

Prospective Validation of Eight Different Adherence Measures for Use with Administrative Claims Data among Patients with Schizophrenia

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ABSTRACT

Objective: The aim of this study was to compare the predictive validity of eight different adherence measures by studying the variability explained between each measure and hospitalization episodes among Medicaid-eligible persons diagnosed with schizophrenia on antipsychotic monotherapy.

Methods: This study was a retrospective analysis of the Arkansas Medicaid administrative claims data. Continuously eligible adult schizophrenia (ICD-9-CM = 295.***) patients on antipsychotic monotherapy were identified in the recruitment period from July 2000 through April 2004. Adherence rates to antipsychotic therapy in year 1 were calculated using eight different measures identified from the literature. Univariate and multivariable logistic regression models were used to prospectively predict all-cause and mental health-related hospitalizations in the follow-up year.

Results: Adherence rates were computed for 3395 schizophrenic patients with a mean age of 42.9 years, of which 52.5% (n = 1782) were females,

and 52.8% (n = 1793) were white. The proportion of days covered (PDC) and continuous measure of medication gaps measures of adherence had equal C-statistics of 0.571 in predicting both all-cause and mental health-related hospitalizations. The medication possession ratio (MPR) continuous multiple interval measure of oversupply were the second best measures with equal C-statistics of 0.568 and 0.567 for any-cause and mental health-related hospitalizations. The multivariate adjusted models had higher C-statistics but provided the same rank order results.

Conclusions: MPR and PDC were among the best predictors of any-cause and mental health-related hospitalization, and are recommended as the preferred adherence measures when a single measure is sought for use with administrative claims data for patients not on polypharmacy.

Keywords: adherence, pharmacy claims, schizophrenia, validation.

Introduction

The International Society for Pharmacoeconomics and Outcomes Research Medication Compliance and Persistence Work Group defines medication adherence as “the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen” [1]. Medication nonadherence is commonly associated with adverse health conditions and increased economic burden to the health-care system [2–6], and is a critical issue especially in case of chronic therapies such as schizophrenia. Adherence measures include direct and indirect techniques. Direct methods include biological assays, whereas indirect methods consist of pill counts, electronic monitors, and use of administrative database claims [7]. Indirect methods and, in particular, use of administrative data are becoming increasingly popular because they afford ease of use and are considered economical; however, there are no clear standards for measuring or calculating adherence with these indirect approaches.

Medication nonadherence rates in patients suffering from schizophrenia range from 20% to 89% based on the adherence

definition used [8]. Adherence measures using pharmacy claims data have been used to predict health-care cost and utilization [9–11]. Svarstad et al. found that persons with schizophrenia with poorer adherence had higher hospitalization rates than their more adherent counterparts. Additional studies have reported similar findings in persons with schizophrenia [5,6]. Non-adherence to the prescribed treatment may account for 40% of the rehospitalizations associated with schizophrenia [8]. Thieda et al. conducted a literature review for the years 1995 through 2002 evaluating the relationship between compliance and the economic costs of schizophrenia [4]. The authors concluded that lower compliance was associated with adverse outcomes such as increased relapse rates with associated costs ranging from \$10,000 to \$26,000. Bearing in mind the economic outcomes associated with medication nonadherence, schizophrenia serves as a favorable condition to determine the predictive validity of various adherence measures.

Because of their usefulness in recent years, administrative claims data have been one of the most commonly used sources for calculating medication adherence. Medication adherence measured using pharmacy claims has been validated using other adherence measures such as patient reports, pill counts, questionnaires, and interviews [12–17]. Despite these validation studies, there are no standards for the mathematical calculation of adherence using claims data. A systematic review by Andrade et al. [18] identified 136 studies that employed administrative claims

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to calculate medication adherence and persistence. About 57% of the studies considered medication possession ratio (MPR) and related measures, 10% used medication gaps, and 43% used switching and discontinuation in calculating medication adherence and persistence. Even among the 57% that considered MPR and related measures, the follow-up period definitions varied, ranging from a specified follow-up period (e.g., 1 year) to the period between the first and last refill. This study emphasized the lack of consensus among definitions and methods used to calculate adherence using administrative claims. Hess et al. published a study that identified 11 different adherence measures calculated using administrative claims data, and initiated the idea of standardizing adherence measures [19]. This study, however, did not empirically validate these measures.

The primary aim of this study was to prospectively validate administrative claims-based adherence measures using hospitalization as the end point for persons with schizophrenia. Medication adherence was measured in terms of adherence to monotherapy within a class of drugs prescribed for treating schizophrenia. This study sought to identify adherence measures which had the best predictive validity, in an effort to offer practitioners and researchers an empirical basis for selecting an adherence measure among eight unique measures based on administrative claims data.

Methods

To assess the predictive validity of each adherence measure, the adherence rates among schizophrenia patients were compared with hospitalization rates. Our primary hypothesis is that an increase in adherence will be associated with lower hospitalization rates. This was a prospective study where adherence was assessed in year 1 following an index prescription, and hospitalization rates were determined in the subsequent year.

The study used patient-linked administrative claims data for the Arkansas Medicaid population representing adjudicated paid claims for services rendered from January 1, 2000 through April 30, 2005. A schematic representation of the study periods is shown in Figure 1. Patients with schizophrenia were identified using the ICD-9-CM code of 295.xx (recorded in the medical and inpatient claims file) during the “enrollment period” July 1, 2000 through April 30, 2004. An “index date” defined as the date on which the first prescription for oral antipsychotic medication (conventional: fluphenazine, haloperidol, loxapine, pimozide, perphenazine, trifluoperazine, chlorpromazine, thioridazine,

molindone, thiothixene; atypical: risperidone, quetiapine, olanzapine, aripiprazole, clozapine, ziprasidone) was filled by the patient in the enrollment period. Adherence rates, defined below, were computed using eight different adherence definitions for the 1-year period starting from the index date.

Subjects

The following inclusion and exclusion criteria were used to select study subjects:

1. Primary diagnosis for schizophrenia (ICD-9-CM = 295.** [6,20] recorded in the medical and inpatient claims file during the period July 1, 2000 through April 30, 2004 (starting cohort size N = 11,587);
2. Patients with at least one prescription for oral antipsychotic medication in a 1-year period between July 1, 2000 and April 30, 2004 (N = 9025; patients excluded N = 2562);
3. Excluded patients less than 18 years of age at the index date and Qualified Medicare Beneficiaries (N = 7552; patients excluded N = 1473);
4. Continuous eligibility for the 6 months before and 24 months after the index date (N = 6344; patients excluded N = 1208);
5. At least two paid claims for an oral antipsychotic medication in a 1-year period during the period July 1, 2000 through April 30, 2004 (N = 5936; patients excluded N = 408);
6. Excluding patients taking two different oral antipsychotic medications simultaneously (N = 3971; patients excluded N = 1965);
7. Patients were required to have at least one inpatient, outpatient, pharmacy, or nursing home claim during the post-index period. This inclusion criterion was imposed to verify that patients were utilizing Medicaid benefits in the post-index period (N = 3957; patients excluded N = 14);
8. Excluding patients with a nursing home claim during the index period (final cohort size N = 3395; patients excluded = 562).

This study was approved by the Institutional Review Board at the University of Arkansas for Medical Sciences.

Variables

Measures of Medication Adherence

Medication adherence was measured in terms of adherence to monotherapy within a class of drugs prescribed for treating

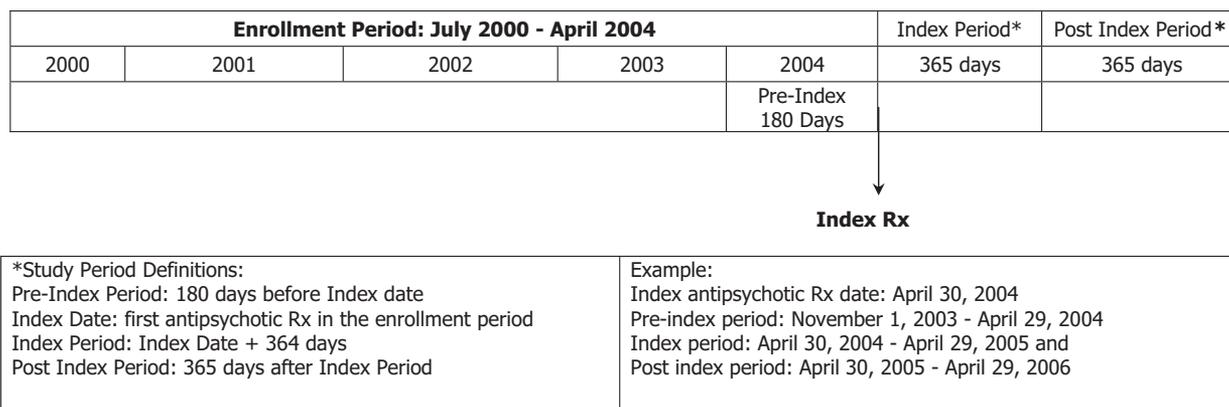


Figure 1 Description of study periods for a person diagnosed with schizophrenia.

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