Assessing and communicating heterogeneity of treatment effects (HTE) for patient subpopulations: challenges and opportunities

Symposium
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Food and Drug Administration (FDA)
and
Johns Hopkins University
Center of Excellence in Regulatory Science & Innovation (JHU CERSI)

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Today's Agenda

- Opening presentations
- Sessions 1-3- overview presentation on session topic followed by panel discussions
  - Session 1: HTE in Diverse Populations
  - Session 2: HTE Considerations in Design & Analysis
  - Session 3: Communicating HTE to Key Stakeholders
  - Each panelist has a challenge question(s) they will address in a 5 min. presentation (see handout)
  - Q & A at the end of each panel
- Session 4- overview presentations followed by discussant & Q & A
  - HTE from the perspective of Patient-Centered Outcomes Research Institute (PCORI)
- Final thoughts/ Wrap-up at the end of the day

Today's Logistics for Attendees

- Please use microphones in room to ask questions
- Remote attendees can type questions in Adobe Q & A box
- Cell phone: please mute or turn off ringers
- Breaks/Lunch – snacks, lunch options, and coffee are available for purchase at kiosk- please pre-order lunch by 10:40 am or earlier
- WiFi information is included on last page of agenda
- Symposium recording and slides will be available on FDA and JHU CERSI websites with speaker's permission after the symposium (see links in agenda)
- Questions? Please stop by the registration table outside of the room

What is HTE?

- Often, individuals respond differently to the same treatment

- Treatment response variation = explainable variation + random fluctuation

- HTE is the explainable variation in treatment response that is attributable to individual characteristics

Why is HTE Important?

- *If it were not for the great variability between the individuals, medicine might as well be a science, not an art* (William Osler, 1892)

- *The paradox of the clinical trial is that it is the best way to assess whether an intervention works, but is arguably the worst way to assess who benefits from it* (Mant, 1999)

ITE and Subgroup Analysis

- Ideally we would like to estimate individualized treatment effect (ITE)

- But ITE is not identifiable

- We can consider groups of similar individuals and estimate a group-specific treatment effect
  - Subgroup analysis
  - Prediction models

HTE Assessment is Perilous

- HTE estimation entails greater variance due to reduced information content

- Increases false-positive (type-I) and false-negative (type-II) errors

- <u>Central challenge</u>: how to reliably identify individuals or groups likely to benefit from the treatment

- There is a need to leverage prior knowledge, good designs, clever analysis