

SUPPLEMENTARY MATERIAL

Systematic Review of Real-World Treatment Patterns of Oral Antipsychotics and Associated Economic Burden in Patients With Schizophrenia in the United States

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Supplementary Table S1
PRISMA Checklist

Section and Topic	Item #	Checklist Item	Location Where Item Is Reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	2-3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	3-4, Supplementary Table S6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary Tables 2-5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	3-4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	3-4
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	NA
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	4
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	NA

Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	3-4
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	4
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	4
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	4
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	NA
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	NA

Supplementary Table S2

Embase Search Strategy for Economic Burden

Search Number	Search String	Hits (June 1, 2018)
Population		
1.	'schizophrenia'/exp OR 'schizophrenia' OR 'schizophrenia':ab,ti OR 'schizophrenic':ab,ti	203,904
Economic Burden		
2.	'economics'/exp OR 'health economics'/exp OR 'pharmacoeconomics'/exp OR 'cost of illness'/exp OR 'cost':ab,ti OR 'costs':ab,ti OR 'budget*':ab,ti OR 'expenditure*':ab,ti OR 'resource utilization':ab,ti OR 'resource use':ab,ti OR 'economic*':ab,ti OR 'pharmacoeconomic*':ab,ti OR 'productiv*':ab,ti OR 'work loss':ab,ti OR 'absenteeism' OR 'presenteeism' OR 'emergency room':ab,ti OR 'ER visit' OR 'outpatient visit':ab,ti OR 'incarceration':ab,ti OR 'societal':ab,ti OR 'hospitalization':ab,ti OR 'hospital*':ab,ti OR 'length of stay':ab,ti OR 'health care resource utilization' OR 'HRU'	3,048,300
3.	#1 AND #2	26,295
Limiters		
4.	[2008-2018]/py	14,458
5.	[english]/lim AND [humans]/lim	12,321
6.	#5 NOT ('book'/exp OR 'book':it OR 'chapter':it OR 'conference abstract'/exp OR 'conference abstract':it OR 'conference paper'/exp OR 'conference paper':it OR 'conference review'/exp OR 'conference review':it OR 'editorial'/exp OR 'editorial':it OR 'erratum'/exp OR 'erratum':it OR 'letter'/exp OR 'letter':it OR 'review'/exp OR 'review':ab,ti OR 'case report'/de OR 'case report':it OR 'quality control'/exp OR 'quality control'/de OR 'practice guideline'/exp OR 'practice guideline'/de OR 'methodology'/de)	5315
7.	#6 NOT ('randomized controlled trial'/exp OR random*:ti OR placebo:ti OR ((singl*:ti OR doubl*:ti OR trebl*:ti OR tripl*:ti) AND (mask*:ti OR blind*:ti OR dumm*:ti)) OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR 'random allocation':ti OR 'placebo'/exp OR 'randomization'/exp OR 'nonhuman'/de OR 'randomized controlled trial (topic)'/de)	4757
8.	#7 NOT ('animal cell'/exp OR 'animal cell'/de OR 'animal experiment'/exp OR 'animal experiment'/de OR 'animal model'/exp OR 'animal model'/de OR 'cancer cell culture'/de OR 'biological model'/de OR 'human tissue'/exp OR 'human tissue'/de OR 'cell culture'/de OR 'nonhuman'/de OR 'diagnostic test accuracy study'/de)	4706
9.	#8 NOT (France:ti or china:ti or UK:ti or 'United Kingdom':ti or Canada:ti or Japan:ti or Africa:ti or Spain:ti or German:ti or Italy:ti or Europe:ti or Australia:ti or Switzerland:ti or Sweden:ti or Netherlands:ti or brazil:ti)	4440
Results		
TOTAL		4440

Supplementary Table S3

PubMed Search Strategy for Economic Burden

Search Number	Search String	Hits (June 1, 2018)
Population		
1.	"Schizophrenia"[Mesh] or schizophrenia[tiab] or schizophrenic[tiab]	134,289
Economic Burden		
2.	"Economics"[Mesh] or "Cost of Illness"[Mesh] or cost[tiab] or costs[tiab] or budget*[tiab] or expenditure*[tiab] or "resource utilization"[tiab] or "resource use"[tiab] or economic*[tiab] or pharmacoeconomic*[tiab] or productiv*[tiab] or "work loss"[tiab] or absenteeism[All Fields] or presenteeism[All Fields] or "hospitalization"[tiab] or hospital*[tiab] or "length of stay"[All Fields] or "emergency room"[tiab] or "ER visit" or "outpatient visit"[tiab] or "incarceration"[tiab] or "societal"[tiab] or "health care resource utilization"[All Fields] or "HRU"[All Fields]	2,178,773
3.	#1 AND #2	15,473
Limiters		
4.	#3 Limited to studies published from January 1, 2008 through June 1, 2018	5928
5.	#4 Published in human subjects and English language	4133
6.	#5 NOT ("clinical trial"[ptyp] or "case reports"[ptyp] or letter[ptyp] or news[ptyp] or comment[ptyp] or "case report"[tiab] or "editorial"[tiab] or "letter"[tiab])	3526
7.	#6 NOT (randomized controlled trial[pt] OR randomized controlled trials as topic[mh] OR random allocation [mh] OR double-blind method[mh] OR single-blind method[mh] OR random*[tw] OR "Placebos"[Mesh] OR placebo[tiab] OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw] OR dumm*[tw])))	3165
8.	#7 NOT (France[ti] or china[ti] or UK[ti] or "United Kingdom"[ti] or Canada[ti] or Japan[ti] or Africa[ti] or Spain[ti] or German[ti] or Italy[ti] or Europe[ti] or Australia[ti] or Switzerland[ti] or Sweden[ti] or Netherlands[ti] or brazil[ti])	2988
9.	#8 NOT ("animal experimentation"[Mesh] OR "animal cell" OR "animal experiment" OR "animal model" OR "cancer cell culture" OR "biological model" OR "human tissue" OR "cell culture" OR "nonhuman" OR "diagnostic test accuracy study")	2984
Results		
TOTAL		2984

Supplementary Table S4

Embase Search Strategy for Treatment Patterns

Search Number	Search String	Hits (June 1, 2018)
	Population	
1.	'schizophrenia'/exp OR 'schizophrenia' OR 'schizophrenia':ab,ti OR 'schizophrenic':ab,ti	203,904
	Treatment Patterns	
2.	((((treatment OR therapy OR therapies OR medication OR prescription) NEAR/2 (management OR pattern* OR use OR utilization OR prescribing OR trend* OR switch OR switching OR failure OR discontinuation OR augment* OR adheren* OR complian* OR persisten*)):ab,ti) OR (((treatment OR therapy OR therapies OR medication OR prescription) NEAR/3 (management OR pattern* OR use OR utilization OR prescribing OR trend* OR switch OR switching OR failure OR discontinuation OR augment* OR adheren* OR complian* OR persisten*)):ab,ti) OR 'treatment change':ab,ti OR 'therapy change':ab,ti OR 'drug change':ab,ti OR 'claims database':ab,ti OR 'pharmacy database':ab,ti OR 'pharmacy claim':ab,ti OR 'prescription claim':ab,ti	356,314
3.	'neuroleptic agent'/exp OR (antipsychotic*) OR (neuroleptic*) OR 'first generation antipsychotic agent':ab,ti OR 'second generation antipsychotic agent':ab,ti OR 'chlorpromazine':ab,ti OR 'droperidol':ab,ti OR 'fluphenazine':ab,ti OR 'haloperidol':ab,ti OR 'loxapine':ab,ti OR 'perphenazine':ab,ti OR 'pimozide':ab,ti OR 'prochlorperazine':ab,ti OR 'thioridazine':ab,ti OR 'thiothixene':ab,ti OR 'trifluoperazine':ab,ti OR 'aripiprazole':ab,ti OR 'amisulpride':ab,ti OR 'asenapine':ab,ti OR 'clozapine':ab,ti OR 'iloperidone':ab,ti OR 'lurasidone':ab,ti OR 'olanzapine':ab,ti OR 'paliperidone':ab,ti OR 'quetiapine':ab,ti OR 'risperidone':ab,ti OR 'sertindole':ab,ti OR 'zotepine':ab,ti OR 'ziprasidone':ab,ti OR 'major tranquilizers':ab,ti OR 'tranquilizers':ab,ti	282,858
4.	#1 AND #2 AND #3	5447
	Limiters	
5.	[2008-2018]/py	3813
6.	[english]/lim AND [humans]/lim	3253
7.	#6 NOT ('book'/exp OR 'book':it OR 'chapter':it OR 'conference abstract'/exp OR 'conference abstract':it OR 'conference paper'/exp OR 'conference paper':it OR 'conference review'/exp OR 'conference review':it OR 'editorial'/exp OR 'editorial':it OR 'erratum'/exp OR 'erratum':it OR 'letter'/exp OR 'letter':it OR 'review'/exp OR 'review':ab,ti OR 'case report'/de OR 'case report':it OR 'quality control'/exp OR 'quality control':de OR 'practice guideline'/exp OR 'practice guideline':de OR 'methodology'/de)	1263
8.	#7 NOT ('randomized controlled trial'/exp OR random*:ti OR placebo:ti OR ((singl*:ti OR doubl*:ti OR trebl*:ti OR tripl*:ti) AND (mask*:ti OR blind*:ti OR dumm*:ti)) OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR 'random allocation':ti OR 'placebo'/exp OR 'randomization'/exp OR 'nonhuman'/de OR 'randomized controlled trial (topic)'/de)	981
9.	#8 NOT ('animal cell'/exp OR 'animal cell':de OR 'animal experiment'/exp OR 'animal experiment':de OR 'animal model'/exp OR 'animal model':de OR 'cancer cell culture'/de OR 'biological model'/de OR 'human tissue'/exp OR 'human tissue':de OR 'cell culture'/de OR 'nonhuman'/de OR 'diagnostic test accuracy study'/de)	972
10.	#9 NOT (France:ti OR china:ti OR UK:ti OR 'United Kingdom':ti OR Canada:ti OR Japan:ti OR Africa:ti OR Spain:ti OR German:ti OR Italy:ti OR Europe:ti OR Australia:ti OR Switzerland:ti OR Sweden:ti OR Netherlands:ti OR brazil:ti)	924
	Results	
	TOTAL	924

Supplementary Table S5

PubMed In-Process Search Strategy for Treatment Patterns

Search Number	Search String	Hits (June 1, 2018)
Population		
1.	"Schizophrenia"[Mesh] or schizophrenia[tiab] or schizophrenic[tiab]	134,289
Treatment Patterns		
2.	((treatment*[tiab] or therapy[tiab] or therapies[tiab]) AND (management[tiab] or pattern*[tiab] or use[tiab] or utilization[tiab] or prescribing[tiab] or trend*[tiab] or survey[tiab] or database[tiab])) or switching or switched or "treatment change" or "therapy change" or failure or discontinuation or augment* or adherence or persisten* or complian* "drug change" or ("claims database" or "pharmacy database" or "pharmacy claims")	2,213,631
3.	"Antipsychotic agents"[Mesh] or (antipsychotic*) or (neuroleptic*) or "first generation antipsychotics"[tiab] or "Chlorpromazine"[tiab] or "Droperidol"[tiab] or "Fluphenazine"[tiab] or "Haloperidol"[tiab] or "Loxapine"[tiab] or "Perphenazine"[tiab] or "Pimozide"[tiab] or "Prochlorperazine"[tiab] or "Thioridazine"[tiab] or "Thiothixene"[tiab] or "Trifluoperazine"[tiab] or "second generation antipsychotics"[tiab] or "Aripiprazole"[tiab] or "Amisulpride"[tiab] or "Asenapine"[tiab] or "Clozapine"[tiab] or "Iloperidone"[tiab] or "Lurasidone"[tiab] or "Olanzapine"[tiab] or "Paliperidone"[tiab] or "Quetiapine"[tiab] or "Risperidone"[tiab] or "Sertindole"[tiab] or "zotepine"[tiab] or "Ziprasidone"[tiab] or "major tranquilizers"[tiab] or "tranquilizers"[tiab]	109,976
4.	#1 AND #2 AND #3	8086
Limiters		
5.	#4 Limited to studies published from January 1, 2008 through June 1, 2018	4212
6.	#5 Published in human subjects and English language	2957
7.	#6 NOT ("clinical trial"[ptyp] or "case reports"[ptyp] or letter[ptyp] or news[ptyp] or comment[ptyp] or "case report"[tiab] or "editorial"[tiab] or "letter"[tiab])	2072
8.	#7 NOT (randomized controlled trial[pt] OR randomized controlled trials as topic[mh] OR random allocation [mh] OR double-blind method[mh] OR single-blind method[mh] OR random*[tw] OR "Placebos"[Mesh] OR placebo[tiab] OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw] OR dumm*[tw])))	1627
9.	#8 NOT (France[ti] or china[ti] or UK[ti] or "United Kingdom"[ti] or Canada[ti] or Japan[ti] or Africa[ti] or Spain[ti] or German[ti] or Italy[ti] or Europe[ti] or Australia[ti] or Switzerland[ti] or Sweden[ti] or Netherlands[ti] or brazil[ti])	1569
10.	#9 NOT ("animal experimentation"[Mesh] OR "animal cell" OR "animal experiment" OR "animal model" OR "cancer cell culture" OR "biological model" OR "human tissue" OR "cell culture" OR "nonhuman" OR "diagnostic test accuracy study")	1563
Results		
TOTAL		1563

Supplementary Table S6

Study Selection Criteria for Systematic Review

Domain	Inclusion	Exclusion
Population	- Adults (aged 18 years or older) with schizophrenia - Mixed populations including both schizophrenia and schizoaffective disorders eligible for inclusion - Patient populations in a criminal justice setting - Study populations evaluating at least 30 adult schizophrenia patients	- Children and adolescents <18 years 100% schizoaffective patient populations - Mixed populations in which the outcomes are not separable for the schizophrenia patients - Studies evaluating fewer than 30 schizophrenia patients
Interventions/ comparators	- Any for economic studies - For treatment patterns evidence, only oral antipsychotic agents will be included	NA
Outcomes	Economic outcomes - Clinical health care resource utilization - Hospitalizations - Length of stay - Readmissions - Duration between hospitalizations - Psychiatric visits - Outpatient Visits (psychiatric and non-psychiatric) - Number of prescriptions - Cost - Direct costs - Total and itemized costs - Outpatient care - Inpatient care - Medication costs - Others as reported - Indirect costs - Productivity - Readiness for work - Work loss - WPAI questionnaire - Employer costs - Societal costs (disability, incarceration, child welfare system, etc.) - Treatment patterns - Oral antipsychotics used - Failure rates - Treatment changes - Switches - To what therapies patients switch - Augmentation Discontinuations - Adherence and compliance/persistence	Economic or treatment pattern outcomes not listed for inclusion
Study design	Observational studies including prospective or retrospective cohort studies (such as case-control, cross-sectional studies, or database/registry studies)	- Randomized controlled trials - Single-arm trials - Systematic review^a - Case reports, editorials, comments/commentary,

Domain	Inclusion	Exclusion
		guidelines, news, or narrative reviews
Time period	January 1, 2008, to June 1, 2018	Studies published prior to January 1, 2008 and after June 1, 2018
Others	- Limited to studies conducted in the US or with separable data for patients from the US - Published in English language	- Studies conducted outside of the US or with mixed locations that include ex-US countries - Studies published in languages other than English

^aSystematic reviews were not included for data extraction; however, the references of recent reviews were checked to ensure comprehensive identification of studies.

NA, not applicable; WPAI, Work Productivity and Activity Impairment.

Supplementary Table S7
Study Characteristics

		Direct Costs	Indirect Costs	Resource Use	
Amos, 2018 [1]	Retrospective, observational	No	No	Yes	Yes
Anderson, 2017 [2]	Retrospective, observational	No	No	Yes	Yes
Ascher-Svanum, 2009 [3]	Retrospective, observational	No	No	Yes	Yes
Baser, 2015 [4]	Retrospective, observational	Yes	No	Yes	No
Beebe, 2016 [5]	Cross-sectional	No	No	No	Yes
Berger, 2012 [6]	Retrospective, observational	Yes	No	No	Yes
Berkowitz, 2012 [7]	Retrospective, observational	No	No	No	Yes
Biskupiak, 2017 [8]	Retrospective, observational	Yes	No	Yes	Yes
Broder, 2012 [9]	Retrospective, observational	No	No	Yes	Yes
Campagna, 2014 [10]	Retrospective, observational	No	No	No	Yes
Chen, 2008 [11]	Retrospective, observational	Yes	No	No	Yes
Chen, 2008 [12]	Retrospective, observational	Yes	No	Yes	Yes
Chitnits, 2015 [13]	Retrospective, observational	Yes	No	Yes	No
Citrome, 2009 [14]	Retrospective, observational	No	No	No	Yes
Cullen, 2012 [15]	Retrospective, observational	No	No	Yes	Yes
Davis, 2014 [16]	Retrospective, observational	No	No	No	Yes
DerSarkissian, 2018 [17]	Retrospective, observational	Yes	No	Yes	No
DiBonaventura, 2010 [18]	Cross-sectional	No	Yes	Yes	Yes
Durkin, 2017 [19]	Retrospective, observational	Yes	No	Yes	No
Dusetzina, 2013 [20]	Retrospective, observational	No	No	No	Yes
Farley, 2010 [21]	Case-control	No	No	Yes	Yes
Farley, 2012 [22]	Retrospective, observational	Yes	No	Yes	Yes
Fisher, 2014 [23]	Retrospective, observational	No	No	No	Yes
Gilmer, 2009 [24]	Retrospective, observational	Yes	No	Yes	Yes
Greene, 2017 [25]	Retrospective, observational	No	No	No	Yes
Greene, 2018 [26]	Retrospective, observational	No	No	No	Yes

Haynes, 2012 [27]	Prospective, observational	Yes	No	No	Yes
He, 2018 [28]	Retrospective, observational	Yes	No	No	No
Horvitz-Lennon, 2013 [29]	Retrospective, observational	No	No	No	Yes
Jiang, 2015 [30]	Retrospective, observational	Yes	No	Yes	Yes
Joshi, 2017 [31]	Retrospective, observational	Yes	No	No	Yes
Karve, 2012 [32]	Retrospective, observational	Yes	No	Yes	No
El Khoury, 2018 [33]	Retrospective, observational	No	No	No	Yes
Kilzieh, 2008 [34]	Retrospective, observational	No	No	No	Yes
Kozma, 2009 [35]	Retrospective, observational	No	No	Yes	Yes
Kreyenbuhl, 2011 [36]	Retrospective, observational	No	No	Yes	Yes
Lafeuille, 2013 [37]	Retrospective, observational	Yes	No	Yes	No
Lafeuille, 2013 [38]	Retrospective, observational	No	No	Yes	Yes
Lafeuille, 2015 [39]	Retrospective, observational	Yes	No	Yes	No
Lafeuille, 2017 [40]	Retrospective, observational	Yes	No	Yes	Yes
Lafeuille, 2018 [41]	Retrospective, observational	Yes	No	Yes	Yes
Lang, 2010 [42]	Retrospective, observational	No	No	Yes	Yes
Lang, 2013 [43]	Retrospective, observational	Yes	No	Yes	Yes
Law, 2008 [44]	Retrospective, observational	No	No	Yes	Yes
Lawson, 2015 [45]	Retrospective, observational	No	No	Yes	Yes
Locklear, 2014 [46]	Retrospective, observational	Yes	No	Yes	Yes
MacEwan, 2016 [47]	Retrospective, observational	No	No	Yes	Yes
Manuel, 2012 [48]	Retrospective, observational	Yes	No	Yes	Yes
Marcus, 2015 [49]	Retrospective, observational	No	No	Yes	Yes
Martin, 2009 [50]	Retrospective, observational	No	No	No	Yes
Mohamed, 2009 [51]	Retrospective, observational	No	No	Yes	Yes
Mullins, 2008 [52]	Retrospective, observational	No	No	Yes	Yes
Nakonezny, 2008 [53]	Prospective, observational	No	No	No	Yes
Nuechterlein, 2011 [54]	Prospective, observational	No	Yes	No	Yes

Offord, 2013 [55]	Retrospective, observational	No	No	Yes	Yes
Offord, 2013 [56]	Retrospective, observational	Yes	No	Yes	Yes
Panish, 2013 [57]	Retrospective, observational	No	No	Yes	Yes
Pesa, 2015 [58]	Retrospective, observational	Yes	No	Yes	No
Pesa, 2017 [59]	Retrospective, observational	Yes	No	Yes	Yes
Pfeiffer, 2008 [60]	Retrospective, observational	No	No	No	Yes
Pilon, 2017 [61]	Retrospective, observational	Yes	No	Yes	Yes
Pilon, 2017 [62]	Retrospective, observational	Yes	No	Yes	Yes
Pilon, 2017 [63]	Retrospective, observational	No	No	Yes	Yes
Pilon, 2018 [64]	Retrospective, observational	Yes	No	Yes	Yes
Rajagopalan, 2017 [65]	Retrospective, observational	No	No	No	Yes
Seabury, 2014 [66]	Retrospective, observational	Yes	No	Yes	Yes
Shah, 2017 [67]	Retrospective, observational	Yes	No	Yes	Yes
Stephenson, 2012 [68]	Retrospective, observational	No	No	No	Yes
Stroup, 2014 [69]	Retrospective, observational	No	No	Yes	Yes
Stroup, 2016 [70]	Retrospective, observational	No	No	Yes	Yes
Tang, 2017 [71]	Retrospective, observational	No	No	No	Yes
Thomas, 2015 [72]	Retrospective, observational	Yes	No	Yes	Yes
Wang, 2014 [73]	Retrospective, observational	No	No	Yes	Yes
Wilk, 2008 [74]	Cross-sectional	No	No	No	Yes
Xiao, 2015 [75]	Retrospective, observational	Yes	No	Yes	Yes
Yan, 2018 [76]	Retrospective, observational	Yes	No	Yes	No
Young-Xu, 2016 [77]	Retrospective, observational	Yes	Yes	Yes	Yes
Yu, 2009 [78]	Retrospective, observational	Yes	No	Yes	Yes
Yu, 2009 [79]	Retrospective, observational	Yes	No	Yes	Yes
Zhu, 2008 [80]	Prospective, observational	Yes	No	Yes	Yes
Zhu, 2008 [81]	Prospective, observational	No	No	No	Yes

REFERENCES

- 1 Amos T, El Khoury A, Vlahiotis A, et al. Treatment patterns and healthcare resource utilization among young adults with schizophrenia treated with paliperidone palmitate or oral atypical antipsychotics [abstract PMH62]. *Value Health*. 2018;21:S190.
- 2 Anderson JP, Icten Z, Alas V, Benson C, Joshi K. Comparison and predictors of treatment adherence and remission among patients with schizophrenia treated with paliperidone palmitate or atypical oral antipsychotics in community behavioral health organizations. *BMC Psychiatry*. 2017;17:346.
- 3 Ascher-Svanum H, Peng X, Faries D, Montgomery W, Haddad PM. Treatment patterns and clinical characteristics prior to initiating depot typical antipsychotics for nonadherent schizophrenia patients. *BMC Psychiatry*. 2009;9:46.
- 4 Baser O, Xie L, Pesa J, Durkin M. Healthcare utilization and costs of Veterans Health Administration patients with schizophrenia treated with paliperidone palmitate long-acting injection or oral atypical antipsychotics. *J Med Econ*. 2015;18:357-65.
- 5 Beebe LH, Smith K, Phillips C. Descriptions and correlates of medication adherence, attitudes, and self-efficacy in outpatients with schizophrenia spectrum disorders (SSDs). *Arch Psychiatr Nurs*. 2016;30:400-5.
- 6 Berger A, Edelsberg J, Sanders KN, et al. Medication adherence and utilization in patients with schizophrenia or bipolar disorder receiving aripiprazole, quetiapine, or ziprasidone at hospital discharge: a retrospective cohort study. *BMC Psychiatry*. 2012;12:99.
- 7 Berkowitz RL, Patel U, Ni Q, Parks JJ, Docherty JP. The impact of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) on prescribing practices: an analysis of data from a large midwestern state. *J Clin Psychiatry*. 2012;73:498-503.
- 8 Biskupiak J, Yoo M, Kim J, et al. Impact of medication changes during hospital stay on postdischarge hospital readmissions and health care charges: analysis of outcomes among adults with schizophrenia or bipolar disorder admitted to an academic neuropsychiatric hospital [abstract F9]. *J Manag Care Spec Pharm*. 2017;23:S44-S5.
- 9 Broder MS, Bates JA, Jing Y, et al. Association between second-generation antipsychotic medication half-life and hospitalization in the community treatment of adult schizophrenia. *J Med Econ*. 2012;15:105-11.
- 10 Campagna EJ, Muser E, Parks J, Morrato EH. Methodological considerations in estimating adherence and persistence for a long-acting injectable medication. *J Manag Care Spec Pharm*. 2014;20:756-66.
- 11 Chen L, McCombs JS, Park J. Duration of antipsychotic drug therapy in real-world practice: a comparison with CATIE trial results. *Value Health*. 2008;11:487-96.
- 12 Chen L, McCombs JS, Park J. The impact of atypical antipsychotic medications on the use of health care by patients with schizophrenia. *Value Health*. 2008;11:34-43.

- 13 Chitnis A, Sun SX, Dixit S, et al. Changes in patterns of utilization and cost of health care services associated with initiation of asenapine for the treatment of schizophrenia in adults. *Manag Care*. 2015;24:58-64.
- 14 Citrome L, Reist C, Palmer L, et al. Impact of real-world ziprasidone dosing on treatment discontinuation rates in patients with schizophrenia or bipolar disorder. *Schizophr Res*. 2009;115:115-20.
- 15 Cullen BA, McGinty EE, Zhang Y, et al. Guideline-concordant antipsychotic use and mortality in schizophrenia. *Schizophr Bull*. 2013;39:1159-68.
- 16 Davis MC, Fuller MA, Strauss ME, Konicki PE, Jaskiw GE. Discontinuation of clozapine: a 15-year naturalistic retrospective study of 320 patients. *Acta Psychiatr Scand*. 2014;130:30-9.
- 17 DerSarkissian M, Lefebvre P, Joshi K, et al. A comparison of antipsychotic treatment patterns, healthcare resource utilization, and associated costs in veterans with schizophrenia pre- and post-initiation of treatment with once-every-three-month paliperidone palmitate [abstract F17]. *J Manag Care Spec Pharm*. 2018;24:S51-S2.
- 18 DiBonaventura MC, Panish J, Kenworthy D, Wagner JS, Dirani R. The association of well-being, productivity and resource use among community-dwelling patients with schizophrenia using atypical antipsychotics. *J Pharm Health Serv Res*. 2010;1:181-7.
- 19 Durkin M, Song X, Tran O, et al. Two-year acute care utilization and cost outcomes for schizophrenia patients in medicaid treated with paliperidone palmitate or oral atypical antipsychotic [abstract F14]. *J Manag Care Spec Pharm*. 2017;23(3-a suppl):S54.
- 20 Dusetzina SB, Cook BL, Busch AB, Alexander GC, Huskamp HA. Racial-ethnic differences in incident olanzapine use after an FDA advisory for patients with schizophrenia. *Psychiatr Serv*. 2013;64:83-7.
- 21 Farley JF. Medicaid prescription cost containment and schizophrenia: a retrospective examination. *Med Care*. 2010;48:440-7.
- 22 Farley JF, Hansen RA, Yu-Isenberg KS, Maciejewski ML. Antipsychotic adherence and its correlation to health outcomes for chronic comorbid conditions. *Prim Care Companion CNS Disord*. 2012;14.
- 23 Fisher MD, Reilly K, Isenberg K, Villa KF. Antipsychotic patterns of use in patients with schizophrenia: polypharmacy versus monotherapy. *BMC Psychiatry*. 2014;14:341.
- 24 Gilmer TP, Ojeda VD, Barrio C, et al. Adherence to antipsychotics among Latinos and Asians with schizophrenia and limited English proficiency. *Psychiatr Serv*. 2009;60:175-82.
- 25 Greene M, Yan T, Chang E, Hartry A, Broder MS. Medication adherence and discontinuation in medicaid patients with schizophrenia initiating a long acting injectable antipsychotic versus those who change to a different oral antipsychotic [abstract PMH58]. *Value Health*. 2017;20:A302.

- 26 Greene M, Yan T, Chang E, et al. Medication adherence and discontinuation of long-acting injectable versus oral antipsychotics in patients with schizophrenia or bipolar disorder. *J Med Econ*. 2018;21:127-34.
- 27 Haynes VS, Zhu B, Stauffer VL, et al. Long-term healthcare costs and functional outcomes associated with lack of remission in schizophrenia: a post-hoc analysis of a prospective observational study. *BMC Psychiatry*. 2012;12:222.
- 28 He J, Caver M, Vu H, Tariq S. Effect of atypical antipsychotic long-acting injectable utilization on overall healthcare costs [abstract]. *J Manag Care Spec Pharm*. 2018;24(4-a suppl):S51.
- 29 Horvitz-Lennon M, Donohue JM, Lave JR, Alegría M, Normand SL. The effect of race-ethnicity on the comparative effectiveness of clozapine among Medicaid beneficiaries. *Psychiatr Serv*. 2013;64:230-7.
- 30 Jiang Y, Ni W. Health care utilization and treatment persistence associated with oral paliperidone and lurasidone in schizophrenia treatment. *J Manag Care Spec Pharm*. 2015;21:780-92.
- 31 Joshi K, Kamstra R, Pilon D, Lefebvre P, Emond B. Treatment patterns and Medicaid spending in comorbid schizophrenia populations: once-monthly paliperidone palmitate versus oral atypical antipsychotics [abstract]. Presented at: Annual Meeting of the American Psychiatric Association; May 20-24, 2017; San Diego, CA.
- 32 Karve S, Panish JM, Dirani RG, Candrilli S. Health care utilization and costs among medicaid-enrolled patients with schizophrenia experiencing multiple psychiatric relapses. *Health Outcomes Res Med*. 2012;3:e183-e94.
- 33 El Khoury A, Joshi K, Brouillette M, Kalyanaraman A. Treatment patterns in schizophrenia patients initiated on paliperidone palmitate long-acting injectable in a medicaid population [abstract]. Presented at: Annual Meeting of the American Psychological Association; August 9-12, 2018; San Francisco, CA.
- 34 Kilzieh N, Todd-Stenberg JA, Kennedy A, Wood AE, Tapp AM. Time to discontinuation and self-discontinuation of olanzapine and risperidone in patients with schizophrenia in a naturalistic outpatient setting. *J Clin Psychopharmacol*. 2008;28:74-7.
- 35 Kozma CM, Weiden PJ. Partial compliance with antipsychotics increases mental health hospitalizations in schizophrenic patients: analysis of a national managed care database. *Am Health Drug Benefits*. 2009;2:31-8.
- 36 Kreyenbuhl J, Slade EP, Medoff DR, et al. Time to discontinuation of first- and second-generation antipsychotic medications in the treatment of schizophrenia. *Schizophr Res*. 2011;131:127-32.
- 37 Lafeuille MH, Gravel J, Lefebvre P, et al. Patterns of relapse and associated cost burden in schizophrenia patients receiving atypical antipsychotics. *J Med Econ*. 2013;16:1290-9.
- 38 Lafeuille MH, Laliberté-Auger F, Lefebvre P, et al. Impact of atypical long-acting injectable versus oral antipsychotics on rehospitalization rates and emergency room visits among relapsed schizophrenia patients: a retrospective database analysis. *BMC Psychiatry*. 2013;13:221.

- 39 Lafeuille MH, Grittner AM, Fortier J, et al. Comparison of rehospitalization rates and associated costs among patients with schizophrenia receiving paliperidone palmitate or oral antipsychotics. *Am J Health Syst Pharm*. 2015;72:378-89.
- 40 Lafeuille M, Joshi K, Tandon N, et al. Health care costs and resource utilization in patients with schizophrenia and cardiometabolic comorbidities treated with once-monthly paliperidone palmitate versus oral atypical antipsychotics [abstract F17]. *J Manag Care Spec Pharm*. 2017;23:S55-S6.
- 41 Lafeuille MH, Tandon N, Tiggelaar S, et al. Economic impact in Medicaid beneficiaries with schizophrenia and cardiometabolic comorbidities treated with once-monthly paliperidone palmitate vs. oral atypical antipsychotics. *Drugs Real World Outcomes*. 2018;5:81-90.
- 42 Lang K, Meyers JL, Korn JR, et al. Medication adherence and hospitalization among patients with schizophrenia treated with antipsychotics. *Psychiatr Serv*. 2010;61:1239-47.
- 43 Lang K, Federico V, Muser E, Menzin J, Menzin J. Rates and predictors of antipsychotic non-adherence and hospitalization in Medicaid and commercially-insured patients with schizophrenia. *J Med Econ*. 2013;16:997-1006.
- 44 Law MR, Soumerai SB, Ross-Degnan D, Adams AS. A longitudinal study of medication nonadherence and hospitalization risk in schizophrenia. *J Clin Psychiatry*. 2008;69:47-53.
- 45 Lawson W, Johnston S, Karson C, et al. Racial differences in antipsychotic use: claims database analysis of Medicaid-insured patients with schizophrenia. *Ann Clin Psychiatry*. 2015;27:242-52.
- 46 Locklear JC, Wahlqvist P, Gustafsson U, et al. Impact of extended-release quetiapine fumarate on hospitalization length and cost in schizophrenia and bipolar disorder patients: a retrospective, hospital-based, US-cohort analysis. *J Comp Eff Res*. 2014;3:335-44.
- 47 MacEwan JP, Forma FM, Shafrin J, et al. Patterns of adherence to oral atypical antipsychotics among patients diagnosed with schizophrenia. *J Manag Care Spec Pharm*. 2016;22:1349-61.
- 48 Manuel JI, Essock SM, Wu Y, Pangilinan M, Stroup S. Factors associated with initiation on clozapine and on other antipsychotics among Medicaid enrollees. *Psychiatr Serv*. 2012;63:1146-9.
- 49 Marcus SC, Zummo J, Pettit AR, Stoddard J, Doshi JA. Antipsychotic adherence and rehospitalization in schizophrenia patients receiving oral versus long-acting injectable antipsychotics following hospital discharge. *J Manag Care Spec Pharm*. 2015;21:754-68.
- 50 Martin BC, Wiley-Exley EK, Richards S, et al. Contrasting measures of adherence with simple drug use, medication switching, and therapeutic duplication. *Ann Pharmacother*. 2009;43:36-44.
- 51 Mohamed S, Rosenheck R, Harpaz-Rotem I, Leslie D, Sernyak MJ. Duration of pharmacotherapy with long-acting injectable risperidone in the treatment of schizophrenia. *Psychiatr Q*. 2009;80:241-9.

- 52 Mullins CD, Obeidat NA, Cuffel BJ, Naradzay J, Loebel AD. Risk of discontinuation of atypical antipsychotic agents in the treatment of schizophrenia. *Schizophr Res.* 2008;98:8-15.
- 53 Nakonezny PA, Byerly MJ, Rush AJ. Electronic monitoring of antipsychotic medication adherence in outpatients with schizophrenia or schizoaffective disorder: an empirical evaluation of its reliability and predictive validity. *Psychiatry Res.* 2008;157:259-63.
- 54 Nuechterlein KH, Subotnik KL, Green MF, et al. Neurocognitive predictors of work outcome in recent-onset schizophrenia. *Schizophr Bull.* 2011;37 Suppl 2:S33-40.
- 55 Offord S, Wong B, Mirski D, Baker RA, Lin J. Healthcare resource usage of schizophrenia patients initiating long-acting injectable antipsychotics vs oral. *J Med Econ.* 2013;16:231-9.
- 56 Offord S, Lin J, Wong B, Mirski D, Baker RA. Impact of oral antipsychotic medication adherence on healthcare resource utilization among schizophrenia patients with Medicare coverage. *Community Ment Health J.* 2013;49:625-9.
- 57 Panish J, Karve S, Candrilli SD, Dirani R. Association between adherence to and persistence with atypical antipsychotics and psychiatric relapse among US Medicaid-enrolled patients with schizophrenia. *J Pharm Health Serv Res.* 2013;4:29-39.
- 58 Pesa JA, Muser E, Montejano LB, Smith DM, Meyers OI. Costs and resource utilization among Medicaid patients with schizophrenia treated with paliperidone palmitate or oral atypical antipsychotics. *Drugs Real World Outcomes.* 2015;2:377-85.
- 59 Pesa JA, Doshi D, Wang L, Yuce H, Baser O. Health care resource utilization and costs of California Medicaid patients with schizophrenia treated with paliperidone palmitate once monthly or atypical oral antipsychotic treatment. *Curr Med Res Opin.* 2017;33:723-31.
- 60 Pfeiffer PN, Ganoczy D, Valenstein M. Dosing frequency and adherence to antipsychotic medications. *Psychiatr Serv.* 2008;59:1207-10.
- 61 Pilon D, Tandon N, Lafeuille MH, et al. Treatment patterns, health care resource utilization, and spending in Medicaid beneficiaries initiating second-generation long-acting injectable agents versus oral atypical antipsychotics. *Clin Ther.* 2017;39:1972-85.e2.
- 62 Pilon D, Muser E, Lefebvre P, et al. Adherence, healthcare resource utilization and Medicaid spending associated with once-monthly paliperidone palmitate versus oral atypical antipsychotic treatment among adults recently diagnosed with schizophrenia. *BMC Psychiatry.* 2017;17:207.
- 63 Pilon D, Amos TB, Germain G, et al. Treatment persistence and hospitalization rates among patients with schizophrenia: a quasi-experiment to evaluate a patient information program. *Curr Med Res Opin.* 2017;33:713-21.
- 64 Pilon D, Alcusky M, Xiao Y, et al. Adherence, persistence, and inpatient utilization among adult schizophrenia patients using once-monthly versus twice-monthly long-acting atypical antipsychotics. *J Med Econ.* 2018;21:135-43.

- 65 Rajagopalan K, Wade S, Meyer N, Loebel A. Real-world adherence assessment of lurasidone and other oral atypical antipsychotics among patients with schizophrenia: an administrative claims analysis. *Curr Med Res Opin.* 2017;33:813-20.
- 66 Seabury SA, Goldman DP, Kalsekar I, et al. Formulary restrictions on atypical antipsychotics: impact on costs for patients with schizophrenia and bipolar disorder in Medicaid. *Am J Manag Care.* 2014;20:e52-60.
- 67 Shah A, Xie L, Kariburyo F, Zhang Q, Gore M. Treatment patterns, healthcare resource utilization and costs in schizophrenia patients treated with long-acting injectable vs oral antipsychotics: a real-world study [abstract]. Presented at: Annual Psych Congress; September 16-19, 2017; New Orleans, LA.
- 68 Stephenson JJ, Tunceli O, Gu T, et al. Adherence to oral second-generation antipsychotic medications in patients with schizophrenia and bipolar disorder: physicians' perceptions of adherence vs. pharmacy claims. *Int J Clin Pract.* 2012;66:565-73.
- 69 Stroup TS, Gerhard T, Crystal S, Huang C, Olfson M. Geographic and clinical variation in clozapine use in the United States. *Psychiatr Serv.* 2014;65:186-92.
- 70 Stroup TS, Gerhard T, Crystal S, Huang C, Olfson M. Comparative effectiveness of clozapine and standard antipsychotic treatment in adults with schizophrenia. *Am J Psychiatry.* 2016;173:166-73.
- 71 Tang Y, Horvitz-Lennon M, Gellad WF, et al. Prescribing of clozapine and antipsychotic polypharmacy for schizophrenia in a large Medicaid program. *Psychiatr Serv.* 2017;68:579-86.
- 72 Thomas KL, Jiang Y, McCombs JS. Clozapine revisited: Impact of clozapine vs olanzapine on health care use by schizophrenia patients on Medicaid. *Ann Clin Psychiatry.* 2015;27:90-9.
- 73 Wang CC, Maciejewski ML, Rao JK, et al. Examining the relationship between adjunctive psychotherapy use and antipsychotic persistence and hospitalization. *Adm Policy Ment Health.* 2014;41:598-607.
- 74 Wilk JE, West JC, Marcus SC, et al. Family contact and the management of medication non-adherence in schizophrenia. *Community Ment Health J.* 2008;44:377-80.
- 75 Xiao Y, Muser E, Lafeuille MH, et al. Impact of paliperidone palmitate versus oral atypical antipsychotics on healthcare outcomes in schizophrenia patients. *J Comp Eff Res.* 2015;4:579-92.
- 76 Yan T, Greene M, Chang E, et al. All-cause hospitalization and associated costs in patients with schizophrenia or bipolar disorder initiating long-acting injectable antipsychotics. *Curr Med Res Opin.* 2018;34:41-7.
- 77 Young-Xu Y, Duh MS, Muser E, et al. Impact of paliperidone palmitate versus oral atypical antipsychotics on health care resource use and costs in veterans with schizophrenia. *J Clin Psychiatry.* 2016;77:e1332-e41.
- 78 Yu AP, Atanasov P, Ben-Hamadi R, et al. Resource utilization and costs of schizophrenia patients treated with olanzapine versus quetiapine in a Medicaid population. *Value Health.* 2009;12:708-15.

- 79 Yu AP, Ben-Hamadi R, Birnbaum HG, et al. Comparing the treatment patterns of patients with schizophrenia treated with olanzapine and quetiapine in the Pennsylvania Medicaid population. *Curr Med Res Opin.* 2009;25:755-64.
- 80 Zhu B, Ascher-Svanum H, Faries DE, Correll CU, Kane JM. Cost of antipsychotic polypharmacy in the treatment of schizophrenia. *BMC Psychiatry.* 2008;8:19.
- 81 Zhu B, Ascher-Svanum H, Shi L, et al. Time to discontinuation of depot and oral first-generation antipsychotics in the usual care of schizophrenia. *Psychiatr Serv.* 2008;59:315-7.