The National Evaluation System for health Technology Coordinating Center (NESTcc) – Key Learnings in Enhancing the Access to Generate Real-World Evidence (RWE) for Medical Devices

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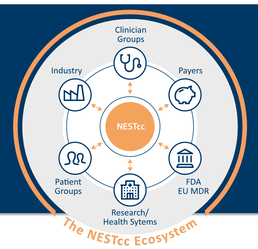
Background

NESTcc was established as an independent coordinating center through a cooperative agreement between the U.S. Food and Drug Administration and the Medical Device Innovation Consortium (MDIC) in 2016. NESTcc aims to drive the quality and efficient use of real-world data (RWD) to inform medical device development and evaluation throughout the total product life cycle (TPLC).

Mission

To catalyze the timely, reliable, and cost-effective development of Real-World Evidence (RWE) to enhance regulatory and clinical decision making.



Vision

To be the leading organization within the health technology and medical device ecosystem for conducting efficient and timely high-quality RWE studies throughout the TPLC.

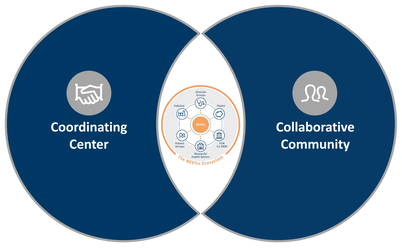
Established by the U.S. Food and Drug Administration, NESTcc is an independent coordinating center driving quality and efficiency in the use of RWD to inform medical device development and evaluation.

Since its inception, NESTcc has established relationships (Master Research Agreements) with 14 institutions shown below. These "Network Collaborators" (NCs) comprise the NESTcc Research Network. The Research Network provides access to an array of RWD sources available for research (electronic health record [EHR], registry, claims, and patient-generated data [PGD]) that have been gathered from health care delivery systems and the routine course of care.

DukeHealth · HealthCore · INSIGHT Clinical Research Network · Lahey Hospital & Medical Center · MAYO CLINIC · MDEpiNet · Mercy · NWEH NorthWest EHealth Discover-NOW · PEDSnet A Pediatric Learning Health System · STAR Stakeholders, Technology, and Research CRN · OneFlorida Clinical Research Consortium · VANDERBILT UNIVERSITY MEDICAL CENTER · Weill Cornell Medicine · Yale NewHaven Health

141 million+ Total Population
3,075 Outpatient Practices/Clinics
291 Specialty Clinics
162 Hospitals/Medical Centers

NESTcc serves as a coordinator facilitating collaborations in the health technology ecosystem. As a central point to bridge stakeholders to researchers, NESTcc provides the means to conduct high-impact studies with the appropriate oversight, quality control, and compliance.



> **As we move to a digitized world for device evaluation and surveillance, NEST can serve as a vehicle to drive evidence generation and enable new models of oversight to better meet the needs of patients.**
>
> *Jeff Shuren, M.D., J.D., Director of the U.S. Food and Drug Administration's Center for Devices and Radiological Health, and NESTcc Governing Committee member*

As a **coordinating center** offering services to organizations seeking to sponsor medical device/technology research based on high-quality RWD.

As a **collaborative community** comprised of representatives from across the medical device ecosystem, including FDA, working together to coalesce teams of diverse stakeholders around common needs and initiatives.

Introduction

- NESTcc awarded a diverse slate of "Test-Case" research studies to examine the capabilities of the Research Network in various clinical areas, regulatory uses, and analytical approaches.
- NESTcc maintained closed oversight through periodic study reports to ensure the success of the study, but also to learn from the study experience (e.g., programmatic efficiencies, collaborations, scientific/technical activities).
- Utilizing these study progress reports, a thematic analysis was conducted to capture the overarching themes across the successes and challenges of generating RWE.
- Key learnings have been generated to further develop the NEST model, all while answering stakeholder-driven research questions.

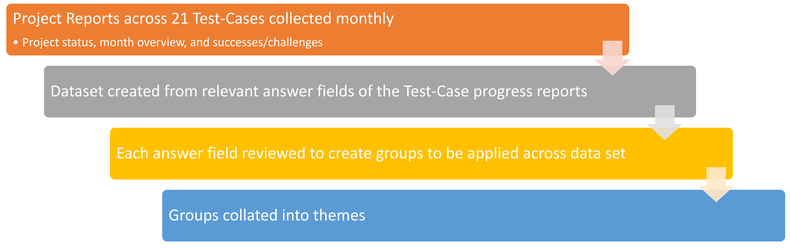
NESTcc Test-Case Overview

Test-Case	Technology of Interest	Disease Area	Device Class	Device Type	Data Sources	Study Design
1	Cardiac Ablation Catheters	Cardiology	III	T	EHR	Retrospective
2	Mechanical Aortic Heart Valves	Cardiology	III	T	EHR; Registry	Retrospective
3	Cardiac Implantable Device Leads	Cardiology	III	T	Claims; EHR	Retrospective
4	Cardiovascular Stent Device	Cardiology	III	T	EHR	Retrospective
5	Apple Watch ECG Diagnostic + mHealth	Cardiology	II	D/S	EHR; PGD	Prospective
6	Iliac Branch Endoprosthesis/Stent	Cardiology	III	T	EHR; Registry	Retrospective
7	Electrode Renal Denervation System	Cardiology	III	T	EHR	Retrospective
8	Craniomaxillofacial Distractors	Dental	II	T	EHR	Retrospective
9	Sutures/Staples/Skin Adhesives	Dermatology	I/II	T	EHR; Claims	Retrospective
10	Ear Tubes	Ear, Nose, & Throat	II	T	Claims; EHR	Retrospective
11	Total Knee Arthroplasty	Orthopedics	II	T	Registry; Claims	Retrospective
12	Total Knee Arthroplasty	Orthopedics	II	T	Registry; Claims	Retrospective
13	Intervertebral Body Fusion Devices	Orthopedics	II	T	EHR	Retrospective
14	Annular Closure Device	Orthopedics	III	T	Claims	Retrospective
15	Knee and Hip Implants	Orthopedics	II/III	T	Registry; Claims	Retrospective
16	mHealth for Insomnia/Prescription Digital Therapeutic (Mobile Medical App)	Psychiatry/Mental Health (Insomnia/Depression)	II	S	EHR; PGD	Prospective
17	Positive Airway Pressure (PAP) Therapy	Respiratory	II	T	EHR; PGD; Claims	Prospective
18	IVD Lung Cancer Diagnostic	Respiratory (Oncology)	II/III	D	EHR; Registry	Retrospective
19	Surgical Ablation Device	Surgery (Oncology)	II	T	EHR	Retrospective
20	Surgical Mesh	Urology	II	T	EHR; Registry	Retrospective
21	mHealth for Surgical Mesh (Mobile App)	Urology	II	S	PGD; Registry	Retrospective /Prospective

Device Types: T – T (non-IVD/imaging); S – Software or mobile health; D – Diagnostic;

Methods

- To assess successes and challenges in the conduct of the study, semi-structured progress reports were developed to collect study experiences across the full slate of Test-Cases in a consistent manner.
- Based on the collective monthly progress reports, a dataset for analysis was created from select answer fields deemed relevant to the assessment.
- Each answer field of the dataset was reviewed initially to identify constructs contributing to the successes and challenges of the study. These constructs were interpreted into groups that may be applied across the dataset.
- Considering the known issues surrounding RWE studies and how the progress reports were framed to capture details of these issues, a hybrid approach of inductive and deductive analyses was applied in identifying themes.



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Results

- The number of progress reports collected for review varied by Test-Case due to their individual start dates, award delays, and study timelines. A total of 119 reports were reviewed from 3 completed (29 reports) and 18 (90 reports) ongoing Test-Cases.
- The most notable themes of the reports related to ensuring consistent data quality, appropriate use of data standards, and RWE methods application. Although initial contracting delays were most prevalent, administrative challenges were not considered as a central theme in this analysis, as the focus was on insights in the execution of research.

Themes	Category	Examples
Ensuring Data Quality	Successes	- Novel approaches to validate computable phenotypes using a variety of sources (link to registry, natural language processing on clinical notes, chart reviews, labs, etc.) - Use of already established and recognizable resources/infrastructure to support quality of aggregate data
	Challenges	- Limitation of available cases to be included in study due to missing variables or outcomes of interest - Variability in quality, systems, and standards of data between partnered sites affects quality of aggregate data - Infrequency of unique device identifier utilization and/or integration
Methods Application	Successes	- Collaborative approach in analysis decisions, covariate/outcome selections and validation, and sharing insights between stakeholders involved in study - Public feedback solicitation on protocol
	Challenges	- In certain studies, small sample sizes limit method applications such as matching or meaningful statistical analyses
Appropriate Use of Data Standards	Successes	- Study data across partnered sites was harmonized at a central location, if data was shared - Data submitted from partnered sites received guidance/training on relevant fields to use - Existing data standards of registry, common data models, or study-specific case report forms were used to collect data from partnered sites
	Challenges	- Differences in data standards between partnered sites require building study specific requirements, then a crosswalk to the study requirement per site

Conclusion/Implications

- Research-driven collaborations yielded unique learning opportunities in enhancing the availability of siloed data sources for research.
- Additional efforts will need to be made to further apply methodological and data quality safeguards that may improve research integrity without burdening the progress of the study.
- Despite initial challenges in convening relevant RWD sources and expertise, NESTcc is well situated to catalyze research through clear and consistent guidance, expertise, and scientific standards in the conduct and validation of RWE studies.
- Further programmatic efficiencies and additional data quality/research methods guidance are being developed and applied at NESTcc.

Upcoming NESTcc Initiatives

- Continuous expansion of the Research Network based on geography, available data, and RWE research experience.
- Development of a national post-market active surveillance system capable of device adverse event (AE) signal detection and refinement to complement the current passive and voluntary mode of AE reporting.
- The NESTcc Research Methods Framework and Data Quality Framework released in 2020 will be refined based on key learnings, maturation of the Research Network, and alignment to the latest RWE research priorities and development.
- Designated by the FDA as a Collaborative Community, NESTcc will have the capacity to convene all stakeholders in working towards patient/public health initiatives.