Importance of Real-World Evidence in Clinical Decision-Making

Rakesh Jain, MD,[1] Craig Chepke, MD,[2] Andrew J. Cutler, MD,[3,4] Hemangi R. Panchmatia, MSc,[5] Michael J. Doane, PhD,[5] Dennis Fried, PhD, MPH, MBA,[5] Madé Wenten, PhD, MPH,[5] Barry Lubarsky, PhD[5]

[1]Department of Psychiatry, Texas Tech University School of Medicine-Permian Basin, Midland, TX, USA; [2]Excel Psychiatric Associates, P.A., Huntersville, NC, USA; [3]Department of Psychiatry, SUNY Upstate Medical University, Syracuse, NY, USA; [4]Neuroscience Education Institute, Lakewood Ranch, FL, USA; [5]Alkermes, Inc., Waltham, MA, USA

- **Real-world data (RWD)** relate to information on patient health status and/or delivery of healthcare that is routinely collected from sources such as insurance claims, patient surveys, electronic health records, patient registries, and digital health tools[1]
- **Real-world evidence (RWE)** entails insights from analyzing RWD to understand how treatments perform in everyday clinical settings[2]
- **RWE complements randomized controlled trials (RCTs)**, the gold standard for establishing treatment efficacy and safety[3]
- **RWE strengthens and builds on these findings** by analyzing larger, more diverse populations in real-world settings, helping to understand effectiveness, informing clinical decision-making post-launch, and assessing utility across generalized patient populations

Common Real-World Data Sources

Insurance Claims

Administrative records created when healthcare providers bill insurance companies for services

What they include

Basic patient details (age, gender, etc), diagnosis codes and procedures, prescription fills, dates and duration of care (eg, hospital stays, emergency department visits), and costs of services

How they're used

- Study medication use patterns—how often patients refill prescriptions, stay on treatment (based on refills), and switch medications
- Understand healthcare use—how often and how long patients are hospitalized or how often they visit the emergency department or another outpatient setting
- Assess relapse—using disease-specific (eg, schizophrenia-related) hospital or emergency department visits as a proxy for relapse

Patient Surveys

Information collected directly from patients through questionnaires or interviews

What can be collected

Demographic characteristics and background information, self-reported symptoms, treatment experiences and side effects, preferences for treatment attributes, perceived effectiveness and satisfaction with care, measures of quality of life and daily functioning

How they're used

- Understand treatment attributes that patients value most and the tradeoffs they are willing to make based on experiences with current treatment/care (eg, efficacy vs safety)
- Capture patients' real-world experiences, preferences, satisfaction, and unmet needs

What are some questions that RWE can help address?

A treatment is clinically effective in RCTs, but how might it affect hospitalization rates in real-world settings?

24% relative reduction in **inpatient admissions**

Rate significantly decreased from 33% at baseline to 25% at follow-up: absolute difference (95% CI), −8% (−11%, −5%); *P*<0.001

Published example[4]: A retrospective claims analysis assessed inpatient admissions in adults with schizophrenia before and after initiating a combination of olanzapine and samidorphan (OLZ/SAM)

Initiating OLZ/SAM was associated with significant reductions in schizophrenia-related inpatient admissions

This study analyzed insurance claims data using diagnosis codes and event counts to compare schizophrenia-related inpatient admissions before and after initiating OLZ/SAM to evaluate its real-world effectiveness

Refer to Limitations of Claims Analysis for study limitations

Takeaway: RWE helps clinicians identify treatments associated with reduced hospitalizations, which may serve as an important indicator of relapse risk in schizophrenia

Are patients more likely to remain adherent with one treatment vs another?

109% higher odds of **being adherent**

Odds ratio (95% CI) **OLZ/SAM vs olanzapine**: 2.09 (1.72, 2.54); *P*0.001

50% lower odds of **discontinuation**

Odds ratio (95% CI) **OLZ/SAM vs olanzapine**: 0.50 (0.40, 0.61); *P*<0.001

Published example[5]: A retrospective claims analysis assessed treatment patterns in adult Medicaid-insured patients with schizophrenia who initiated OLZ/SAM vs olanzapine

Significantly higher adherence and lower likelihood of treatment discontinuation were observed for OLZ/SAM vs olanzapine

This study analyzed insurance claims data to calculate the total days' supply from prescription refills for OLZ/SAM vs olanzapine, which was used to assess and compare adherence to these antipsychotics in the real world

Refer to Limitations of Claims Analysis for study limitations

Takeaway: RWE helps identify treatments associated with better adherence, which may have practical implications in clinical practice

Which treatment is better at reducing hospitalization risk in a real-world setting?

Published example[6]: A retrospective claims analysis evaluated acute care events in adult Medicaid-insured patients with bipolar I disorder (BD-I) who initiated OLZ/SAM vs olanzapine

OLZ/SAM was associated with a significantly lower likelihood of ≥1 BD-I–related inpatient admission vs olanzapine

This study analyzed insurance claims data using diagnosis codes and numbers of events to compare BD-I–related inpatient admissions between OLZ/SAM and olanzapine to evaluate their real-world effectiveness

Refer to Limitations of Claims Analysis for study limitations

92% higher odds of **being relapse-free**[a]

Odds ratio (95% CI) of BD-I–related inpatient admissions, **OLZ/SAM vs olanzapine**: 0.52 (0.38, 0.70); *P*<0.001

[a]Calculated based on odds ratio of BD-I–related IP admissions (used as a proxy for relapse; BD-I–related emergency department visits were not included.

Takeaway: RWE (eg, disease-related hospitalization data) may serve as a proxy for treatment outcomes (eg, relapse)

How do patients prioritize efficacy vs tolerability attributes of treatments?

Published example[7]: An online survey elicited the preferences of patients with schizophrenia or BD-I for 5 attributes of oral antipsychotic medications

Patients preferred treatments with better efficacy and were willing to trade some side effects, such as weight gain, for moderate increases in symptom reduction

This study used a survey to gather patients' feedback on the attributes they value most in oral antipsychotic medications—eg, symptom improvement vs fewer side effects—to identify factors that influence their treatment choices

Refer to Limitations of Patient Surveys for study limitations

Takeaway: RWE may help healthcare professionals weigh treatment tradeoffs that are aligned with patient preferences

RWE complements RCTs by extending their findings to routine clinical practice and providing insights on outcomes relevant to everyday patient care

- Provides insights into real-world treatment effectiveness and outcomes relevant to patient care
- Supports informed, shared decision-making between clinicians and patients
- Plays an increasingly important role in guiding evidence-based practice as healthcare moves toward personalized care

Characteristics of RCTs and RWE

	RCTs	RWE
Population	Highly selected, strict inclusion/exclusion	Broad, heterogeneous patient populations
Setting	Controlled, ideal research conditions	Everyday clinical practice
Outcomes	Safety and efficacy focused	Patient centered, pragmatic
Purpose	Demonstrate causal effect	May support generalizability, guide real-world decisions

Limitations of Claims Analysis

- Claims analyses rely on insurance data, and findings may not be representative of those from uninsured patients
- Claims data do not capture disease severity and are subject to data omissions and/or coding inaccuracies
- The presence of a claim for a filled prescription may not indicate that the medication was consumed
- Although RWE studies may adjust for known potential confounders, other clinical measures that may act as additional confounders may not be available in claims data; no adjustments for multiplicity were made in the presented analyses
- Fixed observation periods in RWE studies may not fully capture the effects of longer-term treatment

Limitations of Patient Surveys

- In patient surveys, diagnoses are patient-reported and not confirmed by clinician assessment
- Survey respondents may overstate their answers in response to hypothetical scenarios
- A patient's clinical course and individual treatment experiences may significantly affect survey responses

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Supported by funding from Alkermes, Inc.

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DISCLOSURES

RJ has been a consultant for AbbVie, Acadia, Adamas, Alfasigma, Alkermes, Almatica, Axsome, Biogen, Boehringer Ingelheim, Cingulate Therapeutics, Corium, Eisai, Evidera, Impel, Janssen, Lilly, Lundbeck, Merck, Neos Therapeutics, Neurocrine Biosciences, Osmotica, Otsuka, Pamlab, Pfizer, Sage Therapeutics, Shire, Sunovion, Supernus, Takeda, Teva, Transcend Therapeutics, and Viatris; received speaker/promotional honoraria from AbbVie, Alkermes, Almatica, Axsome, Corium, Eisai, Intra-Cellular Therapies, Ironshore Pharmaceuticals, Janssen, Lilly, Lundbeck, Merck, Neos Therapeutics, Otsuka, Pamlab, Pfizer, Shire, Sunovion, Takeda, Tris Pharmaceuticals, and Viatris; served on an advisory board for Adamas, Alkermes, Corium, Eisai, Janssen, Lilly, Lundbeck, Merck, Neos Therapeutics, Neurocrine Biosciences, Otsuka, Pamlab, Pfizer, Sage Therapeutics, Shire, Sunovion, Supernus, Takeda, and Teva; and received research funding from AbbVie, Lilly, Lundbeck, Otsuka, Pfizer, Shire, and Takeda.

CC has been a consultant or on an advisory board for or has received grant or research support from Acadia, Axsome, Harmony, Neurocrine, and Teva; has served as a consultant for AbbVie, Alkermes, Arcadia, Axsome, Biogen, Boehringer Ingelheim, Corium, Intra-Cellular, Janssen, Karuna, Lundbeck, MedinCell, Moderna, Neurocrine, Noven, Otsuka, Sage, Sumitomo, Supernus, and Teva; has received payment or honoraria for educational activities from AbbVie, Acadia, Alkermes, Axsome, Bristol Myers Squibb, Corium, Intra-Cellular, Janssen, Karuna, Lundbeck, Merck, Neurocrine, Noven, Otsuka, Sumitomo, and Teva; has received support for attending meetings/travel from AbbVie, Acadia, Alkermes, Axsome, Bristol-Myers Squibb, Corium, Intra-Cellular, Janssen, Karuna, Lundbeck, Merck, Neurocrine, Noven, Otsuka, Sumitomo, and Teva; and has served on an advisory or data safety monitoring board for AbbVie, Acadia, Alkermes, Axsome, Biogen, Bristol-Myers Squibb, Corium, Idorsia, Intra-Cellular, Janssen, Karuna, Lundbeck, Moderna, Neurocrine, Noven, Otsuka, Sage, Sumitomo, and Teva.

AJC has been a consultant or on an advisory board for AbbVie, Acadia, Alfasigma, Alkermes, Anavex Life Sciences, Autobahn Therapeutics, Axsome, Biogen, Biohaven, Boehringer Ingelheim, Brii Biosciences, Bristol Myers Squibb, Cerevel, Corium, Delpor, Evolution Research Group, 4M Therapeutics, Intra-Cellular Therapies, J&J Innovative Medicine, Jazz Pharma, Karuna, LivaNova, Lundbeck, Luye Pharma, MapLight Therapeutics, MedAvante-ProPhase, Mentavi, Neumora, Neurocrine, Neuroscience Education Institute, NeuroSigma, Noven, Otsuka, PaxMedica, Relmada, Sage Therapeutics, Supernus, Teva, Thynk, Tris Pharma, Vanda Pharmaceuticals, and VistaGen; is on the speakers' bureau for AbbVie, Alfasigma, Alkermes, Axsome, Bristol Myers Squibb, Corium, Intra-Cellular Therapies, J&J, Lundbeck, Neurocrine, Noven, Otsuka, Supernus, Teva, Tris Pharma, and Vanda Pharmaceuticals; is on a data safety monitoring board for Alar Pharma, COMPASS Pathways, Freedom Biosciences, and Pain Therapeutics; holds stock options from 4M Therapeutics; and receives no royalties.

HRP, **MJD**, **DF, MW**, and **BL** are or were employees of Alkermes, Inc., and may own stock/options in the company

ACKNOWLEDGMENTS

This study was sponsored by Alkermes, Inc. Medical writing and editorial support were provided by Peloton Advantage, LLC, an OPEN Health company, and funded by Alkermes, Inc.

Supported by funding from Alkermes, Inc.