NESTcc Data Quality & Methods Framework
Public Comment Webinar

Agenda

• Dr. Robbert Zusterzeel, *MDIC/NESTcc*: NESTcc Overview and Data Quality & Methods Introduction
• Dr. Lesley Curtis, *Duke University School of Medicine*: NESTcc Data Quality Framework
• Dr. Sharon-Lise Normand, *Harvard Medical School*: NESTcc Methods Framework
• All: Audience members can submit questions through the Q&A feature
NESTcc Overview
**NESTcc’s MISSION & VISION**

**Mission**

To accelerate the development and translation of new and safe health technologies, leveraging Real-World Evidence (RWE), and innovative research.

**Vision**

To be the leading organization within the health technology and medical device ecosystem for conducting efficient and timely high-quality Real-World Evidence (RWE) studies throughout the Total Product Life Cycle (TPLC).
**NESTcc DEVELOPMENT BEGAN IN 2012**

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>2012</td>
<td>FDA proposed the development of a national system</td>
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<td>2015</td>
<td>NESTcc envisioned as a voluntary data network of collaborators by Planning Board</td>
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<tr>
<td>2016</td>
<td>FDA awarded funding for NESTcc to Medical Device Innovation Consortium (MDIC)</td>
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<td>2017</td>
<td>NESTcc Executive Director named and Governing Committee selected</td>
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<td>2017</td>
<td>NESTcc Strategic and Operational Plan developed</td>
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<td>2018</td>
<td>Initial NESTcc Data Network formed and testing initiated through Round 1 Test-Cases</td>
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<tr>
<td>2018</td>
<td>NESTcc Data Quality and Methods Subcommittees formed</td>
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<td>2019</td>
<td>Interim and Final Results from Round 1 and Round 2 Test-Cases</td>
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<td>2019</td>
<td>NESTcc Version 1.0 is operational</td>
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<td>2022</td>
<td>NESTcc fully launched and operational</td>
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Ensuring High-Quality Data & Analysis Methods
In 2018, NESTcc established multi-stakeholder subcommittees to support its efforts to conduct real-world evidence studies for medical devices, leveraging ongoing initiatives including expertise from MDEpiNet, PCORnet, and Sentinel.

**DATA QUALITY SUBCOMMITTEE**

- Chaired by Dr. Lesley Curtis, Duke University School of Medicine
- 12-person subcommittee includes representation from:
  - 6 health systems, including Network Collaborators
  - 3 medical device manufacturers
  - FDA

**METHODS SUBCOMMITTEE**

- Chaired by Dr. Sharon-Lise Normand, Harvard Medical School
- 9-person subcommittee includes representation from:
  - 3 health systems, including Network Collaborators
  - 4 medical device manufacturers
  - FDA
DATA QUALITY & METHODS SUBCOMMITTEES

NESTcc has established Data Quality and Methods Subcommittees to support its efforts to conduct real-world evidence studies for medical devices.

<table>
<thead>
<tr>
<th>Member Name</th>
<th>Organization</th>
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<tbody>
<tr>
<td>Jesse Berlin</td>
<td>Johnson &amp; Johnson</td>
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<tr>
<td>Mitchell Krucoff</td>
<td>Duke University Medical Center/Duke Clinical Research Institute (DCRI)</td>
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<tr>
<td>Heng Li</td>
<td>U.S. Food and Drug Administration (FDA)</td>
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<tr>
<td>Nilsa Loyo-Berrios</td>
<td>U.S. Food and Drug Administration (FDA)</td>
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<td>Joao Montiero</td>
<td>Medtronic</td>
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<td>Didier Morel</td>
<td>Becton Dickinson</td>
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<tr>
<td><strong>Sharon-Lise Normand</strong>*</td>
<td>Harvard Medical School</td>
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<tr>
<td>Nilay Shah</td>
<td>Mayo Clinic</td>
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<td>Scott Snyder</td>
<td>Cook Research Incorporated</td>
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*Subcommittee Chair

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<tr>
<td>Jeffrey Brown</td>
<td>Harvard Pilgrim HealthCare Institute/Harvard Medical School</td>
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<td><strong>Lesley Curtis</strong>*</td>
<td>Duke University School of Medicine</td>
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<tr>
<td>John Laschinger</td>
<td>U.S. Food and Drug Administration (FDA)</td>
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<tr>
<td>Aaron Lottes</td>
<td>Cook Research Incorporated</td>
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<tr>
<td>Keith Marsolo</td>
<td>Cincinnati Children's Hospital Medical Center</td>
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<tr>
<td>Frederick Masoudi</td>
<td>University of Colorado Anschutz Medical Campus</td>
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<tr>
<td>Joe Ross</td>
<td>Yale University</td>
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<tr>
<td>Art Sedrakyan</td>
<td>Weill Cornell Medicine</td>
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<tr>
<td>Kara Southall</td>
<td>Medtronic</td>
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<tr>
<td>James Tcheng</td>
<td>Duke University Health System</td>
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<tr>
<td>Karen Ulisney</td>
<td>U.S. Food and Drug Administration (FDA)</td>
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<tr>
<td>Charles Viviano</td>
<td>U.S. Food and Drug Administration (FDA)</td>
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DATA QUALITY SUBCOMMITTEE & FRAMEWORK

Charge & Vision

• Develop Data Quality Framework for NESTcc Network Collaborators

• Design a process by which NESTcc Network Collaborators can demonstrate their aptitude with the NESTcc Data Quality Framework

• Develop first, simple, pragmatic, iteration of NESTcc Data Quality Framework that will apply to a “first wave” of NESTcc Network Collaborators

Data Quality Framework Overview

• Initial version lays out the foundation for the capture and use of high-quality data for post-market evaluation of medical devices

• Grounded in the use of real-world data (RWD) gleaned from the clinical care setting and the electronic health record (EHR)

• Data Quality Framework will evolve for a “second wave” of data vendors or similar collaborators with large de-identified datasets

Framework Organization

1. Data Governance Principles
2. Characteristics of Data
3. Data Capture & Transformation
4. Data Curation
5. NESTcc Data Quality Maturity Model
DATA QUALITY: DATA GOVERNANCE PRINCIPLES

• Organizational transparency and integrity
  o Leadership, stewardship, patient-centered, stakeholder engagement, transparency, oversight

• Data access, management, linkage and aggregation, and use

• Submission, management, review, and acceptance of RWD/RWE requests
  o Clear criteria, transparent process, commitment to responsible research, efficiency, commitment to results reporting
DATA QUALITY: CHARACTERISTICS OF DATA

**Question at Hand:**
What data are needed?
- Available or acquired
- Sources and Settings
- Experimental Method

**Data**
- Collected Raw Material - Facts
- High Quality – complete, accurate and timely
- Linkages, modular data sets
- Source traceability
- Reliable – free from errors that matter

**Information**
- Relevant – Scope and content answers question at hand  
  *Fit to Purpose*
- Curation – organization and distillation of data - context
- Informs - Knowledge communicated by facts

**Evidence**
- Combination and analysis of data and information
- Identification and application of appropriate analytic and/or statistical tools
- Supports conclusions
- Makes information Interpretable

**Informed Clinical And Regulatory Decisions**
- Judgment - Formation of sound clinical and scientific opinions or conclusions
- Objective evaluation of all evidence
  *Totality of the Evidence*

**Evidence generation and evaluation:** Actionable insights for informed clinical and regulatory decisions (adapted from Califf RM, Sherman R, What we mean when we talk about data. MassDevice. December 11, 2015. [https://www.massdevice.com/44947-2/]
Data Capture and Transformation

• Improving data quality at the point of care and point of data entry should be the ultimate goal
• Understand how and why data of interest were originally obtained and processed
• Build quality control processes into each step of any ETL process

Data Curation

• Process should address conformance, completeness, plausibility
• Study-specific curation should augment foundational data curation
• Metadata about data provenance guides assessments of data fitness for purpose
• Iterative process that helps to improve data quality over time
NESTcc DATA QUALITY MATURITY MODEL

• The five stages of maturity reflect increasingly advanced and integrated levels of performance for health care systems to partner with the NEST ecosystem
• The stages are at least partially aligned with previous maturity models
• The model can indicate progress and help identify weaknesses and opportunities

<table>
<thead>
<tr>
<th>NESTcc Stage</th>
<th>Description</th>
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<tr>
<td>1. Conceptual</td>
<td>Clinical processes capture data primarily in verbose documents, not as data</td>
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<td>2. Reactive</td>
<td>Able to react to requests for analysis, respond to research requests</td>
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<tr>
<td>3. Structured</td>
<td>Clinical systems manage transactional data types (e.g., orders, transactions, laboratory results, medication prescriptions) as discrete data</td>
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<tr>
<td>4. Complete</td>
<td>Granular and complete clinical data based on standardized clinical CDEs captured in the processes of care, integrated into those care processes</td>
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<tr>
<td>5. Advanced</td>
<td>Data linkage and aggregation across systems enabled and open to external queries</td>
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NESTcc Methods Framework

Sharon-Lise Normand, PhD, MSc
Harvard Medical School

Monday, June 3, 2019
METHODS SUBCOMMITTEE & FRAMEWORK

Charge & Vision

• Develop a “living” Methods Framework for NESTcc addressing device-specific considerations in benefit/risk studies and safety signal detection.

• Develop a research agenda identifying critical issues in Methods for device, imaging, and other diagnostic technologies studies across the TPLC

• Consult on an ad hoc basis to NESTcc to ensure that NESTcc activities employ the most appropriate and rigorous methods of analysis

Methods Framework Overview

• Key: pre-specification of study design & analysis

• Develop a methodological framework to include device-specific considerations by device stage

• A single protocol is utilized for both randomized trials and observational studies

Framework Organization

1. Background: Disease, Available Therapies, and Device Risk
2. Device Description
3. Study Specific Objectives
4. Target Population and Patient Selection
5. Outcomes: Primary, Secondary, Procedural, and Device
6. Device Exposure
7. Study Design
   7.1 Specific Design
   7.2 Blinding (Masking)
   7.3 Units of Randomization and Observation
   7.4 Mechanism of Treatment Assignment
   7.5 Other Covariates
8. Study Procedures
   8.1 Patient Consent
   8.2 Randomization/Estimation
   8.3 Protocol Deviation Handling
9. Required Sample Size
10. Study Registration
11. Monitoring Plan
12. Statistical Analysis Plan
## BACKGROUND

- Introductory material of the protocol should include:
  - Thorough discussion of the underlying disease
  - Available therapies
  - Unmet medical needs
- Goal: demonstrate that based on the information presented, there is a justified rationale for conducting the study

## DEVICE DESCRIPTION

- Detailed device descriptions should be included in the protocol including details on each important:
  - Component
  - Ingredient
  - Material that will be in contact with tissues or body fluids of the study subject

## STUDY SPECIFIC OBJECTIVES

- Protocols should include unambiguous statements of its objectives aligned with its overall purpose
- Objectives should be:
  - Relevant
  - Specific, based on measurable quantities
  - Attainable within a reasonable time-frame
Target Population and Patient Selection

• Provide a description of the population to which the results of the study will apply
• Research participants should closely reflect the population of intended use

Outcomes

• Primary outcomes are directly linked to the primary study objective
• Secondary outcomes provide additional information that are intended to support the primary hypotheses
• Procedural outcomes can include procedure time, physiological and biological data captures as part of the procedure, and procedure-specific data
• Device outcomes depend on risk of the device and could range from device performance to linking device performance mechanistically to outcomes in conjunction with determinations of effectiveness, safety, and benefit/risk
• Control outcomes are used to help justify the unmeasured confounder assumption
DEVICE EXPOSURE

• The main goals of the underlying study should be used to define exposure and outcomes
• Exposure various by device types that are being studies

STUDY DESIGN

• Basic features of study design should include:
  o Number and type of comparison groups
  o Who is blinded to what when
  o Experimental unit of randomization
  o How the device assignment mechanism will occur
    o Randomized or observed

STUDY PROCEDURES

• Study procedures should include
  o How patients are approached and consented
  o How device assignment mechanism will be estimated
  o How data will be collected
  o Definitions of protocol deviations and how those will be treated
  o What constitutes subject withdrawal
  o What strategies will be adopted to minimize missing data
**SAMPLE SIZE, STUDY REGISTRATION, MONITORING PLANS, AND STATISTICAL ANALYSIS PLAN**

- **Required Sample Size:** Sample sizes vary depending on the study, but basic principles include indicating the type of study design, describing the approach to evaluation, and describing and justifying additional features of the study that impact the sample size.

- **Study Registration:** Trials should be registered on [www.clinicaltrials.gov](http://www.clinicaltrials.gov) prior to enrolling the first patient.
  - While registration of observational studies is more controversial, registering selected observational studies is encouraged.

- **Monitoring Plans:** Appropriate monitoring plans help ensure the protection of the rights, welfare, and safety of the human subjects, and the quality of the study data.

- **Statistical Analysis Plan (SAP):** The SAP provides the detailed description of all statistical analyses, such as estimation of treatment effect, approach to missing data, etc., to be conducted once the data are available.
LAUNCHING THE SUBCOMMITTEE FRAMEWORKS

NESTcc Data Quality & Methods Subcommittees’ Framework development will include a public comment period before the first iterations are released.

**NESTcc Data Quality & Methods Frameworks Timeline**

- **May 2019**: Public Comment Period Opens
- **June 2019**: Public Comment Period Closes
- **June 2019**: Version 1 of NESTcc Frameworks Released
- **July 2019**: NESTcc Frameworks Utilized to Inform Test-Cases & Active Surveillance
- **Implementation & Iteration**
NESTcc Data Quality & Methods Frameworks were released for public comment ([http://nestcc.org/opportunities](http://nestcc.org/opportunities)) on **Tuesday, May 28**.

Comments are being collected through Survey Monkey

- Comments should be submitted for the appropriate section of the Framework
- Comments should refer to the line numbers in the Framework documents
Engage with NESTcc
CONNECT WITH NESTcc

Explore opportunities to connect with NESTcc online with the following resources:

Contact us to develop a partnership
NESTcc@mdic.org

Connect with us on Twitter
@NESTccMedTech

Check out our updates on the website
www.nestcc.org

Explore open opportunities for engagement
nestcc.org/opportunities

Initiate a request to use the NESTcc Data Network
nestcc.org/consultation