

PCORI: How heterogeneity of treatment effect informs what we do

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Patient-Centered Outcomes Research Institute (PCORI)



- An independent research institute authorized by Congress in 2010 and governed by a 21-member Board of Governors representing the entire healthcare community
- Funds comparative clinical effectiveness research (CER) driven by patients and other stakeholders information needs
- Seeks answers to real-world questions about what works best for patients based on their circumstances and concerns



Our Broad Mandate

“The purpose of the Institute is to assist patients, clinicians, purchasers, and policy-makers in making informed health decisions by **advancing the quality and relevance of evidence** concerning the manner in which diseases, disorders, and other health conditions can effectively and appropriately be prevented, diagnosed, treated, monitored, and managed through **research and evidence synthesis that considers variations in patient subpopulations...**”

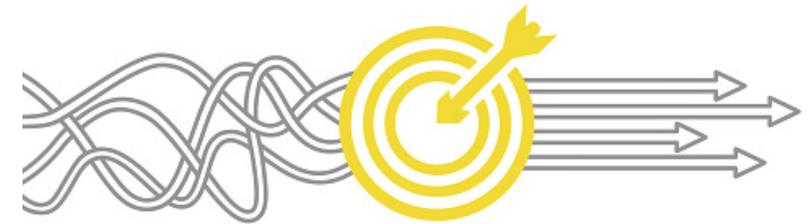
PCORI’s Methodology Committee shall.... improve science and methods of research....(including) **methods by which patient subpopulations can be accounted for** and evaluated in different types of research.”

—from PCORI’s authorizing legislation



Demand for Valid Personalized Evidence is Widespread

- Patients clearly want all health care to be as personalized as possible
- Clinicians are encouraged to utilize shared decision making and apply the logic of personalization to individual clinical decisions without always having the evidence to support them
- Evidence-based guideline developers are increasingly using multivariate risk models to target recommendations traditionally based only on age and sex
- Methods to evaluate treatment heterogeneity and parse those most likely to benefit are proliferating, e.g. through machine-learning and “big data”



Research Examples



Research

JAMA | Original Investigation

Association Between Intensity of Posttreatment Surveillance Testing and Detection of Recurrence in Patients With Colorectal Cancer

Rebecca A. Snyder, MD, MPH; Chung-Yuan Hu, MPH, PhD; Amanda Cuddy, MPH; Amanda B. Francescatti, MS; Jessica R. Schumacher, PhD; Katherine Van Loon, MD, MPH; Y. Nancy You, MD, MHS; Benjamin D. Kozower, MD, MPH; Caprice C. Greenberg, MD, MPH; Deborah Schrag, MD, MPH; Alan Venook, MD; Daniel McKellar, MD; David P. Winchester, MD; George J. Chang, MD, MS; for the Alliance for Clinical Trials in Oncology Network Cancer Surveillance Optimization Working Group

patient demographic tumor → Test use among survivors w/o recurrence (n=6279) → Predict each facility # of tests/pt for all survivors (n=8529) → Facility clustering effect for O/E (P<0.0001 imaging, P<0.0001 CEA) → Compare effectiveness of intensity by facility

JAMA. 2018;319(20):2104-2115. doi:10.1001/jama.2018.5816

¹Stress test options include nuclear stress testing, ultrasound stress testing, or exercise ECG (electrocardiogram) stress testing. Nuclear stress testing and coronary CT angiography include exposure to radiation which has been shown to be related to increased cancer risk over a lifetime. Your doctor can help you explore which option may be best for you.

- Age
- Gender
- Race
- If chest pain is made worse when manual pressure is applied to the chest area
- If there is a history of coronary artery disease
- If the chest pain causes perspiration
- Findings on electrocardiograms (electronic tracings of the heart)
- Initial cardiac troponin result



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Colorectal Cancer Surveillance

A decision-support tool for patients and providers following colon or rectal cancer treatment

RESOURCES

MODULE 1: Learn About Follow-up
Keeping an eye on your health is important! Learn about follow-up care.

Will the Colorectal Cancer Come Back?

RESEARCH

OPEN ACCESS

Shared decision making in patients with low risk chest pain: prospective randomized pragmatic trial

Erik P Hess,^{1,2,3} Judd E Hollander,⁴ Jason T Schaffer,⁵ Jeffrey A Kline,⁵ Carlos A Torres,⁶ Deborah B Diercks,⁷ Russell Jones,⁸ Kelly P Owen,⁸ Zachary F Meisel,⁹ Michel Demers,¹⁰ Annie Leblanc,^{2,11} Nilay D Shah,¹¹ Jonathan Inselman,³ Jeph Herrin,¹³ Ana Castaneda-Guarderas,^{1,2,14} Victor M Montori^{2,15}

How you feel about your follow-up care is important. Help your doctor or healthcare professional understand your preferences

Hess Erik P, Hollander Judd E, Schaffer Jason T, et al. Shared decision making in patients with low risk chest pain: prospective randomized pragmatic trial. *BMJ* 2016; 355:f6165

Download Module 3

pcori PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History

CLINICAL RESEARCH PROGRAM

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

Commission on Cancer

Erik Hess, "Emergency Care For you, or with you" PCORI Annual Meeting Presentation, October 31, 2018.

<https://crdecisiontool.mdanderson.org/>

USPSTF: multivariable outcome risk-stratified recommendations



Recommendation	Stratification Approach	Tool
Aspirin Use to Prevent Cardio-vascular Disease (CVD) and Colorectal Cancer: 2016	10-year ASCVD risk	ACC/AHA Pooled Cohort Equations ASCVD-Risk Estimator
Statin Use for the Primary Prevention of CVD in Adults: 2016	10-year ASCVD risk	ACC/AHA Pooled Cohort Equations ASCVD-Risk-Estimator
Breast cancer-Medications for risk reduction: 2013	5 year and lifetime breast cancer risk	National Cancer Institute's Breast Cancer Risk Assessment Tool (BCRISKTOOL)
Screening for Osteoporosis: 2011	10 year risk of major osteoporotic/hip fracture	FRAX®

Development and deployment of clinical prediction rules/tools is promising but requires more research focus

- **To target preventive interventions**

- **Lung cancer screening:** *Ten Haaf, Jeon J, Tammemägi MC, et.al. Risk prediction models for selection of lung cancer screening candidates: A retrospective validation study. PLoS Med. 2017 Apr 4;14(4.)*
- **Diabetes prevention:** *Hippisley-Cox J, Coupland C. Development and validation of QDiabetes-2018 risk prediction algorithm to estimate future risk of type 2 diabetes: cohort study. BMJ. 2017 Nov 20;359.*

- **For common clinically heterogeneous disease with multiple treatments possible** **Depression:** *Kessler RC, van Loo HM, Wardenaar KJ, et.al. Using patient self-reports to study heterogeneity of treatment effects in major depressive disorder. Epidemiol Psychiatr Sci. 2017 Feb;26(1):22-36.*

- Designing research with common baseline characteristics and core outcomes

- **Predicting differential treatment response** can be more complex than analyses based on outcome risk (although these can also have their critics)

- **Research practice in prognosis and clinical prediction lags behind** where it could be for optimal influence (development >>> validation > impact evaluation) *Ban JW, Empananza JI, Urreta I, Burls A. Design Characteristics Influence Performance of Clinical Prediction Rules in Validation: A Meta-Epidemiological Study. PLoS One. 2016 Jan 5;11(1):e0145779.*

PCORI's Commitment: methods, research, dissemination, engagement



Research Initiatives

- E.g., IPD MA to explore treatment heterogeneity
- Stratifying trial results based on outcome risk:
 - DPPT treatment targeting
 - IRIS treatment targeting

Methods Development

- E.g., Predictive Approaches to Treatment Heterogeneity Resource Center (Tufts University award) 2017-2019
 - Methods white paper
 - Pilot projects (including ability to work with other agencies)
- Meta-research and methods research

Ensuring Value and Reducing Waste

More personalized valid and applicable evidence holds the promise of contributing to improved efficiency, effectiveness and reduced waste in research and in health care.

More standardized, consistent approaches across the research enterprise will help

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