Official Title: Engaging Patients to Promote Deprescribing
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Statistical Power

Based on fiscal year (FY) 2017 data, we estimated that we would mail brochures to at least 1,990 PPI patients, 894 Diabetes-Hypoglycemia patients, and 758 Gabapentin patients during the study. For apriori statistical power analyses, we made the following assumptions based on our pilot data: an overall baseline deprescribing rate of 4.21%, a conservatively high intraclass correlation coefficient (ICC) of 0.05 (for non-independence among patients of the same provider), an average of 20 eligible patients per PCC or WHC provider, and a 20% attrition rate (i.e., patients who receive the intervention brochure but do not attend their clinic visit). With these assumptions, we determined that we would have 80% power (for two-tailed tests at α=0.05) to detect deprescribing rates following the intervention as small as 6.55% overall for these low-end estimates of our projected sample. Moreover, even at these low-end estimates of the projected sample size, we determined we would have 80% power to detect an overall deprescribing rate as low as 15% among the combined intervention cohorts even if the ICC was as high as 0.1, the baseline deprescribing rate was as high as 10%, and/or the attrition rate was as high as 40%. Notably, a deprescribing rate of 15% was reasonable to expect given that we found similar or higher rates in our pilot study.

We conducted analyses using SAS.[3]

Endpoints & Covariates

The primary hypothesis was deprescribing would be greater for Veterans receiving the intervention brochure than for those in the historical control group.

The primary outcome was binary: deprescribing versus not, assessed via pharmacy dispensing data from the VA Corporate Data Warehouse (CDW). More specifically, six months from the index date, an analyst queried the CDW to determine medication outcomes (e.g., complete deprescribing, dose reduction). We selected 6 months because prescriptions are often filled as a 90-day supply and using a shorter observation window might not fully identify that the prescription was not refilled. We removed patients who died within six months from their index data from intervention and historical controls at the analysis stage to avoid misattributing deprescribing to the intervention rather than death.

To identify dose reductions, we calculated the total daily dose (TDD) of the target medication as [dose*(quantity/days supplied)]. [1,2] Substitutions within a medication drug class (e.g., pantoprazole to omeprazole) were standardized to one medication within each class. We only compared TDD at 6 months to that at the index visit for oral medications because insulin dose adjustments are not consistently documented within the electronic health record. Combination insulin products were separated into their long acting and short acting components and analyzed separately. We allowed a 10% buffer for days' supply of PPI, sulfonylurea, and gabapentin (e.g., 33 days for a 30-day supply) to account for missed doses and 100% buffer for insulin due to dispensing requirements (e.g., minimum vials dispensed regardless of dose).

Patient factors and provider characteristics (age, gender, profession) were included as covariates in the model. Based on our conceptual model and using data from CDW, patient factors included age, race, sex, and Elixhauser comorbidities in the year prior to the scheduled primary care visit. [4,5]

Additionally, we planned to examine whether the effectiveness of the brochure intervention was associated with target medication.

Interim & Final Analysis

Our primary comparisons were between "brochure-intervention" patients and "historical control" patients (matched in terms of eligibility) from the same primary care provider. To investigate the impact of the intervention brochure on deprescribing, Hierarchical Generalized Linear Modeling (HGLM) was used to account for the nesting of patients within providers. This approach provided information not just about the average effectiveness of the intervention, but also about how much variation there is in the intervention impact across providers. In all models, Level 1 (patient-level) intercepts and slopes were treated as random effects, and parameters were estimated with robust standard errors. Using this approach of nesting patients within providers at intervention sites, for our primary analysis, we compared the likelihood of deprescribing among patients in the pre-intervention ("historical") period to that for patients in the intervention periods who were mailed the brochure. We predicted that intervention patients would be significantly more likely to have deprescribing than patients in the pre-intervention period with the same eligibility criteria. We then examined whether the

intervention effectiveness was moderated by the target medication. We did not expect a discontinuation rate of 100%, as patients may have an indication to remain on the medication. No adjustments were made to p-values or confidence intervals for multiple comparisons for the primary outcome.

No interim analyses were planned.

Missing Data

We examined the incidence of missing data by medication cohort (PPI vs. DM vs. Gaba). We expected very low rates of missing data, given that our primary analyses rely on CDW data. For missing data, we implemented a series of sensitivity analyses using imputation (coding as "missing" for categorical variables and imputed means for continuous variables) to assess the degree of bias that might be induced by missing data. The results did not change in direction or significance.

Methods for dealing with data transformations

We did not apply any data transformations. All data underwent standard preliminary visualization and quality screening to test for potential violations of assumptions (e.g., distributional assumptions regarding normality, homogeneity of variance, linear relationships, outliers, ceiling/floor effects).

Other analytical subsets

The intervention is designed to target and engage patients, but it is possible that the intervention may be more effective with certain providers. Therefore, a null hierarchical model was used to estimate intraclass correlations to characterize the percent variance explained at the patient, provider, and site levels.

We used HGLM to examine whether the likelihood of deprescribing changes over time at our control sites (instead of from the pre-intervention period) to rule out alternative explanations for the effect of our intervention that rely on temporal trends in deprescribing unrelated to our intervention (e.g., other deprescribing initiatives). We elected not to include temporal deprescribing trends in the manuscript since there was no evidence of significant temporal trends.

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