DRIVERS OF EFFECTIVENESS FOR INFORMED OUTCOMES-BASED AGREEMENTS

Educational Symposium

Cigna

CHIMERIX
Today’s Focus

The future of performance-based, or outcomes-based contracts, and the role of Drivers of effectiveness in their planning and execution
Speakers

Christopher Bradbury
Senior Vice-President, Integrated Clinical Solutions & Specialty Pharmacy
Cigna Pharmacy Management

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Vice President, Market Access
Chimerix Inc.,

Helene Karcher
Managing Vice-President, Global Head, Real World Modeling
LASER Analytica

Roman Casciano
Executive Vice-President and Head, Value and Access
LASER Analytica
All Headaches Instantly Cured or Money Refunded.

LEGAL GUARANTEE.

6D. EMERSON'S BROMO-SELTZER, the most successful American Remedy, is an effervescent Powder, taken in water. If three doses do not Cure any Headache, no matter how caused, send the Bottle to us, saying where obtained, AND WE WILL AT ONCE REFUND THE PRICE. TRIAL BOTTLE, post free, 6d. Larger Sizes 1s. and 2s. Sold by many Chemists or obtained to order by almost all.

EMERSON DRUG CO., LTD., 46, HOLBORN VIADUCT, LONDON, E.C.

Insist on Full Name—EMERSON'S BROMO-SELTZER

Proscar (1994)
Clozaril (1995)
Zocor (1998)
Diovan (2004)

BMJ. 2005 May 28; 330(7502): 1262–1264
First Major US Deals

CIGNA Signs Outcomes-Based Contract That May Be First Deal for Specialty Drug

April 2011  Volume 8  Issue 4

From Specialty Pharmacy News

Drug Deals Tie Prices to How Well Patients Do

By ANDREW POLLACK  APRIL 22, 2009

Think of it as product guarantees by the drug industry. Pressed by insurance companies, some drug makers are beginning to adjust what they charge for their drugs, based on how well the medicines improve patients’ health.

“We’re going to see a growth in outcomes guarantees for pharmaceuticals, and it’s very healthy,”
But the practicalities of risk sharing to alleviate the cost burden of paying for new innovations raise some difficult questions.
A risk-sharing scheme to supply multiple sclerosis (MS) medicines to patients has been a 'costly failure', experts have said. The NHS could have saved £250 million if the scheme had been properly assessed after two years they said, adding that the money could have been better spent on other treatments.

**Costly failure of a risk sharing scheme**

The NHS is paying for thousands of patients with multiple sclerosis to receive drugs that monitoring data suggest are not effective. James Raftery examines what went wrong with the access scheme that facilitated their use.
But 2015-16 in US saw a number of new deals

2008-2014:
- Actonel (Sanofi, P&G-Health alliance, 2009)
- Januvia/Janumet (Merck-Cigna, 2009)
- Rebif (EMD Serono-Cigna 2011)

2015 - Today:
- Harvoni/Sovaldi (Gilead-Cigna – Feb 2015)
- Harvoni/Sovaldi (Gilead- Catamaran – Feb 2015)
- Entresto (Novartis-Cigna, Feb 2016)
- Entresto (Novartis-Aetna, Feb 2016)
- Repatha, Praluent (Amgen-Cigna, May 2016)
Value-based Purchasing Tools, including:

“Risk-sharing agreements based on outcomes to link price adjustments for a drug or drugs to clearly defined patient health outcome goals.”
Recent eMax Health Survey

Question: What is the likelihood you will implement an outcomes-based contract over the following time periods?

Very Unlikely | $ | Very Likely
---|---|---

Six Months

One Year

Two Years

Three Years

Payers more strongly than manufacturers that they would implement outcomes-based contracts in the near future.

More than 70% of payers cited a future where “exclusive” contracts were very likely or a certainty.
Recent eMax Health Survey

IMPLEMENTATION BARRIERS
Question: What single barrier is most challenging to successful implementation of an outcomes-based contract?

n=29

- Technical difficulty: 45%
- Resistance to financial risk: 17%
- Corporate structure: 14%
- Lack of perceived value: 10%
- Lack of corporate inertia: 10%
- Other: 4%

The sheer difficulty with the technical aspects of contract implementation ranks as the most challenging barrier to outcomes-based contract implementation.
Health Plan and PBM Perspectives

Christopher Bradbury
Senior Vice-President, Integrated Clinical Solutions & Specialty Pharmacy
Cigna Pharmacy Management

Cigna leadership on OBC’s:

• Januvia/Janumet (Merck-Cigna, 2009)
• Rebif (EMD Serono-Cigna 2011)
• Harvoni/Sovaldi (Gilead-Cigna – Feb 2015)
• Entresto (Novartis-Cigna, Feb 2016)
• Repatha, Praluent (Amgen-Cigna, May 2016)
Industry Perspectives

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Vice President, Market Access
Chimerix Inc.,
Planning and Prediction

Helene Karcher
Managing Vice-President,
Global Head,
Real World Modeling
LASER Analytica
Planning & Predicting Outcomes for Performance-Based Contracts

Hélène Karcher, PhD

ISPOR Washington DC
The tools to get the outcomes right

1. Predicting real-life outcomes

2. Planning: optimizing evidence generation and choice of outcomes
Predicting real-life outcomes
Principle: Use and integrate all relevant data to predict real-world outcomes

- Integrate heterogeneous data via a predictive model
  - Data that are different in nature (e.g., clinical endpoint vs. QoL), in time horizon, in source type (naturalistic, RCT, country-specific, etc.) are considered together
  - Predict effectiveness and quantify uncertainties in RW evidence

- Collect country-specific missing data more optimally
  - Optimal design of pragmatic trials

All relevant data is used, and only minimum necessary amount of additional data is collected.
Step 1: identify your real-word setting

New Real-World Scenario

Please enter a drug name for your product

Drug A

Would you like to evaluate Drug A’s effectiveness alone, or relative to other drug products? (you will need to answer questions about these products too)

- Evaluate effectiveness of your product relative to clinical study comparator
- Evaluate effectiveness of your product relative to real world comparator

Now describe in a few words of the real-world setting in which you wish to learn about relative effectiveness of your product. Just the country can be enough, you can add 'covered under a specific medical insurance', or a specific subpopulation.
Step 1: identify your real-word setting

- Real-Life Comparator
- Population characteristics

Please enter a drug name for your product

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Now describe in a few words of the real-world setting in which you wish to learn about relative effectiveness of your product. Just the country can be enough, you can add ‘covered under a specific medical insurance’, or a specific subpopulation.
Step 2: Use efficacy as measured in clinical trials (patient-level preferable)

- Efficacy
- Clinical trials demographics
Step 3: identity drivers of effectiveness among a few factors

- Drug use factors
  - Patterns of use, dose, treatment duration.
  - Past history of exposure
  - Co-prescriptions

- Health system care delivery factors
  - Coverage
  - Medical Practices
  - Screening policies

- Patient population factors
  - Age, gender, behaviors
  - Co-morbidities
  - Disease stage/severity
  - Other baseline risk factors and genetics relevant to the disease/drug

> Distributions of factors vary between Real-World settings

> Good news: (1) few factors to consider
  (2) interacting effects are universal!
Step 3: identify drivers of effectiveness within drug use factors & patient population characteristics

Drug use factors

Is there a reason to believe patients will be more or less drug use of Drug A in real life than in clinical trials?

- Yes
- No

Is there a reason to believe patients will be more or less drug use of Drug B in real life than in clinical trials?

- Yes
- No

Patient population

How do you expect the real world patient population to differ from the clinical trial population for Drug A?

- Age
Step 4: Build interaction model and apply it to your real-world setting
Results: real-life outcome predictions & impact of each factor (drug use & population factors)

Testing several assumptions helps identify the most acceptable scenarios and outcomes for the Performance Plan.
The tools to get the outcomes right

1. Predicting outcomes

2. Planning: optimizing evidence generation and choice of outcomes
   - Choice of outcomes
   - Evidence generation on the outcome
Choice of outcome for performance-based contracts

Not all characteristics of a “perfect” outcomes are necessary for success:

> Specific to the indication & the drug product
> Sensitive
> Not a proxy of the clinically-relevant outcome
> Measurable in the near-term
> Low inter- & intra-patient variability
> Already routinely measured
Choice of outcome for performance-based contracts: why favor specificity

> Favor specificity (e.g., outcome captures only responders) over sensitivity (e.g., large patient numbers)

- Hospitalizations due to particular type of event
- Ambulation (6-min walk)
- All hospitalizations
- Disability
How to increase accuracy of real-life outcome predictions?
Two ways to improve accuracy of real-life outcome predictions early in clinical development

1. More pragmatic design, i.e., any aspect of study design (population, type of randomization, blinding, monitoring, etc.)

2. Better “analyses tools”, i.e., any aspect of data analyses (statistical or model-based analyses, predictive models, etc.)
Systematic review of methods to incorporate pragmatism pre-authorization: results*

1. Many (39) methodological papers were identified that recommend how to relax trial features to make them more pragmatic, and to adapt analyses.

2. However, this does not translate into many actual Phase 2-3 trials with pragmatic elements – due to scientific and operational hurdles.
   - Systematic review only identified 18 pre-authorization trials with pragmatic elements.
   - Typically only 1-2 selected features are pragmatic.
     - Features required to conduct the trial for authorization.
     - Features that could demonstrate a benefit not present in an RCT setting.

Hurdles to incorporating effectiveness before authorization* (review of 39 articles)

1. Known and unknown confounders in real-world trials may lead to inconclusive effect sizes\(^ {18,25}\)
2. Extensive cost of running such trials due to larger sample size required\(^ {14}\)
3. Operational difficulties in recruiting certain populations, and in minimising measurements/study visits\(^ {30,31}\)
4. Uncertainty in reactions from regulatory bodies\(^ {30,32}\)

Case study 1: Test relaxing eligibility criteria in pre-authorization trials in schizophrenia*

* Karcher, Fu, Efthimiou, Schneeweiss, Nordon, Abenhaim. A practical guide to adding patient heterogeneity into Phase III trials: Results from IMI GetReal WP2. ISPOR Nov 2015.
Real-world study to test eligibility criteria in schizophrenia

1. Extract patient characteristics and interplay between factors and outcome in a real-life schizophrenia population (SOHO cohort)

2. Identify the subpopulation eligible for a typical pre-authorization trial: “reference RCT population”

3. Re-include in this “reference RCT population” a minimal subset of patients who would usually be excluded (=broaden the eligibility criteria)
   - Method of quotas (stratification) for patient inclusion in trials
   - Combined with predictive modeling to evaluate the outcome in the RW population

4. Measure how “efficient” each re-inclusion is

* “Reverse” of the method used in Schneeweiss et al. Increasing Levels of Restriction in Pharmacoepidemiologic Database Studies of Elderly and Comparison With Randomized Trial Results. Med Care. 2007
Identify a reference RCT population within SOHO (observational data source) and predict outcomes

* Leuchet et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. Lancet. 2013
Enriching RCTs to improve predictions

"enriched" RCTs

- efficacy
  - (some RCT patients)

Variability in patient characteristics

+5% excluded patients

Real-life effect
- (full SOHO dataset)

Predict and compare with
- age > 65
- chronicity between 1 and 3
- alcohol abuse
- ...

SOHO dataset
Size of real-world subpopulations that can be re-included in trials differs with each criterion

Patients eligible to enroll into an “enriched” RCT with 1 relaxed criterion (as % of reference RCT population, patients under drug R)

- Disease duration 1-3 years: 19.6%
- 1 past suicide attempt: 18.9%
- Private practice: 15.7%
- Age > 65 years: 7.6%
- Alcohol abuse: 6.9%
- Drug abuse: 6.4%
- BMI < 17 or > 40: 1.7%

Opening the trial to patients with a shorter disease duration enable to tap into a wider patient pool than opening it to patients with alcohol or drug abuse. Assuming all patients are equally difficult to recruit, opening the trial to patients with e.g., a shorter disease duration, enables faster recruitment.
Outcomes for re-included real-world subpopulations slightly differ from the reference RCT population.

ΔCGI-S at 3 months in re-included patients under drug R

As expected, certain subpopulations have a trend to benefit more from treatment. Their re-inclusion is a priori beneficial to trial success.
Prediction accuracy from 4 different RCTs enriched in patients with different characteristics

Prediction accuracy

Target RCT size = 1127

# patients from either of 4 subpopulations

- chronicity between 1 and 3 years
- private practice
- 1 past suicide attempt
- age older than 65 years
The probability of Success of a parallel RCT increases with enrichment in RW subpopulations

Method:
- Simulate a parallel RCT with 250 patients in each arm (drug A vs B)
- Random sampling within (enriched) RCT populations under drug R or AE
- Propensity score matching
- Simulate 1000 trials
Case study 2: Test relaxing eligibility criteria in pre-authorization trials in asthma
Optimizing study populations in clinical development

*Enriched RCT approach – case study in asthma*

> Which patients are typically excluded from clinical trials?
> Impact of re-inclusion of these patients on trial recruitment and outcomes?

Create a Source RW Population from MarketScan®:
- US claims database with ~10M asthma patients Jan 2009-> present

**Review eligibility criteria:**

- **Core:** Criteria which define target patient population
- **Mandatory:** Criteria which minimize patient risk, ethical concerns, etc...
- **May be relaxed:** Eligibility criteria which minimize “technical” risk in clinical trial design

**Identify RCT Populations**
Characterize the patients eligible for RCTs

**Enriched RCT Populations**
Systematically relax these criteria one (or two) at a time and add them back to the RCT population

**Compare Outcomes**
Expandability of the population pool eligible for Phase 3 trials per criterion (prevalence)

<table>
<thead>
<tr>
<th>Subpopulation with a broadened eligibility criterion</th>
<th>Expandability and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD and &gt;50 years</td>
<td>2%</td>
</tr>
<tr>
<td>COPD and ≤50 years</td>
<td>4%</td>
</tr>
<tr>
<td>Stable malignant neoplasms</td>
<td>6%</td>
</tr>
<tr>
<td>Chronic OCS use</td>
<td>7%</td>
</tr>
<tr>
<td>Smokers or former smokers</td>
<td>8%</td>
</tr>
<tr>
<td>Type I and uncontrolled type II diabetes</td>
<td>22%</td>
</tr>
<tr>
<td>Age &gt; 75 years</td>
<td>0%</td>
</tr>
</tbody>
</table>

Expandability:

\[
\text{Number of patients re-included into Phase 3 eligible population} \div \text{Number of Phase 3 eligible population}
\]
### Efficacy and Safety differences in Phase 3 vs re-included real-world populations?

<table>
<thead>
<tr>
<th>Subpopulation with a broadened eligibility criterion</th>
<th>Reduction of exacerbation # (mean, 95% CI) in subpopulation</th>
<th>Relative Risk (mean, 95% CI) in # patients with MACE Subpopulation/population</th>
</tr>
</thead>
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<tr>
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**Blinded results**

Rational decision to relax eligibility criteria based on
1. Expandability of eligible population (prevalence) – linked to recruitment speed
2. Efficacy and safety in the re-included populations

MACE: Major Adverse Cardiac Event
Conclusion

- 4 steps to predicting real-world outcomes using drivers of effectiveness

- Carefully examine eligibility criteria from pre-authorization trials to improve predictions:
  • Can increase both probability of trial success & recruitment speed, – if done by rationally relaxing a few, selected eligibility criteria
Design and Measurement

Roman Casciano
Executive Vice-President and Head, Value and Access
LASER Analytica
Measuring Performance

> What is the best design to measure what we hope to measure?
> How do we interpret what we are seeing in the data?
> What are the necessary caveats and conditions for a win-win agreement?
Measurement – Likely Rationale for Contracts

> To measure performance which is not commonly or not well measured in a trial setting, for example:
  • Adherence and its impact on outcomes
  • Healthcare resource use
  • Hospitalizations
  • Long-term outcomes

> To translate observed findings from RCTs into the real world setting, for example:
  • Differences in real world population
  • Differences in usage patterns/strategies
## Measurement – Options for Study Designs

<table>
<thead>
<tr>
<th>Design/Approach</th>
<th>Challenges</th>
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<tr>
<td>Patient-level Tx response/success</td>
<td>Performance not comparative, disease progress, other Tx changes</td>
</tr>
<tr>
<td>Population-level Impact (pre-post)</td>
<td>Information gaps, changing practices</td>
</tr>
<tr>
<td>Classic Tx vs Control</td>
<td>Inter-group differences</td>
</tr>
<tr>
<td>Ecological Design (world with vs world w/o)</td>
<td>Inter-group differences, practicality, feasibility</td>
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</table>
## Measurement – Possible Designs

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<th>Design/Approach</th>
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<td>Medicare Proposed alternative add-on payment model</td>
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Effectiveness and cost-effectiveness of interferon beta and glatiramer acetate in the UK Multiple Sclerosis Risk Sharing Scheme at 6 years: a clinical cohort study with natural history comparator

Jacqueline Palace, Martin Duddy, Thomas Bregenzer, Michael Lawton, Feng Zhu, Mike Boggild, Benjamin Piske, Neil P Robertson, Joel Oger, Helen Tremlett, Kate Tilling, Yoav Ben-Shlomo, Charles Dobson

“Interpretation: Findings from this large observational study of treatment with interferon beta or glatiramer acetate provide evidence that their effects on disability in patients with relapsing-remitting multiple sclerosis are maintained and cost effective over 6 years. Similar modelling approaches could be applied to other chronic diseases for which long-term controlled trials are not feasible.”

Lancet Neurol 2015; 14: 497–505
The UK MS RSS: So what was all the fuss?

“In absolute terms the EDSS score was 0.10 unit worse than the control data and 0.28 units worse than predicted on the assumption that the disease modifying treatments delay progression of the disease.”

Mike Boggild et al. BMJ 2009;339:bmj.b4677
The UK MS RSS: So what actually was going on?

Mike Boggild et al. BMJ 2009;339:bmj.b4677
The UK MS RSS: Updated Historical Control and Model

(a) mean EDSS

continuous Markov model with one covariate ‘age at onset’
The UK MS RSS: Updated Historical Control and Model
The UK MS RSS: Lessons

> Pre- Post designs can work well, but the choice of control is critical

> Never try to “re-do” your clinical trials

> “figuring it out” along the way often doesn’t go over very well!

> But finally – with proper modeling framework and application of drivers of effectiveness (in this case age), we can do a very good job of prediction in advance
## Measurement – Possible Designs

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Novartis AG’s plan to link the payment for a new heart-failure treatment to the medicine’s performance is meeting skepticism from the largest manager of drug insurance benefits in the U.S.

The problem is that performance-linked prices are difficult to manage because so many things can affect a patient’s outcome, said Steven Miller, chief medical officer of Express Scripts Holding Co., which helps companies and insurance plans manage their prescription benefits.

“If patients on this new drug go out and have a salty pizza and end up in the emergency room, is that the drug’s fault or the patient’s fault?”
Measurement – Drivers of Effectiveness Types

> Factors which influence the base risk (eg. age)

> Factors which influence the relative risk (eg. biomarkers)

> Factors which influence both, two types
  • Base risk predictor and positive effect modifier (eg. non-adherence)
  • Base risk predictor and negative effect modifier (eg. disease severity)
Measurement – Interpretation

What are the possible explanations for the differences we are observing between the clinical trials and real world data?
Increased prevalence of hard to treat patient groups (i.e., negative effect modifiers) in the real world can reduce apparent effectiveness.
However, increased prevalence of a positive effect modifier in the real world can improve real-world effectiveness.

<table>
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Relative Risk 0.88
NNT 52.6

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Relative Risk 0.81
NNT 27.0

RR for non-adh pts 0.67
RR for adherent pts 0.93
Channeling Bias

Channeling can be caused by a number of different circumstances:

> “newness” of treatment (treatment of non-responders or sub-optimal responders to available meds)

> Perceived better effect of treatment in a certain population (optimization of use)

> Perceived higher need of a population (severe population phenomenon)
Channeling of patients to the newer treatment (for example due to perceived higher need) can appear as lack of effectiveness.

**Trial**

- **Treatment**: 18.0%
- **Control**: 27.5%

**Database**

- **Treatment**: 25.5%
- **Control**: 27.5%

**Relative Risk**

- **Trial**: 0.65
- **Database**: 0.93

**NNT**

- **Trial**: 10.5
- **Database**: 50.0

**RR for severe pts**: 0.90
**RR for mild-mod**: 0.60
Measurement – Interpretation

Even a positive effect modifier can create the appearance of lower real world effectiveness in the presence of channeling if the factor (e.g., non-adherence) also predicts higher risk.

Physicians may “channel” no-adherent patients to a depot injection for example, creating the false appearance of lower effectiveness.

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<tr>
<td>Trial</td>
<td>14.6%</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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Relative Risk 0.88

Relative Risk 0.96
Does long-acting injectable risperidone make a difference to the real-life treatment of schizophrenia? Results of the Cohort for the General study of Schizophrenia (CGS)

Lamia Grimaldi-Bensouda a, Frederic Rouillon b, Bernard Astruc c, Michel Rossignol d, Jacques Benichou e, Bruno Falissard f, Frederic Limosin g, Beatrice Beaufils h, Guillaume Vaiva i, Helene Verdoux j, Yola Moride k, Alban Fabre l, Florence Thibaut m, Lucien Abenhaim n,*
and for the CGS Study Group 1

<table>
<thead>
<tr>
<th>ARR† [95% CI]</th>
<th>All</th>
<th>Monotherapy alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>0.66† [0.46; 0.96]</td>
<td>0.50 [0.31; 0.82]</td>
</tr>
<tr>
<td>Principal analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R-LAI use vs. R-LAI non-use</td>
<td>0.53 [0.46; 0.80]</td>
<td>0.49 [0.28; 0.85]</td>
</tr>
<tr>
<td>Secondary analyses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of R-LAI vs. use of oral antipsychotic alone</td>
<td>0.66 [0.44; 1.01]</td>
<td>0.49 [0.28; 0.85]</td>
</tr>
<tr>
<td>R-LAI use vs. use of 1st generation antipsychotic alone</td>
<td>0.58 [0.36; 0.94]</td>
<td>0.41 [0.23; 0.75]</td>
</tr>
<tr>
<td>R-LAI use vs. use of oral 2nd generation antipsychotic</td>
<td>0.50 [0.39; 0.92]</td>
<td>0.51 [0.29; 0.91]</td>
</tr>
<tr>
<td>Sensitivity analyses (matched samples)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R-LAI use vs. R-LAI non-use</td>
<td>0.61 [0.40; 0.94]</td>
<td>0.48 [0.27; 0.86]</td>
</tr>
<tr>
<td>Sensitivity analyses (including indefinite time$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R-LAI use vs. R-LAI non-use</td>
<td>0.71 [0.51; 1.0]</td>
<td>0.52 [0.34; 0.81]</td>
</tr>
</tbody>
</table>

Abbreviations: ARR, Adjusted Rate Ratios; CI, Confidence interval; LAI, long-acting injectable.
† Adjusted for age, gender, type of schizophrenia, educational level, living arrangements, work, guardianship, indicators of global functioning (CGI), suicidality through a propensity scores and for hospitalisation in the previous 12 months, ambulatory status at entry, switching of drugs in the previous trimester and, in the left-hand column, polytherapy (vs. monotherapy).
‡ Primary analysis.
§ Definite exposure counted during one extra month when the drug was switched during the following trimester.
Objective

To assess the effectiveness of a newly marketed drug relative to other drugs for the same psychiatric indication, in routine clinical practice using available electronic health records
Effect of New Drug vs. Old Drugs on Psychiatric Hospitalizations

Adjusted for age, sex, time since first diagnosis, education, number of past-year hospitalizations, number of past-year suicide attempts, number of past year switches, presence of past-year polytherapy, and past-year cumulative hospitalization duration.
Potential for channeling

> New drug belonged to a different drug class
  • Better side effect profile, especially in the long-term

> New drug was packaged in an adherence-optimizing formulation and thus more likely to be differentially dispensed to:
  • Non-adherent patients

> RCTs demonstrated increased efficacy and tolerability of new drug compared to existing alternatives, and thus likely to be dispensed to:
  • Patients not well-managed using existing alternatives
Assessing Comparability of Patient Populations

Perfect Discrimination, c-statistic = 1.0

Treated with Drug B

Treated with Drug A

Predicted Probability of Receiving Drug A

Moderate Discrimination, c-statistic = 0.75

Poor Discrimination, c-statistic = 0.5
Propensity Score Distribution: New Drug (red) vs. Old Drugs (blue)

1 year after market entry
c-statistic: 0.76

2 years after market entry
c-statistic: 0.71

3 years after market entry
c-statistic: 0.67

4 years after market entry
c-statistic: 0.65
Predictors of Receipt of New Drug vs. Other Drugs

- 1-30 days hospitalized in the past year vs. no days
- >30 days spent hospitalized in the past year vs. no days

Odds Ratio

Year 1 | Year 2 | Year 3 | Year 4
--- | --- | --- | ---
2.3 | 1.9 | 1.6 | 1.4

Year 1 | Year 2 | Year 3 | Year 4
--- | --- | --- | ---
2.5 | 2.0 | 1.7 | 1.4
Effect of New Drug vs. Old Drugs on Psychiatric Hospitalizations

Adjusted for age, sex, time since first diagnosis, education, number of past-year hospitalizations, number of past-year suicide attempts, number of past year switches, presence of past-year polytherapy, and past-year cumulative hospitalization duration.
Effect of New Drug vs. Old Drugs on Psychiatric Hospitalizations

Adjusted for age, sex, time since first diagnosis, education, number of past-year hospitalizations, number of past-year suicide attempts, number of past year switches, presence of past-year polytherapy, and past-year cumulative hospitalization duration.
Conclusions

Channeling evident in uptake of the product

- Stratification and propensity score analysis useful in detecting channeling

- Evolution of unadjusted AND adjusted comparative estimates suggests both measured and unmeasured confounding

- Additional information or an alternative analytic design may be necessary to adequately address confounding due to channeling
Implications RE OBC’s

> Dynamics of treatment patterns, switching behaviors, pent up demand for new Tx in the specific setting should be known and understood (historical analogs, market research)

> Need to determine critical variables necessary to explain results (ie what might be my confounders/caveats)

> Lack of adequate information should not compel the use of poor metrics – point of care collection of data is improving and is possible

> Sufficient time post market entry should be allowed for “stabilization” of use
“Make everything as simple as possible, but not simpler.”
—Albert Einstein