Real-World Evidence?
Then Disrupt The Outdated Regulatory Infrastructure

ANIRBAN BASU
basua@uw.edu
@basucally

NISS-Merck Meet-Up on Real World Data
October 4, 2018

THE CHOICE INSTITUTE
School of Pharmacy

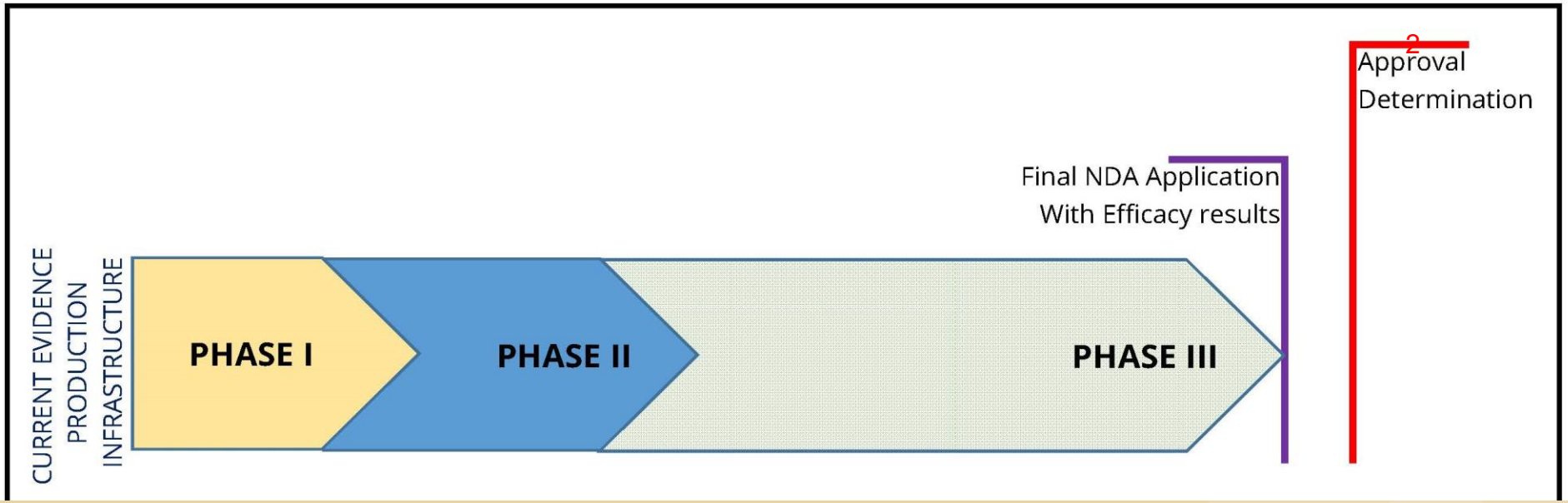
Challenges in decision-making

Questions

> How should manufacturer price their drug at launch?
> Should health plans put a drug on their formularies? Which tier?
> Which drug would a patient most benefit from?

Challenges in answering these question

> How can we produce evidence to answer all of these questions in timely fashion?
> How can we maintain quality of evidence?
> How can we achieve equity in the timely access to innovative medicine


2
Approval
Determination
Final NDA Application
With Efficacy results
CURRENT EVIDENCE
PRODUCTION
INFRASTRUCTURE
PHASE I
PHASE II
PHASE III

Phase III evidence informing decisions

- Evidence collected on typically 1% of the target population
  - Population usually have inequitable access to Phase III trials
- Treatment response believed to be heterogeneous across patients
- Debate as to why efficacy, not effectiveness, should guide decision-making

Challenges

Statistical theory of hypothesis testing is not a theory of decision making

- Mansky, *Health Economics* 2018

Precision **in answering a narrow question in Phase III trials almost always leads to substantial** ***imprecision*** **in answering a different, more decision-relevant question.**

Real-World Evidence

> **We need it to decrease imprecision in answering many different decision-relevant questions.**

Should a product be marketed based on a data set that speaks to a limited and rigidly constructed circumstance, when the clinical use, and in turn the evidence we might have to evaluate the product, could have been far richer, far more diverse, and more informative?

- Scott Gottlieb, FDA Commissioner

Real-World Evidence

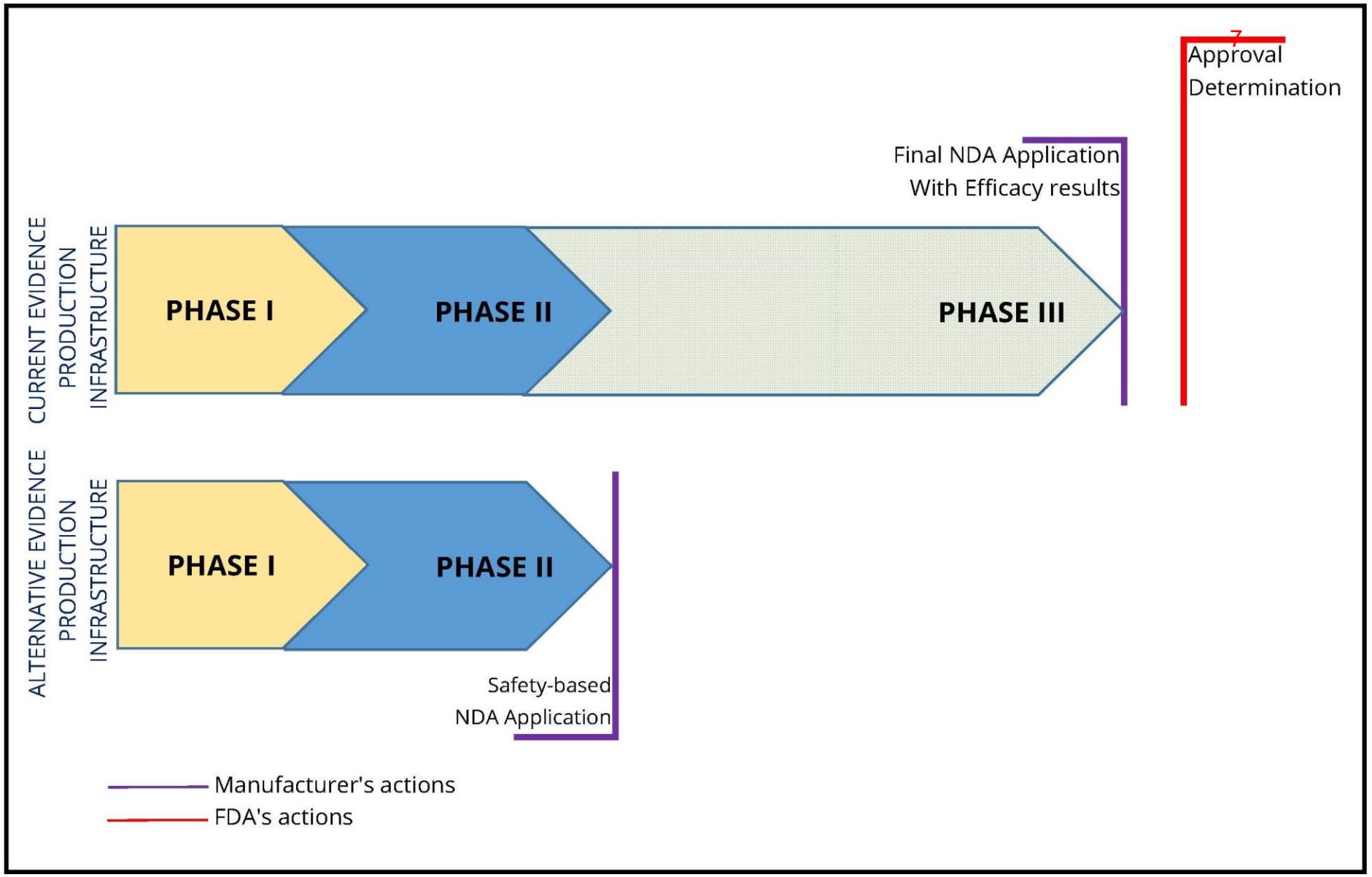
> **We need it to decrease imprecision in answering many different decision-relevant questions.**

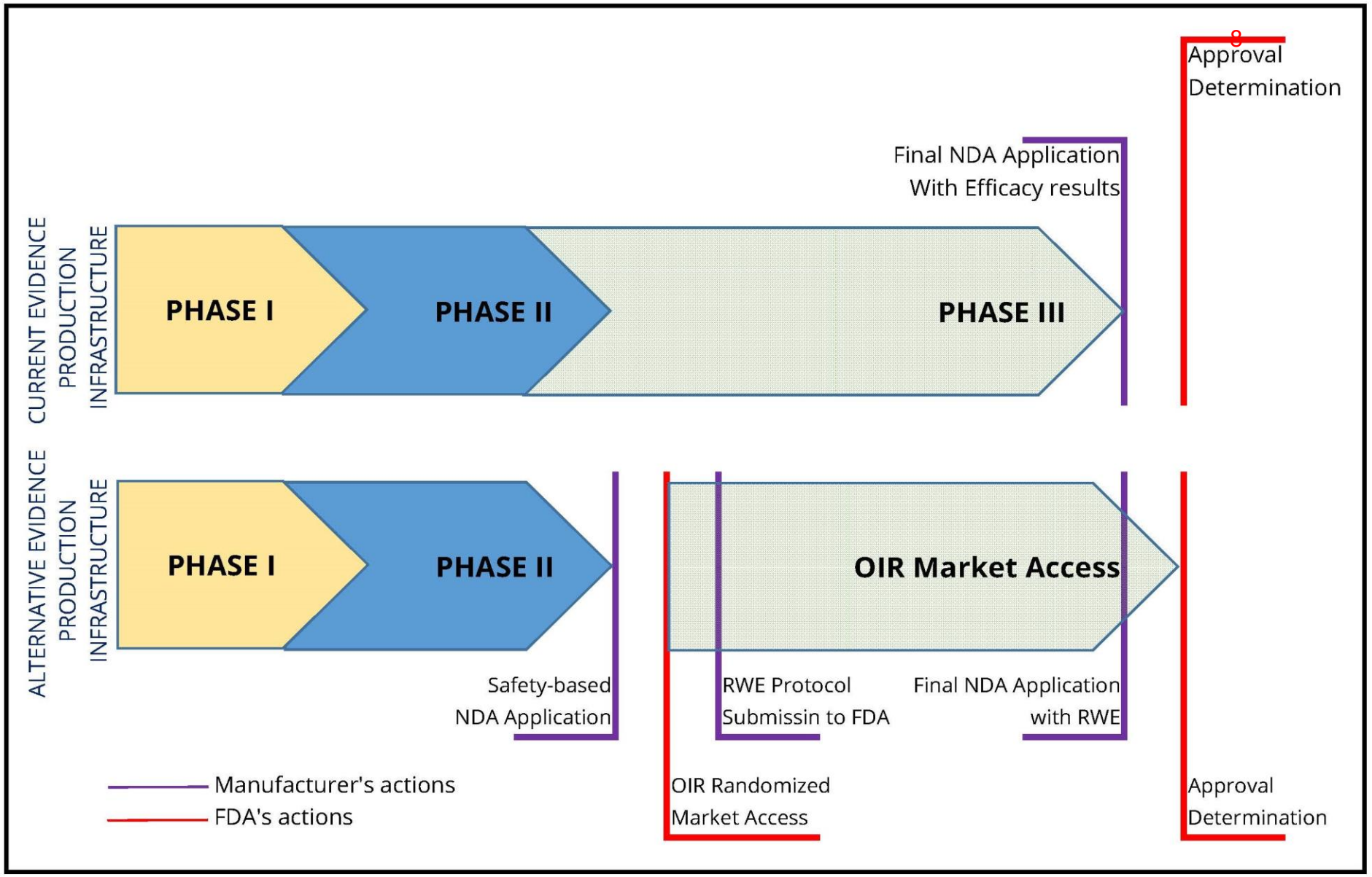
Should a product be marketed based on a data set that speaks to a limited and rigidly constructed circumstance, when the clinical use, and in turn the evidence we might have to evaluate the product, could have been far richer, far more diverse, and more informative?

- Scott Gottlieb, FDA Commissioner

Progress has been incremental at best:

- Use observation data to design Phase III trials
- Use historic RW controls for orphan drugs
- Use post-marketing data to generate signals on safety and effectiveness


Approval
Determination
Final NDA Application
With Efficacy results
CURRENT EVIDENCE
PRODUCTION
INFRASTRUCTURE
PHASE I
PHASE II
PHASE III
ALTERNATIVE EVIDENCE
PRODUCTION
INFRASTRUCTURE
PHASE I
PHASE II
Safety-based
NDA Application
Manufacturer's actions
FDA's actions



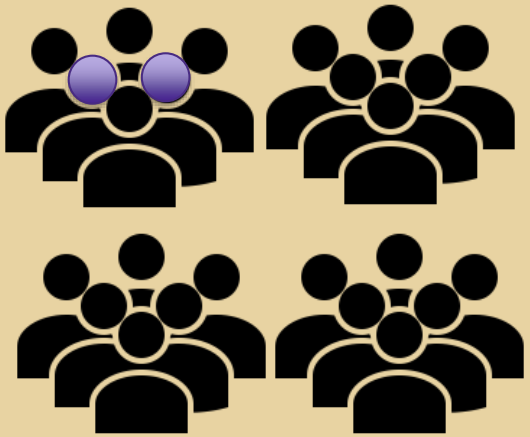
OIR: ”Only-in Research” Designation

Most Important and Disruptive Part of OIR

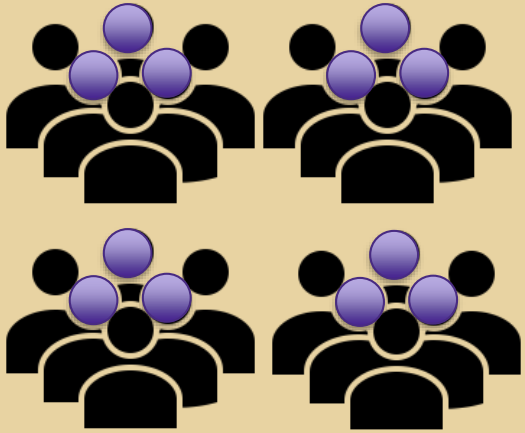
> Earlier market access to the drug based on Phase II results but only to a random subset of patients in the population.

> Ethical challenge: non-uniformity in access to the OIR product.

PHASE III



OIR



- Operates under same information on safety from Phase II
- Maintains physician autonomy
- More equitable access during OIR phase
- Real comparators, even do nothing option.

Tremendous Advantages of OIR

- Early and equitable access to patients
- Randomized access at the population level
  - Directly answer the question on the value of access
  - larger sample sizes
  - explore heterogeneity, and comparative safety
  - allow providers, payers, and policy makers to better target the use of new, often very expensive, drugs to those who would benefit the most.
- Enhance replicability of effectiveness studies in the OIR phase
- Manufacture bound to price modestly during OIR phase

Challenges to FDA

- How to implement randomized access?
  - Allow physicians to prescribe the drug for a random group of patients in the population during the OIR phase (e.g. birthdate)
  - Allow insurance companies to cover the drug for a random group of patients in the population during the OIR phase

- Go beyond just approval decisions
  - Use the population-level randomization instrument, to produce valuable information for different levels of decision making that are often absent in the current process.

Disruptive Innovation to Regulatory Infrastructure

- Current infrastructure of Phase III trials fails to remove decision uncertainty for most real-world decision-relevant questions
- Evidence production in inequitable, and slow
- We need disruptive innovation, not only in how we use evidence, BUT HOW WE PRODUCE IT
- OIR could be a promising alternative for this purpose.

Health Affairs

TOPICS JOURNAL BLO

HEALTH AFFAIRS BLOG DRUGS AND MEDICAL INNOVATION

RELATED TOPICS:
ACCESS TO CARE | PHARMACEUTICALS | MARKETS | DECISION MAKING | PATIENT SAFETY | INSURANCE COVERAGE AND BENEFITS | QUALITY OF CARE | PATIENT HARM | FDA APPROVALS PROCESS | COMPARATIVE EFFECTIVENESS

Want Drug Regulators To Consider Real-World Evidence? Then Disrupt Their Outdated Regulatory Infrastructure

Anirban Basu

NOVEMBER 2, 2017 10.1377/hblog20171030.999857

https://www.healthaffairs.org/do/10.1377/hblog20171030.999857/full/