost.

eTable 8. Logistic regression model estimates for secondary outcomes: Odds ratios and marginal effects

	Intervention effect estimate [95% CI] (percent/percentage point change)	
	Odds ratio [95% CI]	Marginal effect [95% CI]
Outcome:		
Mail-order pharmacy	1.29 [1.13, 1.47]	1.9% [0.9%, 2.8%]
90-day supply	1.14 [0.86, 1.50]	2.0% [-2.4%, 6.4%]

Notes: Order-level outcomes of interest are whether an order was a mail-order prescription and whether the order was for a 90-days supply versus 30-days supply. The analysis on the probability of a 90-days supply medication order includes only orders with 30- or 90-days supply, which comprise 89.2% (n=32,485) of the full analytic sample. The adjusted intervention effect is estimated also with linear regression and includes the following covariates: indicators for specialty type, indicators for drug pharmaceutical class, categorical age bins ([18, 40), [40,65), 65+)), sex, and insurance type (Medicare, Medicaid, private, other). Heteroskedasticity- robust standard errors clustered at the level of randomization, the practice profile, are reported. In addition to odds ratios, we translate estimates to marginal effects to facilitate comparison to our main results.

eTable 9. Sensitivity analyses: Stratification by whether an order and its alternatives were in distinct medication classes

Outcome: out-of-pocket cost (log $)	(1) Estimate [95% CI]	(2) Estimate [95% CI]	(3) Estimate [95% CI]	(4) Estimate [95% CI]
Strata:				
Orders with all alternatives in same medication class (n=31,777)	-18.7% [-20.9%, -16.4%]	-8.4% [-11.2%, -5.5%]	-11.3% [-13.6%, -8.8%]	-11.2% [-13.6%, -8.7%]
Orders with at least one alternative in a different medication class (n=4,642)	-19.5% [-26.1%, -12.4%]	-7.3% [-15.3%, 1.4%]	-13.8% [-19.9%, -7.3%]	-14.3% [-20.3%, -7.9%]
Specialty fixed effects		X	X	X
Drug class fixed effects			X	X
Patient characteristics				X

Notes: Order-level outcome of interest is the out-of-pocket (log-transformed) stratified by whether or not potential alternative drugs are of the same drug pharmaceutical class. Sample size for orders in which potential alternatives are the same drug pharmaceutical class is n=31,777 orders, and sample is n=4642 orders in which potential alternatives belong to more than 1 drug pharmaceutical class. The out-of-pocket cost outcome is log-transformed, and the corresponding effect estimate has been transformed to indicate the percent change implied by the coefficient estimate. The unadjusted intervention effect (1) is estimated via linear regression of the outcome on an indicator for the intervention group with no other covariates. Model (2) additionally includes indicators for specialty of the practice from which the prescription was ordered. Model (3) adds drug class fixed effects. Model (4) adds patient factors which are: categorical age bins ([18, 40), [40,65), 65+)), sex, and insurance type (Medicare, Medicaid, private, other). Heteroskedasticity- robust standard errors clustered at the level of randomization, the practice profile, are reported.

eTable 10. Ten most frequent drug classes by quartiles based on average drug class out-of-pocket cost

Quartile 1 (< $19.80)		Quartile 2 ($19.80 - $47.70)		Quartile 3 ($47.70 - $106.50)		Quartile 4 (> $106.50)	
Drug class	Avg out-of-pocket (30-day adjusted	Drug class	Avg out-of-pocket (30-day adjusted	Drug class	Avg out-of-pocket (30-day adjusted	Drug class	Avg out-of-pocket (30-day adjusted
BETA-ADRENERGIC BLOCKING AGENTS ($14.40	14.4	ANTIHYPERLIPIDEMIC-HMGCOA REDUCTASE INHIB(STATINS)	19.8	ADRENERGICS, AROMATIC, NON-CATECHOLAMINE	70.50	CEPHALOSPORIN ANTIBIOTICS - 3RD GENERATION	214.80
SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRIS)	13.5	THYROID HORMONES	24.9	LIPOTROPICS	106.20	OPIOID ANALGESIC AND NON-SALICYLATE ANALGESICS	142.50
ANTIHYPERTENSIVES, ANGIOTENSIN RECEPTOR ANTAGONIST	19.2	PROTON-PUMP INHIBITORS	32.7	TETRACYCLINE ANTIBIOTICS	82.50	ANTIMIGRAINE PREPARATIONS	225.30
CALCIUM CHANNEL BLOCKING AGENTS	13.2	ANTICONVULSANTS	38.1	ANTIVIRALS, GENERAL	47.70	ANTIVIRALS, HIV-SPEC, NUCLEOSIDE-NUCLEOTIDE ANALOG	405.00
NSAIDS, CYCLOOXYGENASE INHIBITOR - TYPE ANALGESICS	12	BETA-ADRENERGIC AGENTS, INHALED, SHORT ACTING	30	GLUCOCORTICOIDS	58.50	LAXATIVES AND CATHARTICS	1281.60
ANTI-ANXIETY - BENZODIAZEPINES	17.4	BENIGN PROSTATIC HYPERTROPHY/MICTURITION AGENTS	22.2	ANTIPARKINSONISM DRUGS,OTHER	68.40	ANTIHYPERGLY,INCRETIN MIMETIC(GLP-1 RECEP.AGONIST)	139.80
THIAZIDE AND RELATED DIURETICS	11.1	SKELETAL MUSCLE RELAXANTS	27.9	COLCHICINE	72.30	DRUGS TO TREAT ERECTILE DYSFUNCTION (ED)	108.00
ANTIHYPERTENSIVES, ACE INHIBITORS	12	SEDATIVE-HYPNOTICS,NON-BARBITURATE	21.9	ANTICONVULSANT - BENZODIAZEPINE TYPE	73.80	VASODILATORS,CORONARY	118.80
LOOP DIURETICS	8.4	ANTIHYPERGLYCEMIC, BIGUANIDE TYPE	38.7	DIRECT FACTOR XA INHIBITORS	81.30	ANTIFUNGAL AGENTS	793.50
SEROTONIN-NOREPINEPHRINE REUPTAKE-INHIB (SNRIS)	16.8	ANGIOTENSIN RECEPTOR ANTAG.-THIAZIDE DIURETIC COMB	25.8	OPIOID ANALGESICS	50.10	RIFAMYCINS AND RELATED DERIVATIVE ANTIBIOTICS	757.50
ALPHA/BETA-ADRENERGIC BLOCKING AGENTS	13.2	TOPICAL ANTI-INFLAMMATORY STEROIDAL	40.8	OVERACTIVE BLADDER AGENTS, BETA-3 ADRENERGIC RECEP	104.70	ANTI-ULCER PREPARATIONS	194.10
ANTIHYPERGLYCEMIC, INSULIN-RELEASE STIMULANT TYPE	8.4	ANTINEOPLASTIC - AROMATASE INHIBITORS	33.9	ANTIHYPERGLYCEMIC, DPP-4 INHIBITORS	100.20	TOPICAL LOCAL ANESTHETICS	109.50
HISTAMINE H2-RECEPTOR INHIBITORS	11.7	CHOLINESTERASE INHIBITORS	35.7	VAGINAL ESTROGEN PREPARATIONS	84.30	ANTIHYPERGLYCEMIC, DPP-4 INHIBITOR-BIGUANIDE COMBS.	115.20
NOREPINEPHRINE AND DOPAMINE REUPTAKE INHIB (NDRIS)	14.7	BONE RESORPTION INHIBITORS	30.9	ANTIPSYCHOTIC,ATYPICAL,DOPAMINE,SEROTONIN ANTAGNST	50.10	MIOTICS AND OTHER INTRAOCULAR PRESSURE REDUCERS	121.20
POTASSIUM SPARING DIURETICS	14.1	URINARY TRACT ANTISPASMODIC/ANTI INCONTINENCE AGENT	40.8	TX FOR ATTENTION DEFICIT-HYPERACT(ADHD)/NARCOLEPSY	79.80	EYE ANTIBIOTIC AND GLUCOCORTICOID COMBINATIONS	340.50

