PCORI: How heterogeneity of treatment effect informs what we do

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November 29, 2018

Patient-Centered Outcomes Research Institute (PCORI)

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

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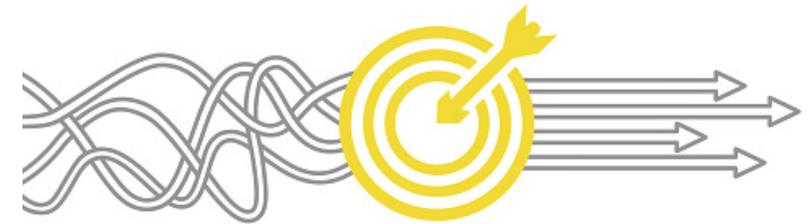
PCORI's Methodology Committee shall…. improve science and methods of research….(including) **methods by which patient subpopulations can be accounted for** and evaluated in different types of research."

—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"

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

https://crcdecisiontool.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, Emparanza 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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