# What is RWE? – 3 Dialectics

- Icons vs Idols
- Arbiter vs Curator
- Validity vs Credibility



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# Icons vs. Idols

- Icon – An exemplar that illuminates or animates
- Idol – A surface appearance that distracts

# Arbiter vs Curator

- Scott Gottlieb: As data become more diverse (to match diverse purposes), FDA may become a curator rather than an arbiter.
- But… what model of curation should we follow?
  - Sundance (Restricted entry, refereed by elites)
  - YouTube (Free entry, refereed by the crowd)

# Validity vs Credibility

- Credible = Simple, but often misleading
- Valid = Accurately predicts, but may be obscure
- Two examples in our discussion:
  - Clinical data vs. traditional evidence
  - Traditional RCT vs. more complex methods

# What is RWE? – Core Qualities

- Generalizable
- Relevant
- Adaptable
- Efficient

# RWE is Generalizable

- Generalizability is more about prediction than resemblance
- Prediction is context-specific, but that's testable
- Predictions are accountable (A scary thought!)

# RWE is Relevant

- Grounded in stakeholder priorities
- Directly addresses decisional needs
- “Fit for purpose” presumes diverse purposes

# RWE is Adaptable

- Must embrace (and attempt to understand) heterogeneity of patients, providers, and systems.
- Answers not expected to apply everywhere and for all time (But how do you regulate with that?)

# RWE is Efficient

- Because answers may be disposable, they should be fast and cheap to create.
- Economy can promote clarity (if we do it right)

# Questions/Challenges

- Is value generalizable?
- How can we increase rigor of observational designs?
- How do we accommodate stakeholders' diverse evidence needs?
- Can we blur the pre-approval/post-approval boundary?
- What's so great about randomization?

# Is value generalizable?

- Components of value:
  - Improvements in function and quality of life
  - Decreased need for other health services
  - Defined in relation to alternatives
- The first may be stable across place and time, the others certainly are not.

# How can we increase the rigor of observational designs?

- Transparency, transparency, transparency
  - Registration is probably MORE important here
  - Secret specs and math can't be trusted (if it's not on GitHub, it didn't happen)
  - Replication in two directions:
    - Different methods on same data
    - Same methods on different data

# How do we accommodate stakeholders' diverse evidence needs?

- Q: How do we simultaneously address questions about effectiveness, tolerability, heterogeneity of treatment effects, and value?
- A: We don't. Amphibious cars still are not a thing.

# Can we blur the pre-approval/post-approval boundary?

- Some research already crosses the boundary (Salford studies, Rare diseases, devices)
- Blending = enrichment and augmentation, not contamination (Thanks, John Doyle)
- Could RWE blur the ACTUAL boundary (driving license analogy)

# What's so great about randomization?

- Strong protection against confounding by indication
- Specified in advance
- Simple and transparent (more credible)

# What holds us back?

- It's less about greed (i.e. perverse incentives)
- And more about fear:
  - It's safer to fail in familiar ways
  - Somebody else might have fun with my stuff
- And trust (which is challenging to scale)