



PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

# **PCORI Methodology Standards: Academic Curriculum**



JOHNS HOPKINS  
SCHOOL *of* MEDICINE



JOHNS HOPKINS  
BLOOMBERG SCHOOL  
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## Module 3: Study Designs

### Category 10: Studies of Diagnostic Tests

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# Definition: Diagnostic Test

- ***Diagnostic test:***

- ▶ An intervention, such as imaging or laboratory test, used to determine the nature or severity of a medical condition or used to predict response to therapy

# Definition: Comparative-Effectiveness Research (CER)

- ***Comparative-effectiveness research (CER):***
  - ▶ Institute of Medicine:
    - The generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care
  - ▶ PCORI:
    - A field of research designed to compare the effectiveness of two or more interventions or approaches to health care, examining their risks and benefits
- **Which intervention works best, for whom, under what circumstances?**
- The purpose of CER is to assist consumers, clinicians, purchasers, and policy makers make informed decisions that will improve health care at both the individual and population levels

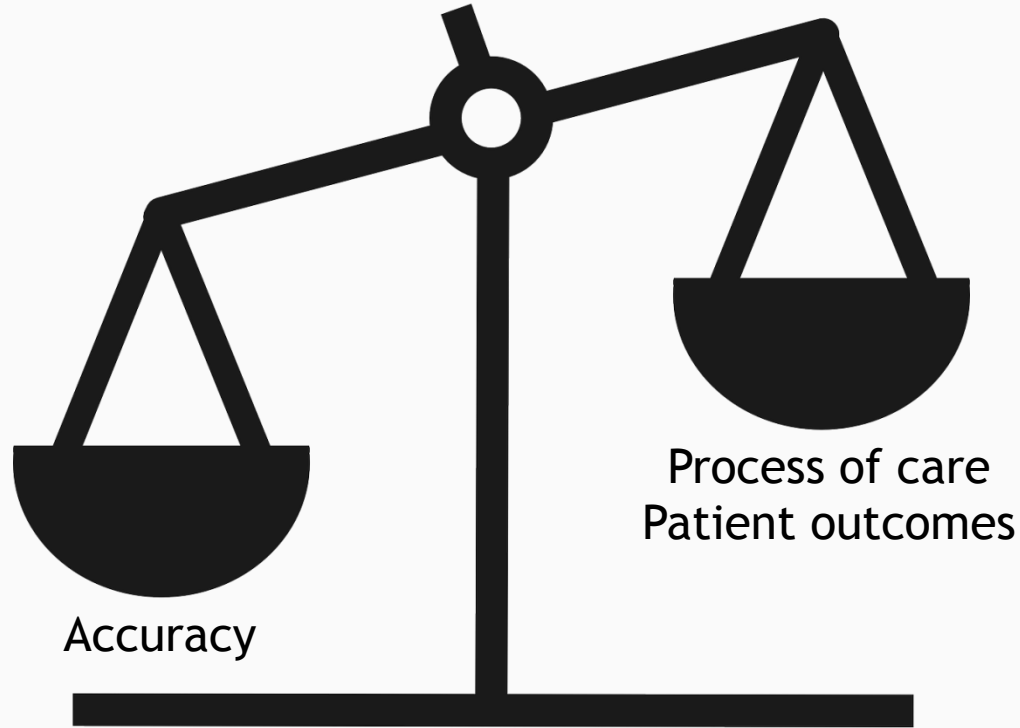
# Developmental Age of a Diagnostic Test

- **Phase I (Discovery):**
  - ▶ Establishment of technical parameters, algorithms, and diagnostic criteria
- **Phase II (Introductory):**
  - ▶ Early quantification of performance in clinical settings
- **Phase III (Mature):**
  - ▶ Comparison to other testing modalities in prospective, typically multi-institutional studies
- **Phase IV (Disseminated):**
  - ▶ Assessment of the procedure as utilized in the community at large

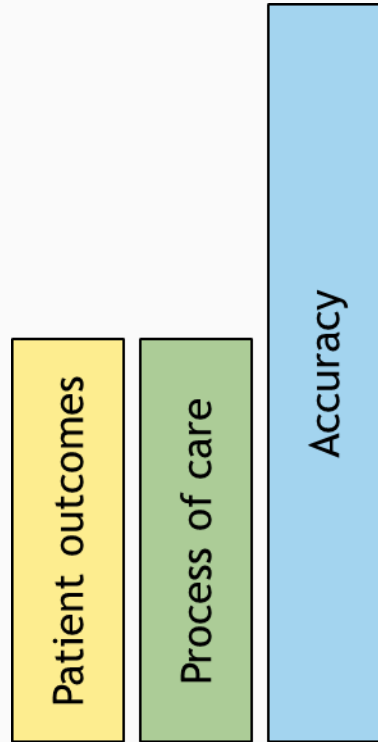
# Guiding Questions in the Clinical Evaluation of a Diagnostic Test

- Accuracy:
  - ▶ How accurate is the test in its diagnostic or predictive task?
  
- Impact on process of care:
  - ▶ Does the test outcome influence subsequent diagnostic and/or therapeutic interventions?
  
- Impact on patient outcomes:
  - ▶ Does the test influence patient outcomes, such as morbidity, mortality, functioning, and quality of life?

# Uneven Development of Evaluation Methods



# Developmental Age of a Diagnostic Test



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# Study Designs for CER on Diagnostic Tests

- Prospective randomized design
- Observational design
- Modeling / simulation / decision analysis
- Systematic review / meta-analysis

# Randomized Controlled Trials

## ■ Strengths

- ▶ Use of randomized design minimizes problems of selection bias and confounding due to indication
- ▶ Use of prospective design minimizes problems of temporal ambiguity between diagnostic findings and patient outcomes

## ■ Limitations

- ▶ Expensive, resource intensive
- ▶ Homogenous study population

# Examples of Randomized Clinical Trials of Diagnostic Tests

## ■ National Lung Screening Trial (NLST, 2011)

- ▶ Prospective randomized comparison of CT versus x-ray screening
- ▶ Assessment of intervention on:
  - Lung cancer incidence
  - Patient mortality
  - Quality of life

## ■ SIGGAR Trial (Halligan, et al., 2007)

- ▶ Multicenter randomized comparison of CT colonography versus standard-of-care investigation (barium enema / colonoscopy)
- ▶ Assessment of intervention on:
  - Colon cancer incidence
  - Incidence of colonic polyps
  - Physical morbidity
  - Psychological morbidity

# Observational Studies

## ■ Strengths

- ▶ Observational studies are less costly and often take less time to complete than do randomized trials
- ▶ Observational studies can be more ethical or practical in certain scenarios—e.g., randomization may not be plausible if a new technology has completely diffused into common usage; it would be difficult to recruit participants to use a former standard of care (Hillman and Gatsonis, 2008)

## ■ Limitations

- ▶ Unidentified biases and confounder may weaken the level of evidence
- ▶ Secondary databases, such as registries or electronic medical records (EMRs), have limited access to information and often lack key factors necessary to evaluate diagnostic performance

# Simulation Studies and Systematic Reviews

- Simulation, modeling, decision analysis, and systematic reviews can be used to perform CER on diagnostic tests
- These methods can also be used to inform study designs for randomized trials or observational studies
- Modeling can be used in comparative accuracy studies to characterize the range of values a new test would need to supersede an older standard of care
- Information from systematic reviews can be used to review the pertinent evidence base, put the study in clinical context, and help inform study design (e.g., what has worked in prior studies, what has not)

# References

- Carlos, R., Gareen, I., Gatsonis, C., Gorelick, J., Kessler, L., Lau, J., Rutter, C., Schmid, C., Tosteson, A. N. A., Trikalinos, T. (2012). *Standards in the Design, Conduct and Evaluation of Diagnostic Testing for Use in Patient Centered Outcomes Research*. PCORI. Available at: <http://www.pcori.org/assets/Standards-in-the-Design-Conductand-Evaluation-of-Diagnostic-Testing-for-Use-in-Patient-Centered-Outcomes-Research.pdf>. Accessed August 7, 2015.
- Fryback, D. G., & Thornbury, J. R. (1991). The efficacy of diagnostic imaging. *Medical Decision Making*, 11(2), 88-94.
- Halligan, S., Lilford, R. J., Wardle, J., et al. (2007). Design of a multicentre randomized trial to evaluate CT colonography versus colonoscopy or barium enema for diagnosis of colonic cancer in older symptomatic patients: the SIGGAR study. *Trials*, 8, 32. <http://doi.org/10.1186/1745-6215-8-32>
- Hillman, B. J., & Gatsonis, C. A. (2008). When is the right time to conduct a clinical trial of a diagnostic imaging technology? *Radiology*, 248(1), 12-15. <http://doi.org/10.1148/radiol.2481072190>
- National Lung Screening Trial Research Team, Aberle, D. R., Adams, A. M., Berg, C. D., et al. (2011). Reduced lung-cancer mortality with low-dose computed tomographic screening. *The New England Journal of Medicine*, 365(5), 395-409. <http://doi.org/10.1056/NEJMoa1102873>