Projections to Real-World Population

Potential Impact of Using Paliperidone Palmitate Long-Acting Injections Among Medicaid Beneficiaries With Schizophrenia

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Introduction

- Well established traditional methods to generate RWE, such as pragmatic trial designs and observational data methods
  - Requires time and substantial resource investments
  - Are they necessary for every new technology?

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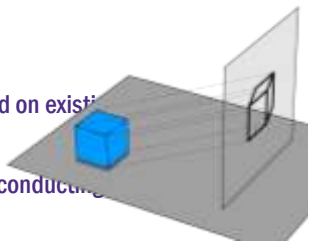
- Well established traditional methods to generate RWE, such as pragmatic trial designs and observational data methods
  - Requires time and substantial resource investments
  - Are they necessary for every new technology?

- Alternative methodological approaches
  - project the real-world impact of a new therapy based on existi… trial data
  - can provide valuable information to payers without conduct… extensive and time-consuming research.
  - for example, propensity score weighting methods.

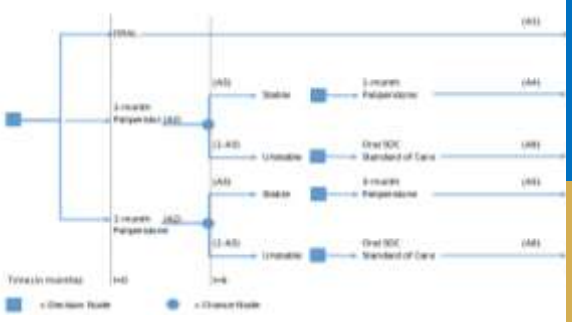


Goal

> To project the impact of using 1-month or 3-month (PP3M) paliperidone-palmitate(PP1M) on psychiatric (PSYCH) and all-cause (AC) hospitalization rates over a period of 18 months in patients with schizophrenia receiving Medicaid and being treated with oral antipsychotic (OA) drugs.

> To base this projection on a decision model, informed by data from three randomized clinical trials.

Decision Model



Treatment strategy #1: Initiating with OA and switching only to OA.

Treatment strategy #2: Initiating PP1M and continuing on PP1M if stabilized at 6 months. Those who discontinued were switched back to receive OAs.

Treatment strategy #3: Initiating PP1M and switching to PP3M if stabilized at 6 months. Those who discontinued were switched back to receive OAs.

Data Sources - 3 different randomized controlled trials

PRIDE was a 15-month prospective, real world, randomized, comparative study of daily OAs (aripiprazole, haloperidol, olanzapine, paliperidone, perphenazine, quetiapine, and risperidone) and PP1M in patients with schizophrenia who had recent criminal justice involvement

Trial 3001 was a 12-month study that compared efficacy and tolerability of PP1M to that of placebo among patients with schizophrenia who had been stabilized (PANSS total score ≤75) on PP1M for 6 months

Trial 3012 compared the efficacy and tolerability of PP3M to that of placebo among patients with schizophrenia who were stabilized on PP1M for 6 months

Data Sources

- The Truven Multi-State Medicaid claims database (2009-2013) provided the real-world data for Medicaid patients treated with oral antipsychotics
  - Inclusion/exclusion criteria from PRIDE were applied to identify OA-treated Medicaid beneficiaries limited to those initiating OA (index) within 90 days of Medicaid enrollment to approximate the PRIDE population.

Inclusions/Exclusion Table

CRITERIA	Exclusions	No. Patients
Total patients enrolled in Medicaid Managed Care from 2009 - 2013		232016
Age between 18 and 60 years as of Jan 1, 2009	50404	181612
Observed to enroll during 2009-2013, i.e. to proxy release from incarceration.	99882	81730
Restrict enrollment date to Jan 2009 to June 2012 so that they could potentially have 18 months of enrollment	12719	69011
Remain enrolled for atleast three months post their first instance of enrollment during 2009 -2013.	839	68172
At least one service with schizophrenia ICD-9 code within 90 days of enrollment	35987	32185
No ICD-9 code for opioid dependence within 90 days of enrollment.	916	31269
Any Antipsychotic RX within 90 days of enrollment	24943	6326
No clozapine within 90 days of index date for oral antipsychotic Rx.	146	6180
No injectable antipsychotics within 90 days of index date for oral antipsychotic Rx.	350	5830
No oral polytherapy on index date and daysupply on monotherapy >= 15 days	1221	4609

Decision Model

PRIDE OA arm projected to & compared to Medicaid OA pop.

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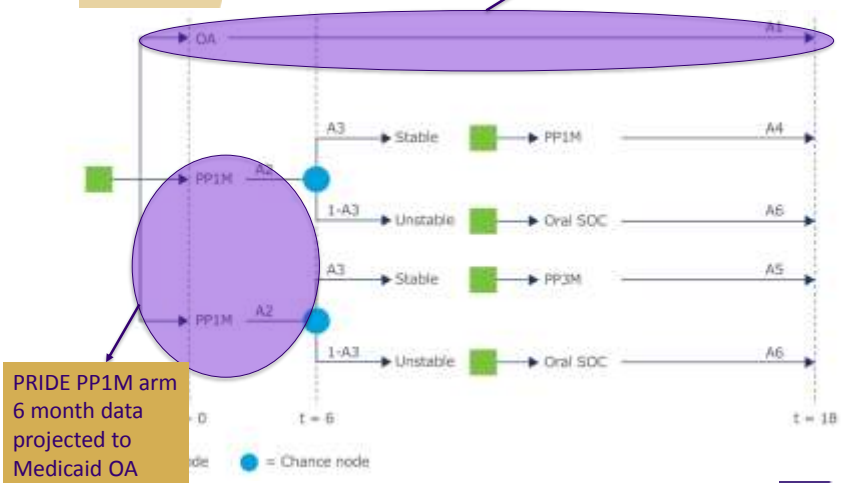
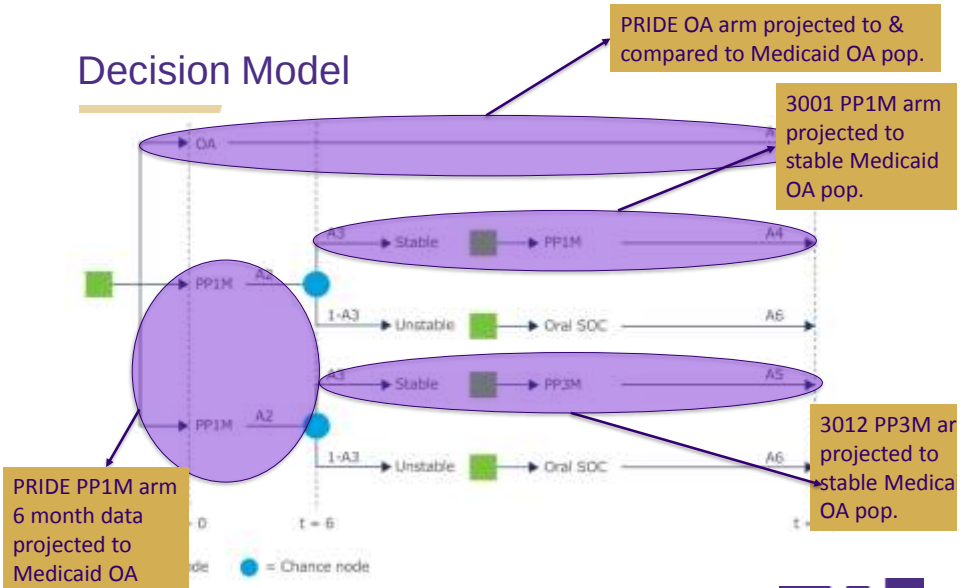


PRIDE PP1M arm 6 month data projected to Medicaid OA pop.

Decision Model

PRIDE OA arm projected to & compared to Medicaid OA pop.

3001 PP1M arm projected to stable Medicaid OA pop.



3012 PP3M ar projected to stable Medica OA pop.

PRIDE PP1M arm 6 month data projected to Medicaid OA pop.

Statistical Steps

Step	Data Source	Covariates used to estimate the propensity score of belonging to Medicaid	Utilizations modelled using IPWs	Utilizations estimated at
1	PRIDE-OA arm+ Medicaid (N=4609)	age, gender, race categories, pre-period time, utilization levels during the pre-period time, distribution of specific oral antipsychotics used at initiation	1) Psych related hosp (PSYCH), 2) All-Cause hospitalization (AC), 3) Prob of OA discontinuation <=6 months of initiation	18 months
2	PRIDE-PP1M arm + Medicaid (N=4609)	age, gender, race categories, pre-period time, utilization levels during the pre-period time		6 months
3	Trial 3001-PP1M arm + Medicaid (N=1814, stable pop)	age, gender, race categories	1) PSYCH 2) AC	12 months post-stabilization of 6 months
4	Trial 3012- PP3M arm+ Medicaid (N=1814, stable)	age, gender, race categories	1) PSYCH 2) AC	12-months post-stabilization of 6 months

Validation exercises

> **Compare projected utilizations of the PRIDE OA arm to the observed utilizations of the Medicaid sample initiating on OAs.**

> **Compare projected utilizations from the PP1M → PP1M arm to the projected 18-month results from the PRIDE PP1M.**

Results

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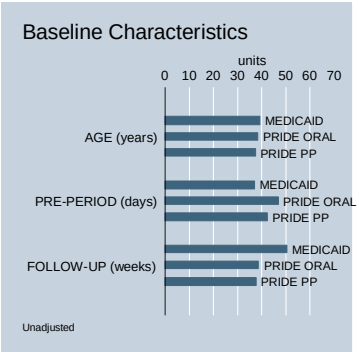
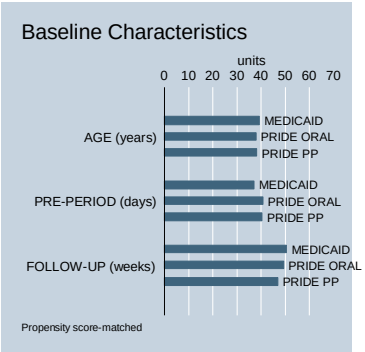
Indexing of PRIDE trial against Medicaid population

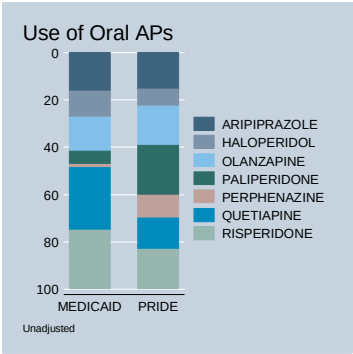


Compared to PRIDE data, Medicaid population looks similar in terms of age, pre and post period duration in this study.

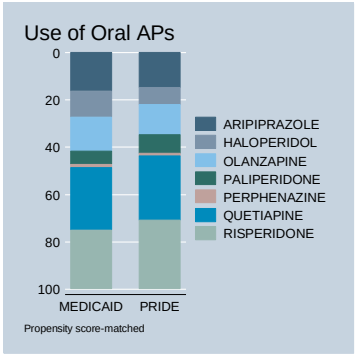


After propensity score matching, age and pre and post period durations balance well across MEDICAID & PRIDE arms.

Indexing of PRIDE trial against Medicaid population



Compared to PRIDE data, Medicaid population lower rates of oral paliperidone and perphenazine, while higher rates of quetiapine at index oral prescription date.



After propensity score matching, oral antipsychotic at index date balance well across MEDICAID & PRIDE arms.

Indexing of Trials 3001 & 3012

	Observed			Projected	
Characteristics	Trial 3001 PP1M N = 160	Trial 3012 PP3M N = 160	Medicaid N = 1,814	Trial 3001 PP1M, N = 160	Trial 3012 PP3M, N = 160
Female, %	47.4	26.0	46.5	46.0	47.6
Age, years	37.3	37.1	41.4	41.9	41.8
White, %	67.5	65.0	57.0	57.3	58.9
Black, %	13.1	15.0	31.0	31.2	28.2
Hispanic, %	8.1%	17.5%	2.0	1.0	2.1

Projected utilizations from PRIDE

Outcomes	PRIDE Trial (observed)[a]			Medicaid (observed)[a]	PRIDE Trials (projected)[b]		
	ORAL N = 212	PP1M N = 219	Diff	ORAL N = 4,609	ORAL N = 212	PP1M N = 219	Diff
Hospitalizations over 18 months							
AC, mean (SE)	0.55	0.37	0.18	0.83 (0.04)[c]	0.59	0.40	0.19
	(0.15)[c]	(0.09)[c]	(0.18)		(0.28)[c]	(0.15)[c]	(0.32)
PSYCH, mean (SE)	0.42	0.22	0.20	0.50 (0.03)[c]	0.50	0.24	0.26
	(0.15)[c]	(0.07)[c]	(0.18)		(0.28)	(0.09)[c]	(0.29)

[a]Adjusted for censoring; [b]Adjusted for censoring and projected to reflect the Medicaid sample; [c]P <0.05; [d]P < 0.10; standard errors obtained via 1,000 bootstrap replicates.

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Projected utilizations from PRIDE (contd.)

Outcomes	PRIDE Trial (observed)[a]			Medicaid (observed)[a]	PRIDE Trials (projected)[b]		
	ORAL N = 212	PP1M N = 219	Diff	ORAL N = 4,609	ORAL N = 212	PP1M N = 219	Diff
Hospitalizations over first 6 months							
AC, mean (SE)	0.42	0.19	0.23	0.64 (0.02)[c]	0.44	0.13	0.31
	(0.13)[c]	(0.05)[c]	(0.15)		(0.17)[c]	(0.04)[c]	(0.17)[d]
PSYCH, mean (SE)	0.37	0.11	0.26	0.38 (0.03)[c]	0.38	0.08	0.30
	(0.13)[c]	(0.04)[c]	(0.14)		(0.16)[c]	(0.04)[c]	(0.16)[d]

[a]Adjusted for censoring; [b]Adjusted for censoring and projected to reflect the Medicaid sample; [c]P <0.05; [d]P < 0.10; standard errors obtained via 1,000 bootstrap replicates.

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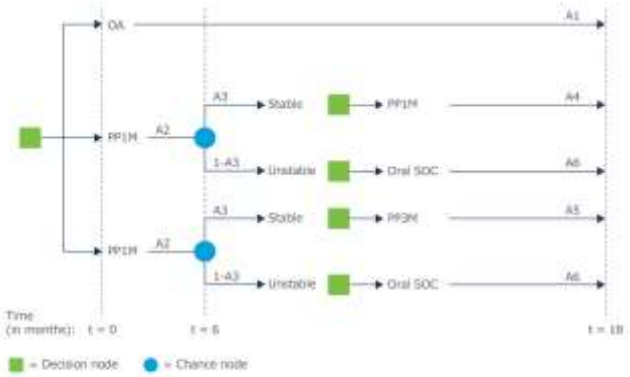
Decision Model



Parameters	Description	Source Data	Estimate Source	Psych	All-cause	Distribution
A1	18-month events with Oral Rx	PRIDE projected on to Medicaid	Table 2	0.50 (0.28)	0.59 (0.28)	Normal
A2	First 6 month events with 1-mo PP	PRIDE projected on to Medicaid	Table 2	0.08(0.04)	0.13 (0.04)	Normal
A3	Pr(Stable at 180 days with 1-mo PP)	PRIDE projected on to Medicaid	Table 2	0.60 (0.04)	0.60 (0.04)	Beta
A4	7 to 18-month events with 1-mo PP among stable	Trial 3001 projected onto Medicaid	Table 4	0.11 (0.05)	0.11 (0.05)	Gamma
A5	7 to 18-month events with 3-mo PP among stable	Trial 3012 projected onto Medicaid	Table 4	0.04 (0.045)	0.05 (0.05)	Gamma
A6	7 to 18-month events with oral Rx among unstable	Observed Medicaid data	Table 2	0.20 (0.03)	0.29 (0.04)	Gamma

Final results from probabilistic simulation model

Outcomes mean (SE)	OA	PP1M → PP1M	PP1M → PP3M	OA – (PP1M→ PP1M)	OA – (PP1M→ PP3M)	(PP1M→ PP1M) (PP1M →PP3M)
Hospitalizations						
AC	0.59 (0.28)	0.31 (0.05)	0.28 (0.05)	0.28 (0.28)	0.31 (0.28)	0.03 (0.07)
PSYCH	0.50 (0.28)	0.23 (0.05)	0.19 (0.05)	0.27 (0.35)	0.31 (0.28)	0.04 (0.07)

Potential monetization of impact (not savings)

- The incremental estimates were used to calculate potential savings for the total Medicaid population of 62 million
- Based on our exclusion inclusion-criteria, the target population size would be 1.23 million ([4609/232016] *62 million)
- Assuming a cost of $10,000 per AC hospitalization, following the PP1M → PP1M strategy for a period of 18-months would eliminate 344,400 AC hospitalizations worth **$3.4 billion**.
- Similarly, following the PP1M → PP3M strategy for a period of 18 months would eliminate 381,300 AC hospitalizations worth **$3.8 billion**.

Limitations and Conclusions

- Inherent reliance on observed and common patient characteristics between the trial and real world data to project outcomes to the real world.
  - Validation exercises are important
- Projecting trial results to a larger and more heterogeneous population also increases uncertainty in the projection estimates.
  - May alter the value of future information/studies

Backup

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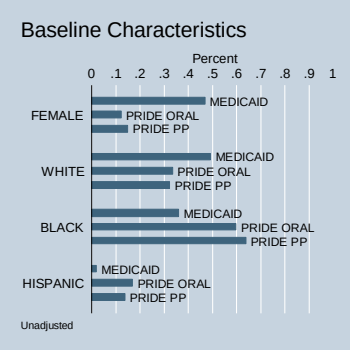
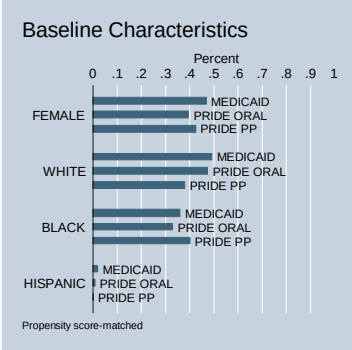
Indexing of PRIDE trial against Medicaid population



Compared to PRIDE data, Medicaid population has higher proportion of females and whites, while lower levels of blacks and Hispanics.



After propensity score matching, demographics balance well across MEDICAID & PRIDE arms.

Statistical Steps (contd.)

- For steps 1-4, modeling of utilizations accounted for censoring within corresponding trial data. Un-projected estimates were compared using IPW and pattern mixture models to deal with censoring and were found to produce similar effects.
- A pattern mixture modeling approach (a simple regression of utilization outcome on time to follow-up, the censoring indicator, and the interaction between the two) was selected used to deal with censoring and projection.
- Expected utilizations were estimated for 18 months (step 1), 6 months (in step 2), and 12 months post-stabilization (steps 3 and 4) of follow-up.
- Standard errors for each projected parameter were estimated based on 1000 bootstrapped replicates on the corresponding analytical sample.
- All analyses were performed using Stata 13.0 software

Probabilistic Simulation Model

- Results from Steps 1-4 were pooled in a fully probabilistic simulation model
- The probabilistic simulation model incorporated all sources of uncertainty in the parameter estimates.

Projected utilizations from PRIDE (contd.)

Outcomes	PRIDE Trial (observed)[a]			Medicaid (observed)[a]	PRIDE Trials (projected)[b]		
	ORAL N = 212	PP1M N = 219	Diff	ORAL N = 4,609	ORAL N = 212	PP1M N = 219	Diff
Probability of continuation ≥180 days	0.47 (0.03)	0.59 (0.03)	–0.12 (0.04)[c]	0.39 (0.01)	0.46 (0.05)[c]	0.60 (0.04)[c]	–0.14 (0.06)[c]

[a]Adjusted for censoring; [b]Adjusted for censoring and projected to reflect the Medicaid sample; [c]$P < 0.05$; [d]$P < 0.10$; standard errors obtained via 1,000 bootstrap replicates.

Projected utilizations from trials 3001 & 3012

	Observed		**Projected**	
Outcomes	Trial 3001 PP1M N = 160	Trial 3012 PP3M N = 160	Trial 3001 PP3M N = 160	Trial 3012 PP3M N = 160
Hospitalizations per 12 months				
AC, mean (SE)	0.10 (0.03)	0.05 (0.04)	0.11 (0.05)	0.05 (0.05)
PSYCH, mean (SE)	0.08 (0.02)	0.01 (0.01)	0.11 (0.05)	0.04 (0.045)

Standard errors obtained via 1,000 bootstrap replicates.