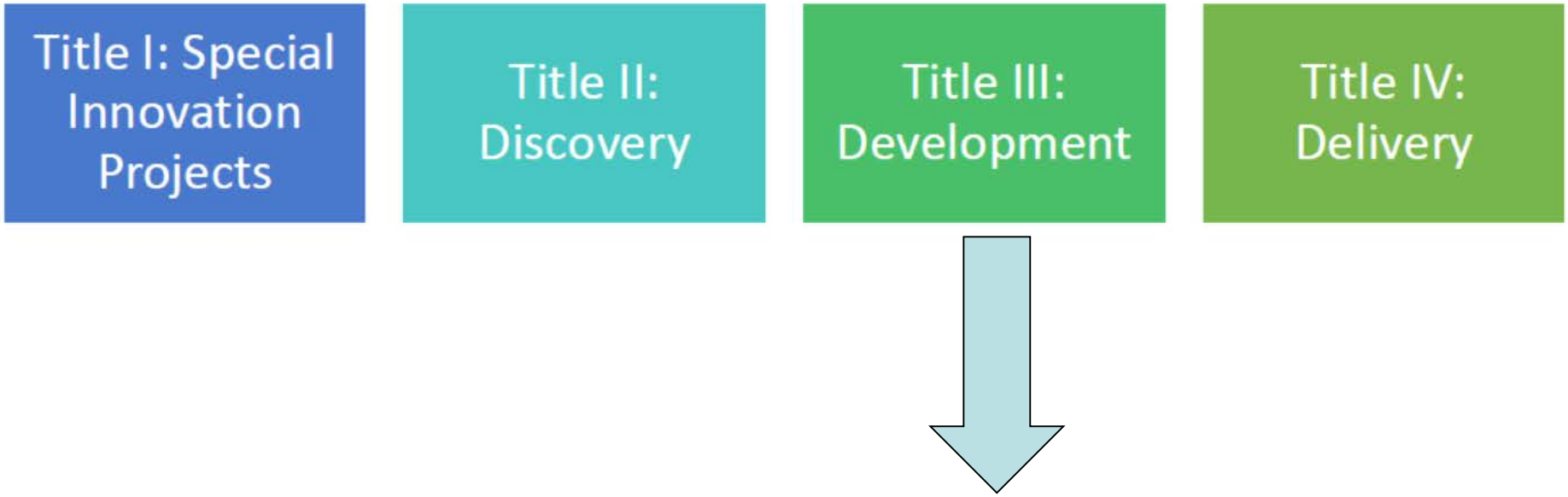
Is there anything described in the 21st Century Cures Act that would benefit from greater attention to HTE?

Jodi Segal, MD, MPH
Professor of Medicine, Epidemiology,
Health Policy and Management

Where is HTE most relevant?

Public Law 114–255
114th Congress



Modern Trial Design and Evidence Development

Novel Clinical Trial Designs (Sec. 3021)

- Requires FDA to hold a public meeting and issue guidance documents that would assist sponsors in incorporating adaptive designs and novel statistical modeling into new drug applications
- Such guidance should include:
  - Use of such clinical trial designs, including how these designs can satisfy the substantial evidence of effectiveness standard
  - How sponsors can obtain feedback from FDA on technical issues related to modeling and simulations
  - The types of qualitative and quantitative information that should be submitted for review
  - Recommended analysis methodologies

Real World Evidence (Sec. 3022)

- Requires FDA to establish a program to evaluate the potential use of real world evidence to:
  - Help support the approval of new indications for an approved drug
  - Help support or satisfy post approval study requirements

Cures definition of RWE: "Data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than clinical trials. May also include ongoing safety surveillance, observational studies, registries, claims data, and patient-centered outcomes research activities."

Novel Clinical trial Designs (Sec 3021)

Requires FDA to develop guidance on use of novel clinical trial designs (including pragmatic designs, adaptive designs) ….

Particularly well suited to address HTE as pragmatic trials are ideal for evaluating HTE in the diverse patients recruited from a usual care setting; adaptive trials can be structured to adapt randomization based on heterogeneity in response

Guidance on qualitative and quantitative information for submission

Possibly the guidance should be about how results in subgroups are reported or how IPD is submitted to allow for exploration for HTE by reviewers

Guidance on analysis methods

That appropriately account for multiple subgroups and pre-specification of these subgroups, etc.

Real World Evidence (Sec 3022)

Requires FDA to establish a program to evaluate the potential use of real world evidence to:

- Help support the approval of new indications for approved drugs
- Help support or satisfy post approval study requirements

Contains Nonbinding Recommendations

Use of Real-World Evidence to Support Regulatory Decision-Maki for Medical Devices

Guidance fo dustry and Food and g Administration Staff

Document issued on August 31, 2017.

The draft of this document was issued on July 27, 2016

For questions about this document regarding CDRH-regulated devices, contact the Office of Surveillance and Biometrics (OSB) at 301-796-5997 or CDRHClinicalEvidence@fda.hhs.gov.
For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

No Explicit Discussion of Heterogeneity of Treatment Effect

(Devices)

Important relevance factors that FDA will assess to determine if the RWD are suitable for regulatory use include…

- whether the RWD adequately captures patient medical history and preexisting conditions, as well as the follow-up information needed to evaluate the *question* being addressed

  [hopefully, that question will include whether there is HTE in important subgroups]

- whether sufficient data elements are collected to adjust for confounding factors that may impact the exposure or outcomes of interest

  [or, better yet, to evaluate the HTE that is attributable to these "confounding factors"]

Closing …

21st Century Cures Act opens a lot of room to better incorporate HTE evaluation into FDA's regulatory work