

Health economics and outcomes research: What can be done differently in registration trials and in post-approval trials?

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Outline

- Define some terms
 - Cost effectiveness, cost, and benefit in health care
 - Registration versus pragmatic trials
- What information payers need, and why
 - Value based contracting
 - Pragmatic trials
- Why pharma's response to payer information needs has been so anemic.
- Suggestions on moving forward

Incremental Cost-Effectiveness Ratio (ICER)

$$\frac{\text{Cost}_B - \text{Cost}_A}{\text{Effectiveness}_B - \text{Effectiveness}_A}$$

Measuring cost

- **Direct medical costs** – costs expended for medical care services
 - Physician fees, hospitalization, outpatient services, pharmaceuticals, home nursing care, etc.
- **Indirect costs** – other costs related to care seeking, or a consequence of the immediate disease
 - Transportation to clinics, cost to non-professional caregivers, productivity loss for patient or family, etc.
- **Societal costs** – non-health consequences of the intervention
 - Incremental social services, criminal justice, increased future earnings, etc.

“Costs” must be considered from a perspective. A “cost” has very different meaning if you are a provider, insurer, patient, or community

Measuring benefit: Quality-adjusted life years (QALYs)

- Weighing the years of life remaining as a result of a successful intervention by the quality of life to be enjoyed during those years
- Utility weights are on a scale of 0 to 1, with “0” representing death, and “1” representing perfect health
- The incremental cost-effectiveness ratio (ICER) is used to assess the cost-effectiveness of the health program being evaluated
- The cost/QALY is widely used to make coverage decisions in Canada, the UK and Europe, allowing greater transparency to decision making

Under the ACA, QALYs (or ICERs based on QALYs) are not permitted to be used to make coverage decisions in federal programs

However, few US payers have used QALYs in their decision-making, even before the ACA rejection. Thus, clinical measures or PROs are typically used, reducing the transparency of the basis of the coverage decision

Defining our trials



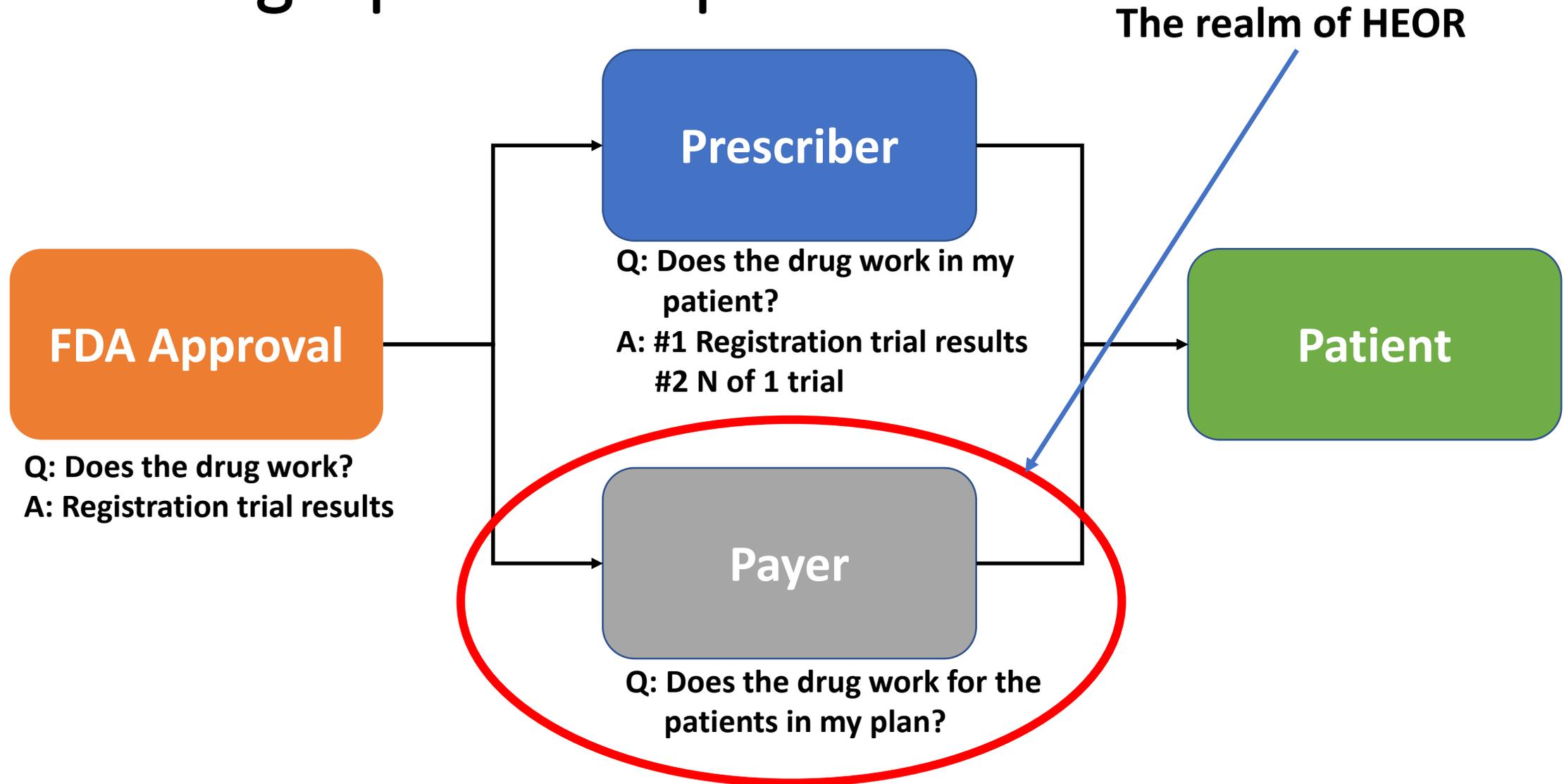
Fully registration

- Ideal responders
- Ideal comparisons
- Outcome defined to maximize response
- Strictly defined intervention
- Treatment protocol enforced
- Expert site investigators
- Patient adherence is enforced
- Aggressive participant follow-up
- Exclusions allowed in analyses

Fully pragmatic

- Treated reflects target population
- Standard of practice comparison
- Outcome relevant to patient or payer
- Intervention treatment as practiced
- Treatments measured but not enforced
- Investigators reflect skill of expected prescribers
- Patient adherence is measured but not enforced
- Aggressive participant follow-up
- No exclusions

Getting a pill to the patient...



What information are payers looking for?

- A payer is responsible for managing the health services cost for a population of beneficiaries, not individual patients or diseases
- Payers seek information on the impact of an intervention on health care utilization and pharmacy spending for the people in their health plan
- Uncertainty and miscalculations can be disastrous for a plan
- “Meaningful” timeframes for a payer are 18 month or less

Direct costs are typically the only costs that enter into payer decision making on coverage and pricing

Value-based contracting

- “Reimbursement only for the value created by avoiding other healthcare treatments, by reaching a certain level of improvement in patient condition, or for cures”
- Shifts risk from the payer to the manufacturer
- The data processing and analysis required to support these contracts in exceptionally complex
- As of early 2018, approximately 25 contracts in place in the U.S.¹

“They are short lived. For me, these contracts are a bridge. Initially, there is enough uncertainty and you are accounting for risk”²

1. From <https://pharmaceuticalcommerce.com/brand-marketing-communications/getting-at-the-value-of-value-based-drug-pricing-models/> accessed 2/19/2019

2. Lundbeck Health Economic Council Advisory Session, September 2018

The value of the pragmatic trial for a payer

Provides evidence for how the drug will work in:

...patients like those in their plan

...following their treatment protocols like patients in their plan

...compared to the current standard of practice

...treated by clinicians like those treating their patients

...with the results from the trial representing treating patients in their plan

...and the results in a metric (i.e., direct costs) that are important to the plan managers

As a rule of thumb, including a prior authorization in a plan will decrease drug utilization by 15% due to the complexity it creates for a prescriber

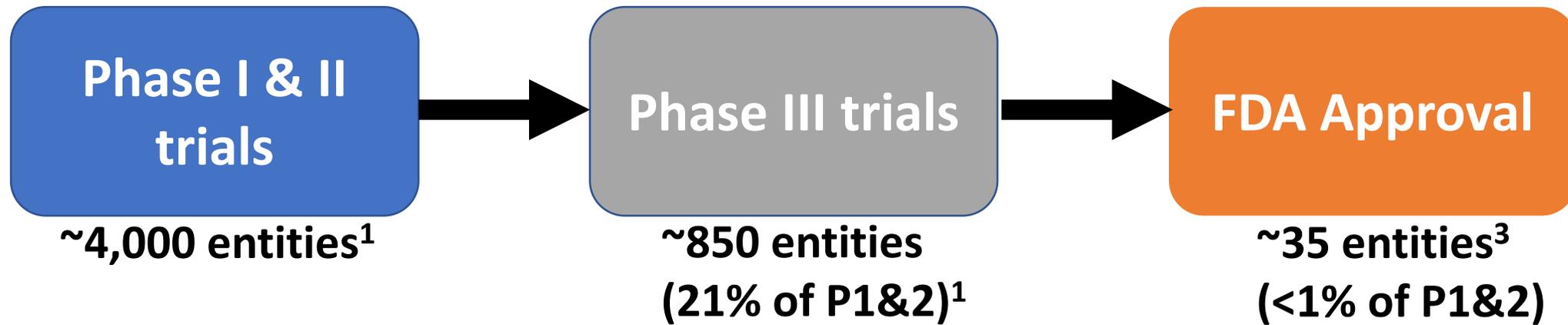
PRIDE: a pragmatic trial

- Compared LAI version of paliperidone palmitate to oral antipsychotics
- Inclusion criteria included a requirement that participants have had been in custody at least twice before enrollment
 - Selectively recruited from homeless shelters and among the homeless
 - Required a reliable contact for follow-up
- Randomized to one of seven medications, but could opt out to up to six proactively
- Outcomes: arrest, hospitalization, treatment augmentation due to efficacy, change due to tolerability or safety, imminent relapse or suicide
 - CGI and PSP were secondary endpoints

PRIDE Results

- Patients on LAI were less likely to have treatment failure
 - 39.8% for LAI versus 53.7% for oral treatment
- Patients on LAI were less likely to spend time in jail or be hospitalized
 - 21.2% versus 29.4%
 - This was the only outcome that was significant
- Non-significant differences in hospitalization, tolerability and failure due to efficacy
- Neither secondary measure (CGI or PSP) was significant
- Injections for LAI and doses dispensed for oral, were comparable.

Financial risk of drug development...



The total cost of Phase III trials in 2011 was over \$89 billion (over \$100 million per entity) or \$2.6 billion per entity approved^{1,2}

1. Mignani et al Why and how have drug discovery strategies in pharma changed? What are the new mindsets? Drug Discovery Today Volume 21, Number 2 February 2016 2. from <https://www.ifpma.org/wp-content/uploads/2016/02/IFPMA-2015-Pharma-by-Numbers.pdf> accessed 1/31/2019 3. from <https://uk.reuters.com/article/us-pharmaceuticals-approvals/new-drug-approvals-fall-to-six-year-low-in-2016-idUKKBN14M08R> accessed 1/31/2019)

A path forward?

- There is an advantage to payer, providers and patients if the results of well designed and conducted pragmatic trials can be available
- It is in the manufacturer's interest to provide stakeholders the most generalizable data available, as early in the product life cycle as is possible.
- This is in conflict with the risk of introducing new data during the pre-approval process which might endanger the regulatory pathway
- Explicit direction from regulators better defining the role of pragmatic trial results in the approval process may encourage greater risk taking for manufacturers