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Prescription Refill Records as a Screening Tool to Identify Antidepressant Non-Adherence

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Abstract

Purpose—Non-adherence is a significant problem with antidepressants. Identifying patients at highest risk for discontinuing antidepressant treatment can be used to target clinical management. Accordingly, our purpose was to determine the shortest gap in medication supply that is predictive of discontinuation, while minimizing false positive results.

Methods—A retrospective cohort study of medical and prescription claims from a national health plan affiliated with i3 Innovus. Sensitivities, specificities, and positive and negative predictive values were calculated for gap lengths to assess how well they predicted discontinuation. Continuously insured individuals aged 18–65 with newly diagnosed major depression and an antidepressant prescription within 45 days of diagnosis were included. Gap length was defined as the maximum number of continuous days without medication supply during acute phase treatment. Discontinuation was defined as a continuous gap of 30 or more days between an expected refill and actual refill.

Results—Of 4,545 eligible patients, 73% discontinued antidepressant treatment during the study period. A maximum continuous gap of 14 days had a sensitivity of 87% and a specificity of 82% for predicting discontinuation. In analyses that varied the way gaps and discontinuation were defined, gap lengths between 8 and 19 days were highly predictive of discontinuation without exceeding a 20% false positive rate.

Conclusions—Based on administrative pharmacy records, screening for gaps in medication supply of at least 14 days can accurately identify 4 of every 5 patients at risk for discontinuing. This early indicator can be used to target clinical interventions.

Keywords

Adherence; screening; depression; prescription refills

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INTRODUCTION

Antidepressants can be effective in treating major depression; however, non-adherence is a significant problem in depressed patients and as many as 76 percent of patients discontinue treatment before completing an acceptable 3 month regimen.[1, 2] Collaborative care interventions that target antidepressant adherence through increased contact with health care professionals have shown promise,[3, 4] but such strategies need to be streamlined to incentivize their adoption by payors.[3] Early targeting of patients who are at high risk for discontinuing therapy is one way to increase the sustainability and marginal benefits of such interventions.

Administrative pharmacy claims data are one potential tool for identifying medication use patterns that are related to discontinuation of therapy.[5, 6] Prescription fill dates and days of treatment supplied for initial and subsequent fills provide an indicator of medication adherence over time. We used pharmacy claims to identify the shortest gap in medication supply that could be used as an accurate predictor of eventual antidepressant discontinuation. We explored the predictive ability of increasing gap lengths for predicting discontinuation by examining the association between gaps in medication supply during acute depression treatment and medication discontinuation during the guideline-recommended treatment period.[7, 8]

METHODS

Study Design

A retrospective cohort design was used to examine the diagnostic accuracy of refill gap length for predicting antidepressant discontinuation.

Population

Patients were identified using insurance claims from a large U.S. health plan affiliated with i3 Innovus (Figure 1). These data represent paid claims for inpatient, outpatient, and pharmacy services for commercially insured individuals. Patients were included if they had newly diagnosed major depressive disorder (ICD-9 code of 296.20–296.24 for single episodes of varying degree) between July 1, 2000 and December 31, 2002, and were continuously eligible for medical and pharmacy benefits.

Antidepressant users were identified by claims for an antidepressant prescription filled within 45 days of the index diagnosis, with the first such claim marking the start of follow-up. Only patients receiving second-generation antidepressants were included because this medication class is most often prescribed for depression and is not associated with the risk of overdose or food-drug interactions with other depression treatments. Patients were excluded if they had an antidepressant claim within 6 months prior to the index diagnosis, were younger than 18 years or older than 65 years, or if they had a diagnosis for another mental health-related condition during the 6-month pre-index diagnosis period.

Individuals with multiple different second-generation antidepressant claims in a single month were assumed to switch treatment, and the start date of the latest medication was their index date for our analysis. Individuals with concurrent claims for more than one second-generation antidepressant over multiple months were excluded, as were those who switched antidepressant medications more than twice during the study period.

Variables

Gaps in medication supply during acute treatment (first 90 days) were used to predict whether patients discontinued antidepressant medication during the first 7 months of treatment (210 days). Treatment gaps during the first 90 days are of interest because problems with non-adherence are common early in treatment and guidelines recommend a minimum acute phase treatment of 6–8 weeks with many patients requiring 10–12 weeks before demonstrating adequate response.[9–11] The period up to 210 days was conceptualized to represent the minimum recommended duration of treatment through the continuation phase.[9–11]

The independent variable, acute treatment phase gap length, was defined by the number of days without medication during the first 90 days of treatment. The gap length was calculated using the date and days supplied by each prescription claim to calculate an expected refill date. If the actual refill date was on or before the expected refill date, we assigned a gap length of zero. When the prescription was refilled after the expected refill date, the gap length was calculated as the number of days between the actual and expected refill date. This calculation was adjusted for medication switching and potential surplus from previous fills. For our primary analysis, we used the gap length that corresponded to the longest continuous gap in medication supply across all refills. Supporting analyses used gaps occurring over more than one dispensing by summing all gaps during the acute treatment phase

The dependent variable, discontinuation, was defined by either the absence of ongoing refills or a gap of 30 days or more during the 210 day study period.[5] Because no clear consensus exists to define the minimum period of time that clinically defines a treatment discontinuation,[6] we conducted supporting analyses that defined discontinuation using a gap length of 15 days. Individuals exceeding the maximum allowable gap at any time during the 210 day study period were classified as discontinuers, regardless of whether a prescription was subsequently filled.

Statistical Analysis

Descriptive statistics were used to summarize population characteristics, gap length variables, and the occurrence of discontinuation. Sensitivities, specificities, positive predictive values (PPV), and negative predictive values (NPV) were calculated for each gap length to assess how well gap length predicts discontinuation. Because the purpose of using refill records is to improve intervention efficiency and identify high risk patients, we focused on minimizing the false positive rate. *A priori*, we set 20% as a threshold for the false positive rate that would be acceptable for clinical application of this method. SAS version 9.1.3 (Cary, NC) was used for all analyses.

RESULTS

Of the 4,545 eligible patients, nearly 73% discontinued their antidepressants during the study period. Women made up the majority of the sample (65%) and the mean age was 39 years at the time of the index prescription. Over the course of follow-up, 29% of patients switched antidepressants one or more times. The most commonly used antidepressants included sertraline (24%), citalopram (20%), paroxetine (17%), fluoxetine (13%), bupropion (11%), and venlafaxine (10%).

The sensitivity, specificity, PPV, and NPV of using varying lengths of gaps in medication supply to predict discontinuation are presented in Table 1. In the primary analysis, a maximum continuous gap of 14 days met our criterion for having a specificity greater than 80% (sensitivity 87%, specificity 82%, PPV 93%, NPV 70%). When using the sum of all

gaps, a total gap length of 19 days met this criterion (sensitivity 88%, specificity 80%, PPV 92%, NPV 71%). Supporting analyses indicated that when the definition of discontinuation was changed from 30 days to 15 days, a maximum continuous gap of 8 days (sensitivity 89%, specificity 80%, PPV 95%, NPV 62%) and a sum of gaps of 12 days (sensitivity 89%, specificity 83%, PPV 96%, NPV 63%) were the earliest times meeting our 80% specificity threshold.

DISCUSSION

Using administrative pharmacy claims, we sought to identify a medication gap length that might be useful in designing prospective interventions. Depending on how gaps and discontinuation were defined, we found that gaps between 8 and 19 days were highly predictive of discontinuation without exceeding a 20% false positive rate.

From a methodological perspective, our analysis is limited by several factors. First, while we adjusted for medication switching, adherence is difficult to accurately measure with claims data when treatment changes. Second, although administrative claims data are believed to capture the majority of medication use, some patients may have additional drug use not captured within the claims data (e.g., samples, cash purchases). Third, we allowed gaps in medication supply to occur simultaneously with the discontinuation outcome. From a clinical perspective, we felt this approach was most appropriate to capture acute phase disruptions in treatment, even though some of these people later resumed treatment.

Translation and implementation of our gap analysis into real-world interventions needs to consider several issues. For instance, the screening tool requires real-time access to prescription records which would entail significant coordination to move from gap identification to clinical intervention. Such implementation would require either that the intervention originates from an insurer or that systems be developed to provide clinicians with pharmacy data. Another important issue is whether the potential improvements in clinician access to this information and efficiency in identification of adherence problems are worth the additional effort. Given the high rate of acute phase discontinuation with antidepressants (73% in our sample) and the fact that antidepressant discontinuation might be appropriate in many cases (e.g., side effects, drug not working, not needed or wanted), the incremental value of implementing a refill screening method needs further study.

Despite these potential limitations and logistical hurdles, we believe that identification of gaps in medication supply is clinically important. Our analysis suggests that gaps ≥ 14 days can accurately identify 4 out of 5 patients who discontinue treatment. Creating a mechanism whereby clinicians are informed of these refill gaps might help stimulate early intervention, or improve the quality of otherwise scheduled clinical encounters. One next step for this work might be to incorporate refill screening into a collaborative care model, where improvements in the quality of depression care have already been well documented.[3] This strategy may lead to a more efficient care model and accelerate adoption of such models by health systems and payors.

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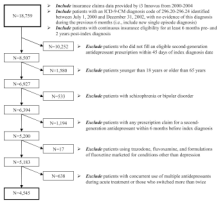

Figure 1.
Flow of Participants

Table 1

Measures of Diagnostic Accuracy of Gap Length in Predicting Discontinuation

	30 Day Discontinuation			
Gap Length	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**Positive Predictive Value (95% CI)**	**Negative Predictive Value (95%CI)**
Maximum Continuous Gap[a]				
3 Day Gap	0.96 (0.95, 0.97)	0.38 (0.35, 0.41)	0.81 (0.79, 0.82)	0.78 (0.75, 0.82)
6 Day Gap	0.93 (0.92, 0.94)	0.56 (0.53, 0.59)	0.85 (0.84, 0.86)	0.75 (0.72, 0.77)
9 Day Gap	0.90 (0.89, 0.91)	0.68 (0.65, 0.71)	0.88 (0.87, 0.89)	0.73 (0.70, 0.75)
12 Day Gap	0.88 (0.87, 0.89)	0.77 (0.74, 0.79)	0.91 (0.90, 0.92)	0.71 (0.69, 0.74)
15 Day Gap	0.86 (0.85, 0.88)	0.83 (0.81, 0.85)	0.93 (0.92, 0.94)	0.70 (0.67, 0.72)
18 Day Gap	0.85 (0.83, 0.86)	0.89 (0.87, 0.90)	0.95 (0.94, 0.96)	0.68 (0.66, 0.71)
21 Day Gap	0.83 (0.82, 0.85)	0.92 (0.91, 0.94)	0.97 (0.96, 0.97)	0.67 (0.65, 0.70)
24 Day Gap	0.82 (0.81, 0.83)	0.95 (0.93, 0.96)	0.98 (0.97, 0.98)	0.66 (0.64, 0.68)
27 Day Gap	0.81 (0.79, 0.82)	0.97 (0.96, 0.98)	0.99 (0.98, 0.99)	0.65 (0.63, 0.68)
30 Day Gap	0.79 (0.78, 0.80)	1.0 (>0.99, 1.0)	1.0 (>0.99, 1.0)	0.64 (0.62, 0.66)
Sum of Gaps[b]				
3 Day Gap	0.96 (0.96, 0.97)	0.36 (0.33, 0.38)	0.80 (0.79, 0.81)	0.79 (0.76, 0.83)
6 Day Gap	0.94 (0.94, 0.95)	0.48 (0.46, 0.51)	0.83 (0.82, 0.84)	0.76 (0.73, 0.79)
9 Day Gap	0.92 (0.92, 0.93)	0.59 (0.56, 0.61)	0.86 (0.84, 0.87)	0.74 (0.72, 0.77)
12 Day Gap	0.91 (0.90, 0.92)	0.67 (0.64, 0.69)	0.88 (0.87, 0.89)	0.73 (0.71, 0.76)
15 Day Gap	0.89 (0.88, 0.90)	0.73 (0.70, 0.75)	0.90 (0.89, 0.91)	0.72 (0.69, 0.74)
18 Day Gap	0.88 (0.87, 0.89)	0.78 (0.76, 0.80)	0.91 (0.90, 0.92)	0.71 (0.69, 0.73)
21 Day Gap	0.87 (0.86, 0.88)	0.82 (0.80, 0.84)	0.93 (0.92, 0.94)	0.70 (0.68, 0.73)
24 Day Gap	0.86 (0.85, 0.87)	0.86 (0.84, 0.88)	0.94 (0.93, 0.95)	0.70 (0.67, 0.72)
27 Day Gap	0.85 (0.84, 0.86)	0.88 (0.86, 0.90)	0.95 (0.94, 0.96)	0.69 (0.66, 0.71)
30 Day Gap	0.84 (0.83, 0.86)	0.92 (0.90, 0.93)	0.96 (0.96, 0.97)	0.69 (0.66, 0.71)

[a] Maximum number of continuous days without a medication supply during the acute phase of treatment (0 to 90 days), truncated at 30 days.

[b] Sum of days without a medication supply during the acute phase of treatment (0 to 90 days), truncated at 30 days.