Alternative and "Off-Label" Uses of Antipsychotic Medications in Medicaid

The Hilltop Institute
analysis to advance the health of vulnerable populations

UMBC
AN HONORS UNIVERSITY IN MARYLAND

Michael T. Abrams,✉ MPH; Jessica R. Kopelke, BS; Osama O. Elfaki, MS, MIA; Susan Chen, MBA; David S. Salkever, PhD

✉ mabrams@hilltop.umbc.edu; The Hilltop Institute and the Department of Public Policy at the University of Maryland, Baltimore County, Baltimore, Maryland, 21250

Introduction

Despite the name, antipsychotic medications are used both on and off label for indications besides severe psychosis (i.e., schizophrenia). "Off-label" means that a drug is prescribed for an indication that has not been approved by the U.S. Food and Drug Administration. Such use is nevertheless quite common and legal in the United States.[1]

Several recent reports have documented the widespread use of antipsychotic medications for indications other than psychosis, such as mania, bipolar disorder, anxiety, autism, and dementia.[2-6] Here we report the magnitude and basic correlates of such use in the context of a single Medicaid program. We further consider if and how off-label use correlates with the experience of each recipient's mental health care provider. Medicaid is the medical insurance program for most individuals with serious mental illness in the United States.[7]

Methods

We utilized Medicaid administrative data from the state of Maryland for fiscal year (FY) 2001 (July 2000 – June 2001). This is the base year for a four-year follow-up study of cost outcomes associated with the use of various antipsychotic medications. That study focuses on individuals with diagnoses in the schizophrenia domain (i.e., ICD-9 codes beginning with 295). Our interest in alternative diagnoses (the focus of this poster) is tied to efforts to generate instrumental variables characterizing a given provider's predilection for one drug over another.[8] One approach we have taken in generating such an instrument is to consider the extent to which prescribers use antipsychotics for indications other than schizophrenia (the main and original on-label indication).

From FY 2001 administrative Medicaid data we created an analytic file of all adults (≥18 years old) who filled an antipsychotic prescription (n=26,579). We then removed all individuals with one or more schizophrenia diagnoses, thus reducing the population of interest to 16,337 unique individuals.

To those unique-person records we linked age, gender, Medicaid eligibility, and mental health diagnostic fields. Based on the diagnostic fields, we further created a flag indicating whether a given individual had an on-label (bipolar, mania, or other psychosis) or only off-label (see Table 1) diagnosis evident in their Medicaid record. Finally, we created a flag indicating whether each individual had at least one contact during the year with a clinical provider that is "experienced" in the use of antipsychotics.

Here we define an "experienced provider" as one who treated at least 20 individuals with schizophrenia during the year of our study. In total we found 114 such "experienced providers," and they were the most frequent providers for 74% of our schizophrenia population of 9,259 individuals who had at least 1 inpatient or 2 outpatient Medicaid transactions including a diagnosis of schizophrenia. Of those 114 "experienced providers," 23 were individually named physicians (e.g., John Smith, M.D.), and the rest were facility names (e.g., Rehab House, Inc.).

Using the above-described analytic file, we generated the following summary statistics to describe the alternative use (i.e., other than to treat schizophrenia) of antipsychotics in Maryland's Medicaid program and consider which factors we isolated correlated with off-label use.

Table 1. Mental Disorder Diagnostic Flags (ICD-9 Code)

On-Label	Off-Label
Episodic mood disorders (296)	Dementia (290)
	Transient mood disorders (293)
	Persistent mental disorder due to other conditions (294)
	Pervasive developmental delay (299)
	Anxiety disorders (300)
	Personality disorders (301)
	Sexual & gender identify disorders (302)
	Physiologic malfunction from mental factors (306)
Delusional disorders (297)	Special symptoms, NOS (307)
	Acute reaction to stress (308)
	Adjustment reaction (309)
Other non-organic psychoses (298)	Mental disorders due to brain damage (310)
	Depression, NOS (311)
	Conduct Disorders (312)
	Emotional disorders of childhood & adolescence (313)
	Hyperkinetic syndromes (314)
	Specific delays in development (315)
	Psychic factors associated w/other disease (316)
	Mental retardation (317-319)
	Absence of any diagnoses in this table

Results

Table 2. Demographics Summary

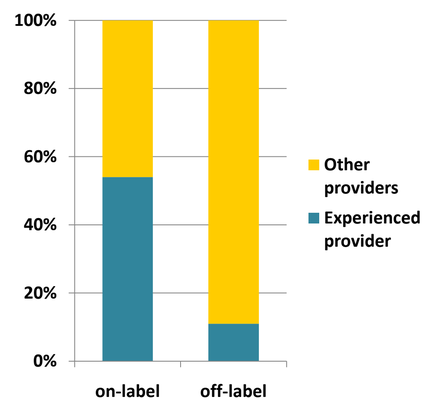
Variable	On-Label (n=6,783)	Off-Label (n=9,554)	Stat
Age in years, mean (std)	49 (19)	66(22)	t=50 (p<0.0001)
Sex (% female)	62%	66%	Chi-sq = 18 (p<0.0001)

Table 3. Medicaid Eligibility Summary (*chi-sq* = 2,400, *p*<0.0001)

Coverage Category	On-Label (n=6,783)	Off-Label (n=9,554)
ABD, Medicare, Pharmacy	67%	38%
ABD, LTC	19%	54%
HCBS Waiver	2%	4%
F&C	9%	2%
All others	3%	2%
	100%	100%

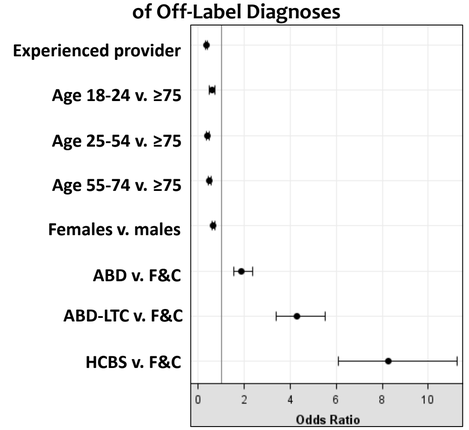
ABD = aged, blind, and disabled; LTC = long-term care; HCBS = home and community-based services; F&C = Families & Children

Figure 1. Percentage Who Visited an Experienced Provider*



*A doctor or clinic that was the most frequent provider to at least 20 Medicaid clients with schizophrenia in FY 2001

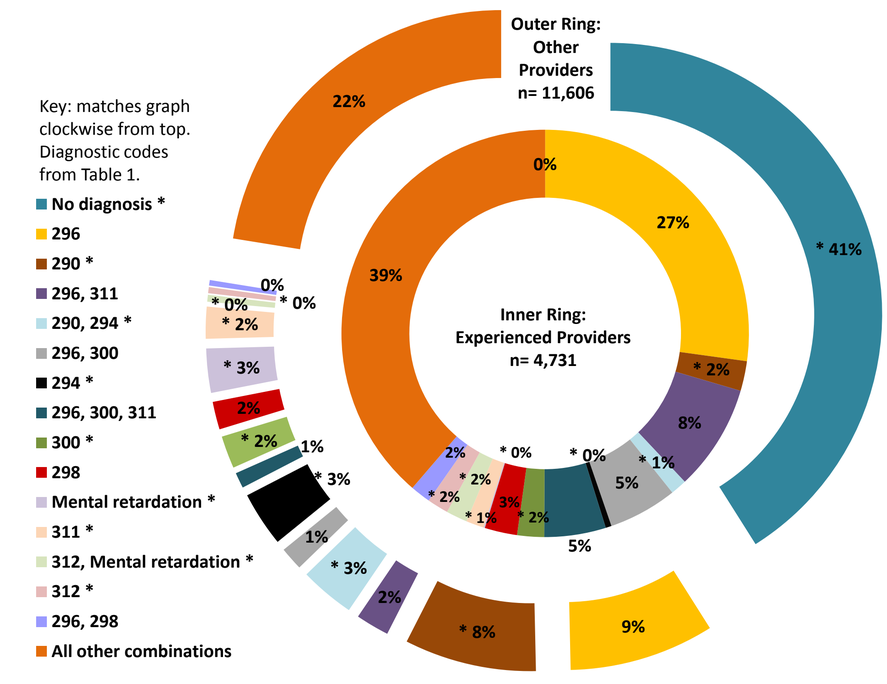
Figure 3. Logistic Regression Predicting Odds of Off-Label Diagnoses



Notes: Excludes those with no diagnosis. (n=11,320, 4,716 off-label). Plot shows estimate and 95% CI.

ABD = aged, blind, and disabled; F&C = Families & Children; LTC = long-term care; HCBS = home and community-based services

Figure 2. Percentage of the Top Diagnostic Combinations



Notes: Stratified by contact with "experienced" (inner ring) or other providers (outer ring). Co-morbid diagnoses (e.g., 296 and 311) need only be coincident in year. Highest off-label uses are starred (*).

Discussion

Basic and regression statistics both demonstrate that non-schizophrenia, off-label use of antipsychotics is higher in Medicaid clients who are older, male, and in need of skilled nursing care (e.g., Long-term care). Also, these methods show that experienced providers appear to avoid off-label use (adjusted-odds ratio = 0.35 95% confidence interval: 0.32-0.39).

Frequency review also demonstrates that off-label use is substantial at 58% if the absence of any mental disorder in Table 1 is included in the definition of off-label, and 42% if such undiagnosed individuals taking antipsychotics are excluded. Two factors may explain the absence of diagnoses: 1) other diagnoses (e.g., substance use disorders) led to antipsychotic use, or 2) non-Medicaid providers were involved (e.g., Medicare or Community Health Centers).

The most common alternative indication is bipolar disorder/mania (ICD-9 code = 296). Relatively common off-label indications are dementia, persistent mental disorders due to other conditions, anxiety, mental retardation, and conduct disorder.

Since 2001, off-label use of antipsychotics to treat depression in older adults has likely waned because of the substantial risk of adverse effects.[9] Episodic mood disorders (e.g., mania and bipolar disorder) are a newer—but established indications for antipsychotics.[4, 5]

References

1. Clark, M. E. (ed.) (2007). *Pharmaceutical law*. BNA Books.
2. Rijcken, C. A., et al. (2003). *Pharmacopsychiatry, 36*(5): 187-91.
3. Barbui, C. A., et al. (2004). *Acta Psychiatr Scand, 109*(4): 275-8.
4. Domino, M. E., & Swartz, M. S. (2008). *Psychiatr Serv, 59*(5): 507-14.
5. Kamble, P. J., et al. (2010). *Psychiatr Serv, 61*(2): 130-6.
6. Leslie, D. L., et al. (2010). *Psychiatr Serv, 610*(9): 1175-81.
7. Frank, R. G., & Glied, S. A. (2006). *Better but not well*. JHU Press.
8. Duggan M., (2005). *J Health Econ*, 24:1-31.
9. Schneider, L. S., et al. (2006). *NEJM, 355*(15): 1525-38.

Acknowledgements

NIMH Grant #5R03MH083208

Maryland Department of Health and Mental Hygiene IRB #09-64

UMBC IRB #Y07DS19230