NEST Overview and Future Vision

Rachael Fleurence, Ph.D.

Executive Director

NESTcc

Rachael Fleurence, Ph.D.

Rachael L. Fleurence, PhD is the inaugural Executive Director of the newly formed National Evaluation System for health Technology (NEST) Coordinating Center. Under the umbrella of a public-private partnership, NESTcc's mission is to establish clear pathways within the medical device ecosystem to support the timely, reliable, and cost-effective development of evidence using Real-World Data sources for key stakeholders, including the medical device industry, regulators, payers, patients, clinicians, and health systems.

Dr. Fleurence joins NEST from the Patient-Centered Outcomes Research Institute (PCORI) where she was the Program Director for PCORI's initiative to build the National Patient-Centered Clinical Research Network, or PCORnet, sine 2012. PCORnet has been a transformational effort to engage patients and leverage electronic health data to improve the speed and efficiency of clinical research in the United-States. A 350 million dollar investment involving 130 health institutions across the country, 20 patient powered research networks and covering 110 Million patients, PCORnet launched as an independent foundation in March 2017. Dr. Fleurence was also the inaugural director for the PCORI Methods Program in 2012, working closely with the PCORI Methodology Committee on this effort in its initial years. Dr. Fleurence has served on a number of Boards and Steering Committees, including most recently the National Medical Device Evaluation System Planning (NEST) Planning Board, the Medical Device Innovation Consortium (MDIC) Board and the SMART IRB Steering Committee, an effort to streamline IRB reviews across academic research institutions. She chaired the PCORnet Executive Committee from 2015-2017, and served as the vice-chair of the PCORnet Council.

A health economist and health services researcher by training, Dr. Fleurence received a BA from Cambridge University (United-Kingdom), a MA in business management from ESSEC-Paris (France), and a MSc and PhD in health economics from the University of York (United-Kingdom).

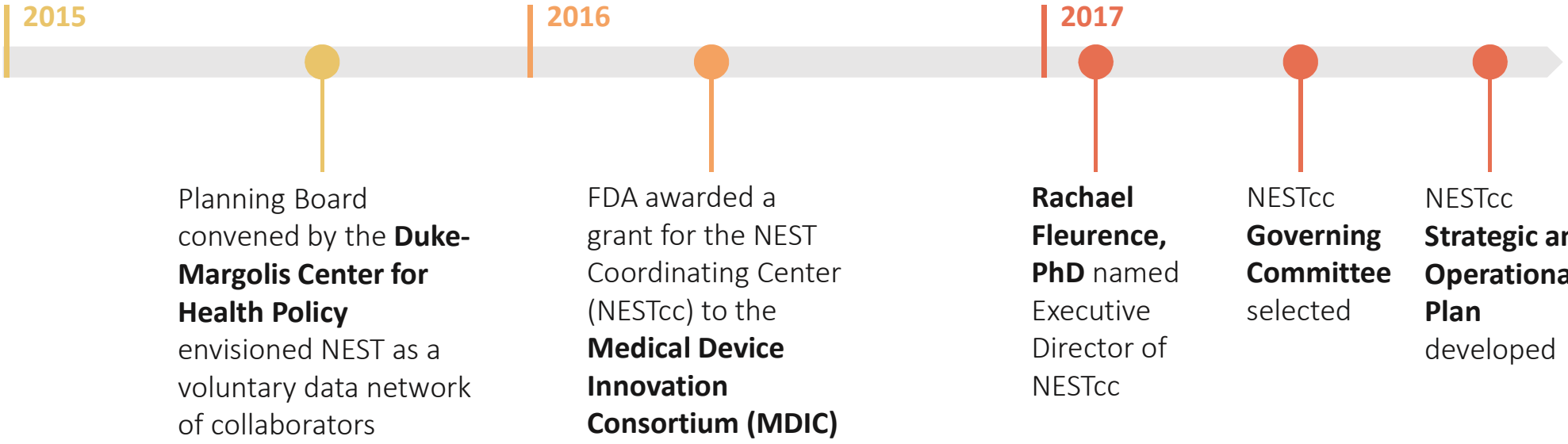
Rachael L. Fleurence, PhD
NESTcc Executive Director

April 19, 2018

Establishing the National Evaluation System for health Technology Coordinating Center (NESTcc)

HISTORY OF NEST

The National Evaluation System for health Technology's (NEST) vision is to improve the use of Real-World Evidence (RWE) generated in the routine course of care.



THE ECOSYSTEM CHALLENGE

The health care ecosystem is united behind the need to improve patients' timely access to safe and effective devices as well as to improve the quality of life for patients with medical devices.

NESTcc was developed to tackle the lack of **high quality, near real-time,** and **low cost evidence** to support:

Regulatory decision-making across the Total Product Life Cycle (TPLC) for the **FDA and medical device industry**

Clinical decision-making for **patients and clinicians**

Purchasing decisions and quality of care for **health systems**

Coverage decisions for public and private **payers**

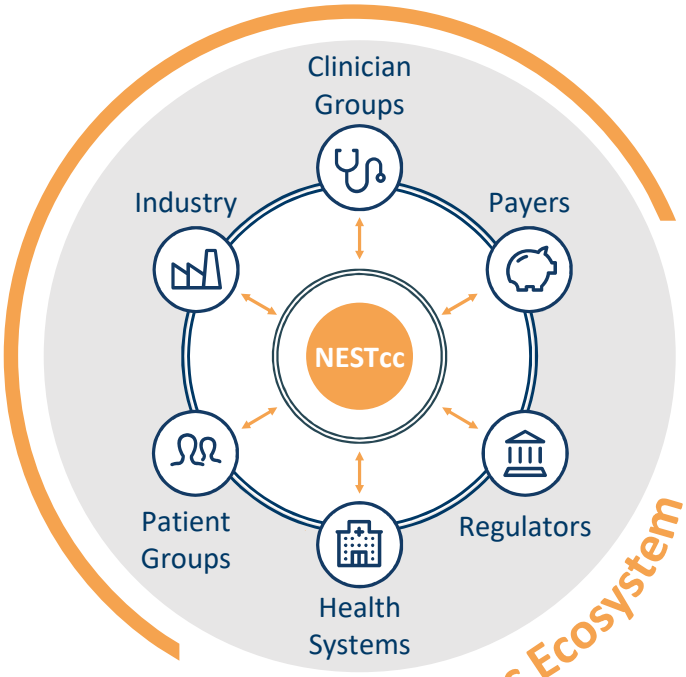
NESTcc'S ROLE IN THE ECOSYSTEM

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).



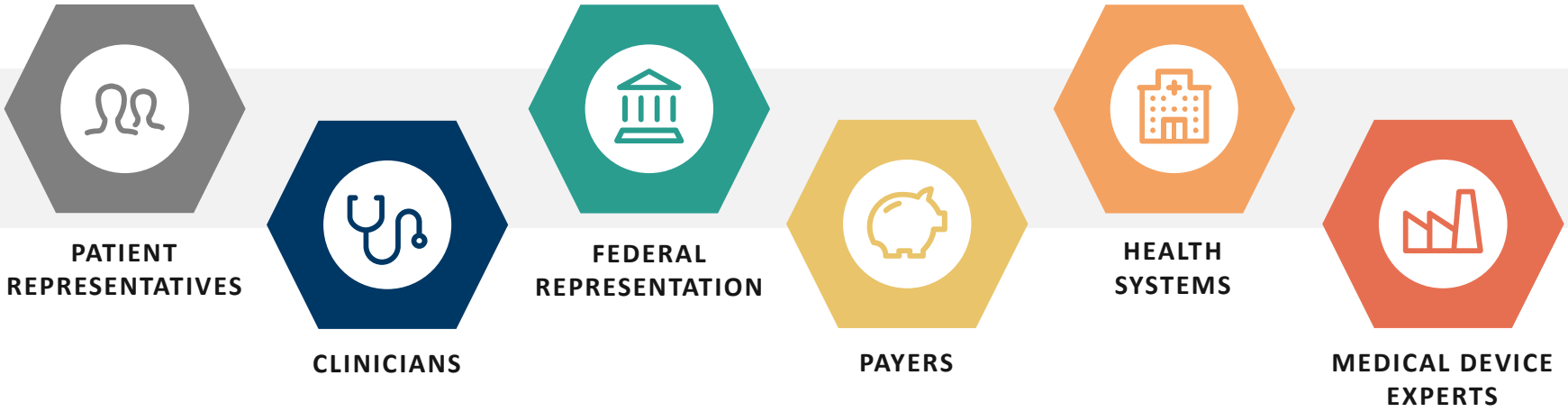
The NESTcc Ecosystem

What value is NESTcc adding to the ecosystem that is not already there ?

ESTABLISH NESTcc GOVERNANCE

Through an open call for nominations published in January 2017, the inaugural NESTcc Governing Committee was formed.

The NESTcc Governing Committee represents a **diverse set of stakeholder groups**, including:



NESTcc GOVERNING COMMITTEE

The NESTcc Governing Committee represents stakeholders across the medical device ecosystem.

NAOMI ARONSON
Blue Cross Blue Shield Association (BCBSA)

KATHLEEN BLAKE
American Medical Association (AMA)

MARK DEEM – MDMA Nominee
The Foundry, LLC

PAMELA GOLDBERG
Medical Device Innovation Consortium (MDIC)

BILL HANLON – ACLA Nominee
LabCorp/Covance

ADRIAN HERNANDEZ
Duke Clinical Research Institute (DCRI)

HARLAN KRUMHOLZ
Yale University

ELIZABETH MCGLYNN
Kaiser Permanente

MICHELLE MCMURRY-HEATH – AdvaMed Nominee
Interim Governing Committee Chair
Johnson & Johnson Medical Devices

VANCE MOORE
Mercy Health

JEFFREY SHUREN
FDA, CDRH

SHARON TERRY
Genetic Alliance

DIANE WURZBURGER – MITA Nominee
GE Healthcare

MARC BOUTIN
National Health Council

TAMARA SYREK JENSEN
Center for Clinical Standards and Quality, CMS

■ Trade Association Nominees

Launching the NESTcc Data Network

DEVELOP NESTcc'S ROLE

NESTcc will develop its role to build a sustainable network of collaborators committed to advancing RWE generation.

Engage

- Designated 11 **NESTcc Demonstration Projects** to learn opportunities and challenges of using RWE to meet regulatory and coverage requirements
- Initiated **analysis of the value for industry stakeholders of RWE**

Leverage

- Executed MOUs with initial set of **11 NESTcc network collaborators** to begin to establish NESTcc's Data Network launch
- Began implementing feasibility testing with network collaborators for **test-cases** from industry

Transform

- In 2018, will identify barriers for **research-ready medical device data infrastructure** and work to address these
- In 2018, will establish **data quality** and **methods standards**

DEVELOP NESTcc'S ROLE: DEMONSTRATION PROJECTS

NESTcc is focusing on leveraging RWE in use cases across the total product life cycle.

Ability to Support Use Cases Across the Total Product Life Cycle (TPLC)

Engage

Leverage

Transform

Principle Investigator(s), Demonstration Project	Pre-Market: Pre-Market Approval, 510(k), De Novo	Label Expansion	Post-Market: including Post-Approval Studies (PAS)	Surveillance	Coverage
Morales, Cronenwett, Thatcher: RAPID	○				
Kong, White, Krucoff: SAFE-STEMI	○				
Dreyer: Lung-RADS	△		△		
Waters: SHIELD			□		
Goodney, Sedrakyan: Vascular Implant Networks				○	
Resnic: ICD-DELTA				○	
Dujmovic, Hinrichs, Johnson, Slotwiner: EP PASSION			○		
Atwater & Piccini: Medicare & Implantables			○		
Lampert: mHealth			○		
Johnson & Drozda: EHR-Based Data Network	○				
Ross & Shah: mHealth			○		

Pre-Market — Regulatory Decision — Post-Market

Key: △ Imaging, □ Diagnostics, ○ Traditional

DEVELOP NESTcc'S ROLE: DEMONSTRATION PROJECTS

NESTcc Demonstration Projects are studies that contribute to the field of RWE within the medical device ecosystem. While ranging in scope and size, Demonstration Projects are expected to:

- Develop, verify, and operationalize methods of evidence generation and data use in the pre- and post-market space
- Demonstrate scalability across healthcare systems, device types, and manufacturers
- Demonstrate impact on patients by stimulating innovation in medical device innovation and decreasing the timeline for development and market launch
- Inform NESTcc's strategy as it builds out critical functions and processes for a future sustainable organization

DEVELOP NESTcc'S ROLE: DEMONSTRATION PROJECTS

Demonstration Projects derive value across the development of NESTcc, informing NESTcc's strategy and execution.

Engage

Leverage

Transform

DEMONSTRATION PROJECTS:

- **Serve as Proof-of-Concept to Establish the Value of RWE**
- **Contribute to Methods Development**
- **Support NESTcc's Data Network**
- **Share Lessons Learned for using RWE**

DEVELOP NESTcc'S ROLE: TEST-CASES

NESTcc solicited submissions from industry for RWE test-cases that we will seek to implement with network collaborators.

Engage

Leverage

Transform

Test-cases were sought to assess feasibility and are intended to explore the network collaborators' ability to capture the data needed to support a range of studies and analyses.

GOALS OF TEST-CASES

- Solicit test-cases from medical device manufacturers to understand their **evidence generation needs**
- Explore NESTcc **network collaborators'** ability to capture the data needed to support a range of studies and analyses
- Test and understand the unique **capabilities** of the NESTcc Data Network
- Assess the **feasibility** of NESTcc's envisioned Data Network

DEVELOP NESTcc'S ROLE: TEST-CASES

NESTcc solicited submissions from industry for RWE test-cases to assess feasibility. Test-cases are intended to explore network collaborators' ability to capture data needed to support a range of studies and analyses.

Engage

Leverage

Transform

Submission Deadline – January 31, 2018

NESTcc received **nine test-cases** as a result of its Call for Concepts from medical device manufacturers.

Review and Selection – February 2018

Each concept was reviewed by two to four reviewers from MDIC staff and the FDA through objective evaluation criteria. **Non-MDIC staff were required to disclose COI and sign NDAs with MDIC.**

Feasibility Conversations – March and April 2018

NESTcc network collaborators will be consulted to **assess the feasibility** of test-cases using Concept Proposals submitted by manufacturers

SNAPSHOT OF TEST-CASES

- ✓ Represent both small and large manufacturers
- ✓ Span the Total Product Life Cycle (TPLC) including pre-market, patient management and clinical guidelines, label expansion, post-market surveillance, and quality measurement
- ✓ Cover a range of device types including dermatology, cardiovascular, vascular, orthopedics, and surgery

DEVELOP NESTcc'S ROLE: TEST-CASES

To better understand the capabilities of its Data Network, NESTcc is facilitating collaboration between network collaborators and test-case manufacturers, whose de-identified concepts are summarized below:

Engage

Leverage

Transform

TOTAL-PRODUCT LIFE CYCLE (TPLC) ALIGNMENT	PRODUCT(S)	AREA
Pre-Market Submission	Topical Skin Adhesive	Dermatology
Label Expansion	Devices used in Rx of Atrial Fibrillation	Cardiovascular
Label Expansion	Stent graft component product	Vascular
Move from General to Specific Indication	Device used in surgery	Surgery
Post-market Surveillance	Knee replacement	Orthopedics
Post-market Surveillance	Various Devices	Orthopedics
Patient Management Clinical Guidelines	Anti-coagulation dosage following mechanical heart valve (MHV) replacement	Cardiovascular
Quality Measurement	Endoscopes	General Hospital Device

DEVELOP NESTcc'S ROLE: TEST-CASES

NESTcc has identified two test-cases examining orthopedic devices that are undergoing feasibility testing with network collaborators.

Engage

Leverage

Transform

ORTHOPEDIC TEST-CASE EXAMPLE I

- ✓ Explore the feasibility of using real world data (RWD) for proactive post-market surveillance that fulfills regulatory obligations (necessary data elements, sufficient sample size, and representativeness of the sample for purposes of generalizability to the patient population of users) for three orthopedic devices.
- ✓ The population of interest is patients undergoing craniofacial reconstruction (mostly pediatric patients), spinal decompression/intervertebral body fusion, and ligament/tendon joint attachment.
- ✓ The project will explore proactive surveillance for each device of interest.

ORTHOPEDIC TEST-CASE EXAMPLE II

- ✓ Evaluate the feasibility of combining a limited sample of registry data with private claims payments from NESTcc network collaborators.
- ✓ Project will look at primary total knee replacement surgical procedures and implants in younger (<65 years of age) patients.
- ✓ Outcomes of interest will include readmission, reoperation, and revision (removal of implant).
- ✓ The project will look at 90 day, 1 year, and 2 year post-surgery data, as available from collaborators.

DEVELOP NESTcc'S ROLE: BUILDING A DATA NETWORK

NESTcc has established relationships with network collaborators to advance evaluation and use of high-quality RWD from various sources.

TO DATE, MEMORANDA OF UNDERSTANDING (MOUs) HAVE BEEN SIGNED WITH 11 COLLABORATORS:

Duke University Health System • Healthcore • Lahey Clinic • Mayo Clinic • MDEpiNet • Mercy Health • PEDSnet • University of Florida Health System • Vanderbilt University Medical Center • Weill-Cornell Medical Center • Yale New Haven Health System

DEVELOP NESTcc'S ROLE: BUILDING A DATA NETWORK

NESTcc surveyed its Data Network to determine current capabilities, gaps, and priority areas.

Engage

Leverage

Transform

11

Network Collaborators

Duke University Health System • Healthcore • Lahey Clinic • Mayo Clinic • MDEpiNet • Mercy Health • PEDSnet • University of Florida Health System • Vanderbilt University Medical Center • Weill-Cornell Medical Center • Yale New Haven Health System

Network collaborators represent:

150 Hospitals

3,042+ Outpatient Clinics

Patient data represents:

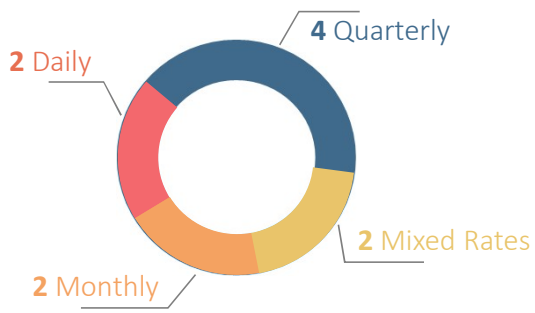
469M+

Patient Records

Common data models:

- ✓ I2b2
- ✓ OMOP
- ✓ PCORnet
- ✓ Sentinel

Collaborators report regular data refreshes:



Most cited expertise:

- ✓ Cardiovascular and Cardiac Surgery
- ✓ Women's Health
- ✓ Neurosurgery
- ✓ Gastroenterology
- ✓ Orthopedic

DEVELOP NESTcc'S ROLE: BUILDING A DATA NETWORK

Collaborators comprising the NESTcc Data Network have access to a range of available data sources, including those listed below.

Engage

Leverage

Transform

AVAILABLE DATA SOURCES

UDI IMPLEMENTATION

***Registries Include (but are not limited to):**

- Anesthesia Quality Institute's National Anesthesia Clinical Outcomes
- Cardiac Catheterization
- Cardiogenic Shock
- Immunization
- Implant registries
- Integrated tumor
- International Consortium Lower-GI
- American College of Surgeons National Surgical Quality Improvement Program
- Oncology
- Pediatric Cardiomyopathy
- Prostate Ablation-Related Energy Devices
- Robotic Surgery
- Society of Thoracic Surgeons National Database
- Society for Vascular Surgery
- Thalassemia Clinical Research Network - Thalassemia Registry
- Vital Records (Birth and Death)

DEVELOP NESTcc'S ROLE: BUILDING A DATA NETWORK

NESTcc will support its Data Network by helping streamline administrative processes, reducing transaction costs, and offering research assistance.

Engage

Leverage

Transform

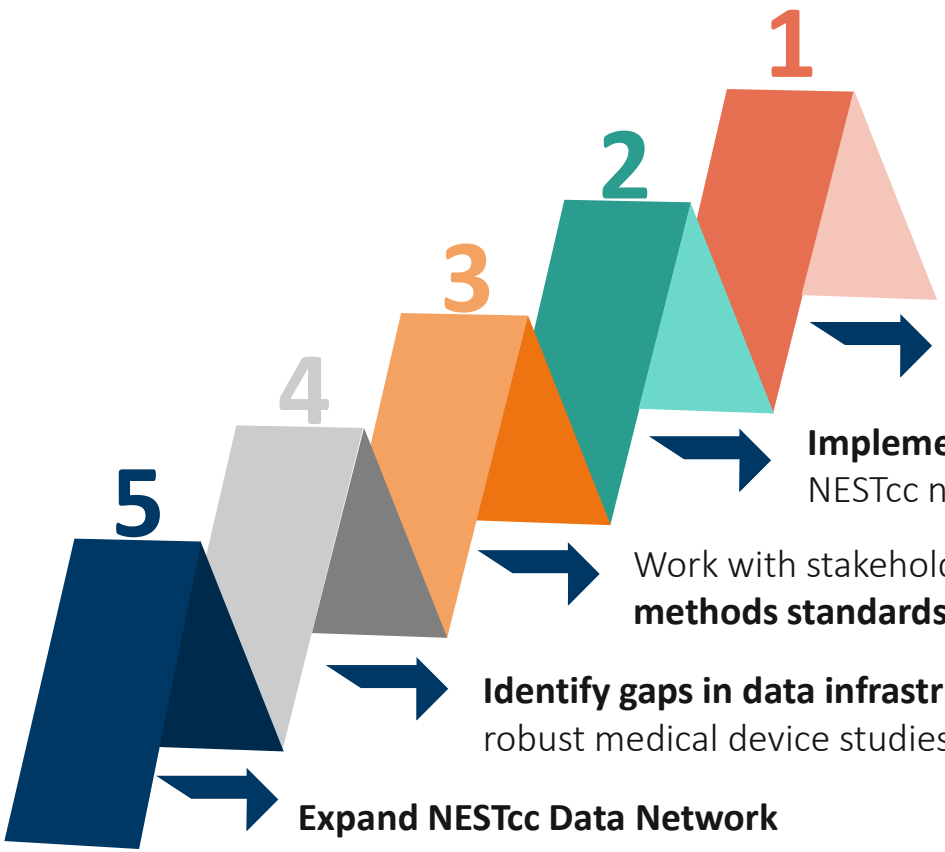
REDUCING TRANSACTION COSTS

- ❑ Putting in place an umbrella non-disclosure agreement (NDA) with NESTcc Network Collaborators
- ❑ Developing a participation agreement defining roles and responsibilities of NESTcc and Network Collaborators
- ❑ Developing a Master Services Agreement between the Network Collaborators and the NESTcc to accelerate contracting time

TYPES OF RESEARCH OFFERED

- ❑ Prep to research questions (e.g. size and type of patient population with a specific condition or device)
- ❑ Identification of patients for clinical trials and identification of clinical trial sites
- ❑ Retrospective observational studies with de-identified data
- ❑ Prospective observational studies with patient consent
- ❑ Patient surveys and patient-generated data with patient consent
- ❑ Interventional/randomized studies (not in the short term)

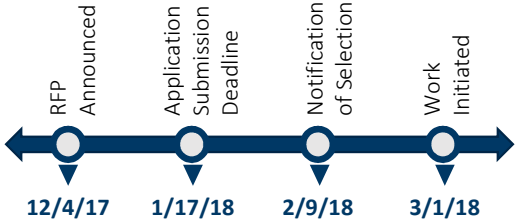
NESTcc DATA NETWORK TIMELINE 2018



1. Establish initial **NESTcc Data Network** with 11 collaborators
2. **Implement test-cases** with manufacturers and NESTcc network collaborators
3. Work with stakeholders to **establish data and methods standards, and operating processes**
4. **Identify gaps in data infrastructure** to support robust medical device studies and find solutions
5. **Expand NESTcc Data Network**

NESTcc PROGRESS: A SNAPSHOT

Selected Teams for RWE Assessment and Value Analysis Initiatives



Initial Data Network Underway

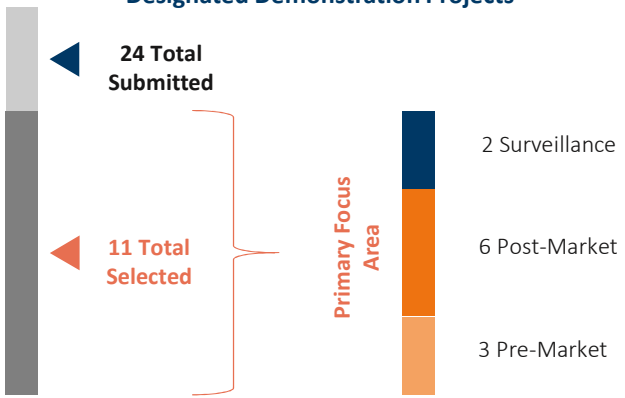
NESTcc Network Collaborators Represent:

11 Collaborators

150 Hospitals

3,042+ Outpatient Clinics

Designated Demonstration Projects



@NESTccMedTech www.nestcc.org

Governing Committee Activity

Seven Governing Committee Meetings

Average attendance of 11/15 members per meeting

Business Plan Input

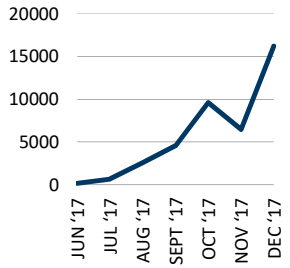
Communications Platforms Launched

June 2017
NESTcc Twitter (@NESTccMedTech)

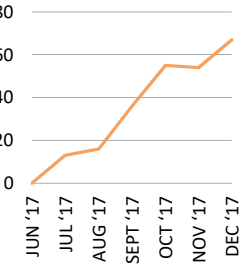
November 2017
NESTcc LinkedIn

December 2017
NESTcc Website (www.nestcc.org)

Social Media Engagement



Twitter Impressions



Twitter Followers

Events and Conferences

2017 Key Conference Presentations

September
- RAPS
- IMDRF Open Stakeholder Day
- NIH Grand Rounds
- AdvaMed MedTech Conference

October
- MDIC Annual Public Forum
- MDEpiNet Annual Meeting
- ICHOM

November
- TCT 2017

Upcoming Events and Conferences

Confirmed
- Health Datapalooza – April 26-27, 2018
- FDA/Xavier MedCon Conference – May 1-4, 2018
- ISPOR Baltimore – May 19-23, 2018

Submitted
- Academy Health 2018 ARM – June 24-26, 2018
- RAPS Regulatory Convergence 2018 – October 1-4, 2018

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@Fleurence

Innovation in Evidence Generation to Support Expedited Access to Medical Device Technologies

Jing Xie, Ph.D.

Vice President

Clinical Affairs & Office of Medical Affairs

Medtronic

Jing Xie, Ph.D.

Dr. Xie currently serves as the Vice President, Clinical Affairs and Office of Medical Affairs at Medtronic Spine. In this role, she strategically leads and directs clinical and medical affairs activities globally.

Prior to Medtronic, Dr. Xie was the Vice President of Clinical Affairs for the Medical Device Innovation Consortium (MDIC) where she worked closely with FDA, payers and industry on identifying challenges and opportunities to advance regulatory science with the mission to expedite patient access to innovative medical device technologies. Prior to that role, Dr. Xie was the Vice President of Global Clinical Affairs for Zimmer Biomet.

Dr. Xie holds a Bachelor of Science degree in analytical chemistry from Xiamen University as well as a Master of Science degree in chemistry and PhD in materials science from the University of Alabama. She also holds a Master of Science degree in computer science from Purdue University.

19 April 2018

INNOVATION IN EVIDENCE GENERATION

SUPPORTING EXPEDITED ACCESS TO MEDICAL DEVICE TECHNOLOGIES

Jing Xie, PhD

VP, Clinical and OMA - Medtronic Spine & Biologics

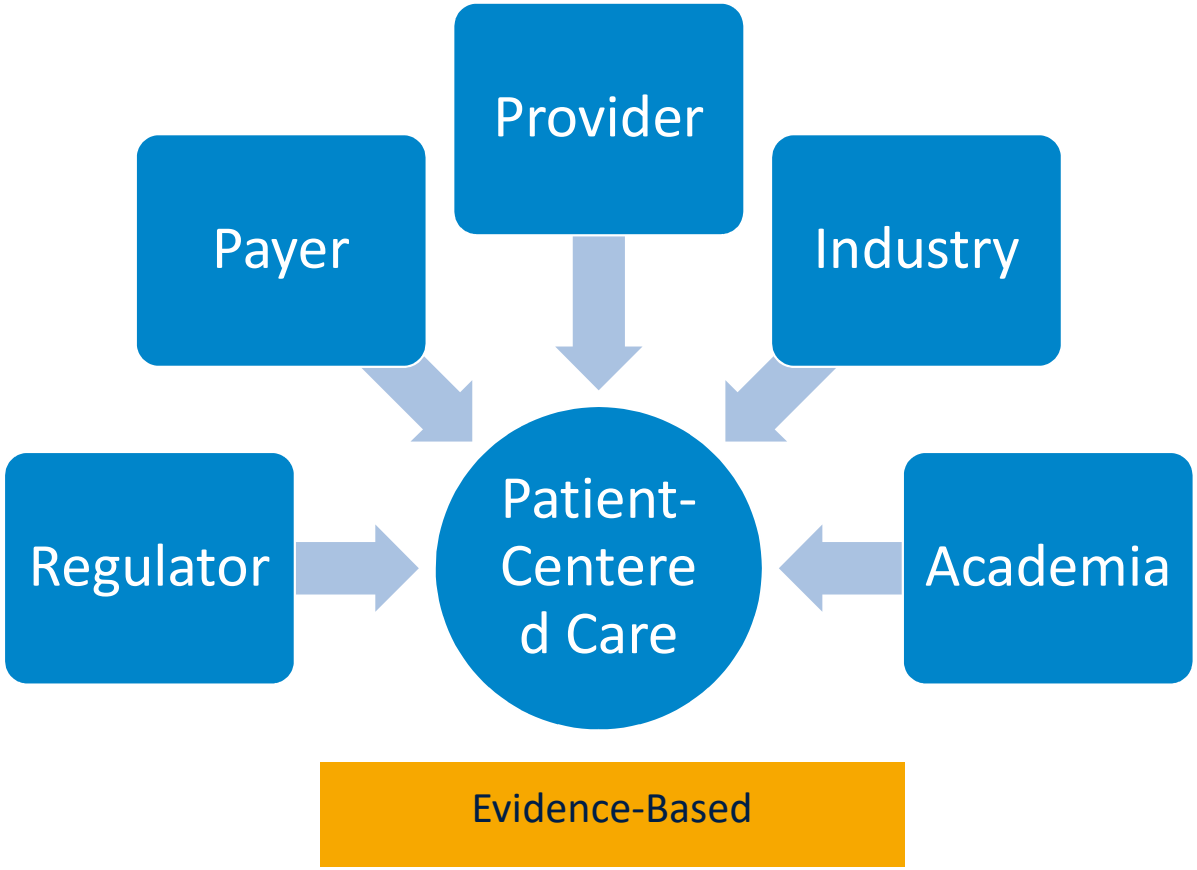
Medtronic

Further, Together

TOPICS

- Driver for Innovation in Evidence Generation
- Transforming Evidence Generation
- Critical Roles of Real-World Data (RWD) and Real-World Evidence (RWE)
- Applications of RWD and RWE
- Optimizing Evidence Generation
- Factors to Successful Adoption of RWD and RWE

HEALTHCARE ECOSYSTEM



DRIVER FOR INNOVATION IN EVIDENCE GENERATION

NEEDS

- Early Access to New Technologies of Public Health Importance
- Evidence-based VBHC
- Evidence to Inform Care Pathway Decision (Multifactorial)
- Patient-centered Care (e.g. which population benefits most?)
- Increased Requirements on Safety Surveillance

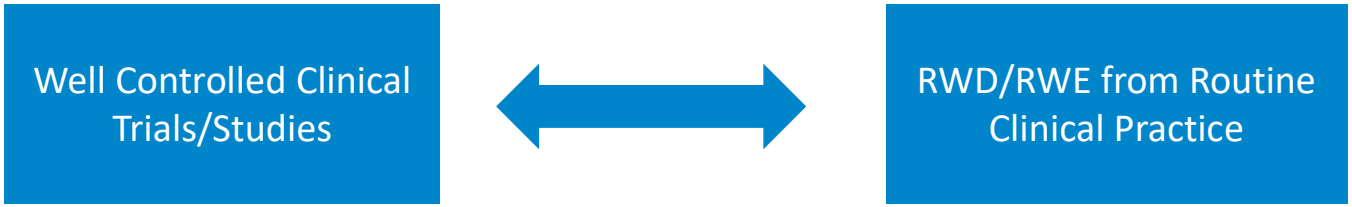
OPPORTUNITIES

- Growing Availability of RWD
- New Data Analytic Methodologies
- IT Infrastructure
- Willingness of Multi-stakeholder Engagement

FAST ACCUMULATION OF DATA

REFLECTING REAL-WORLD PRACTICE

TRANSFORMING EVIDENCE GENERATION



Efficacy

Can It Work?

- Selected populations
- Highly controlled setting
- Optimized to show Efficacy

Effectiveness

Does It Work?

- Diverse patient population
- Diverse surgeon skills
- Diverse hospital settings

TRANSFORMING EVIDENCE GENERATION

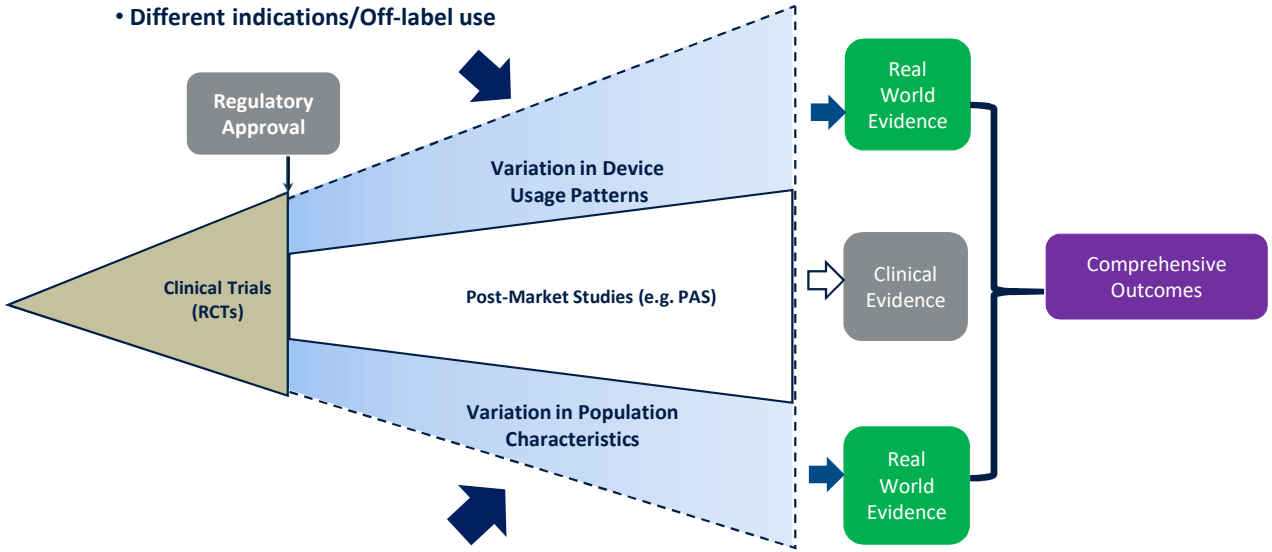
Clinical Trials/Studies

Real World Evidence

*http://medcommsnetworking.com/presentations/shaw_070716.pdf

CRITICAL ROLES OF RWD AND RWE

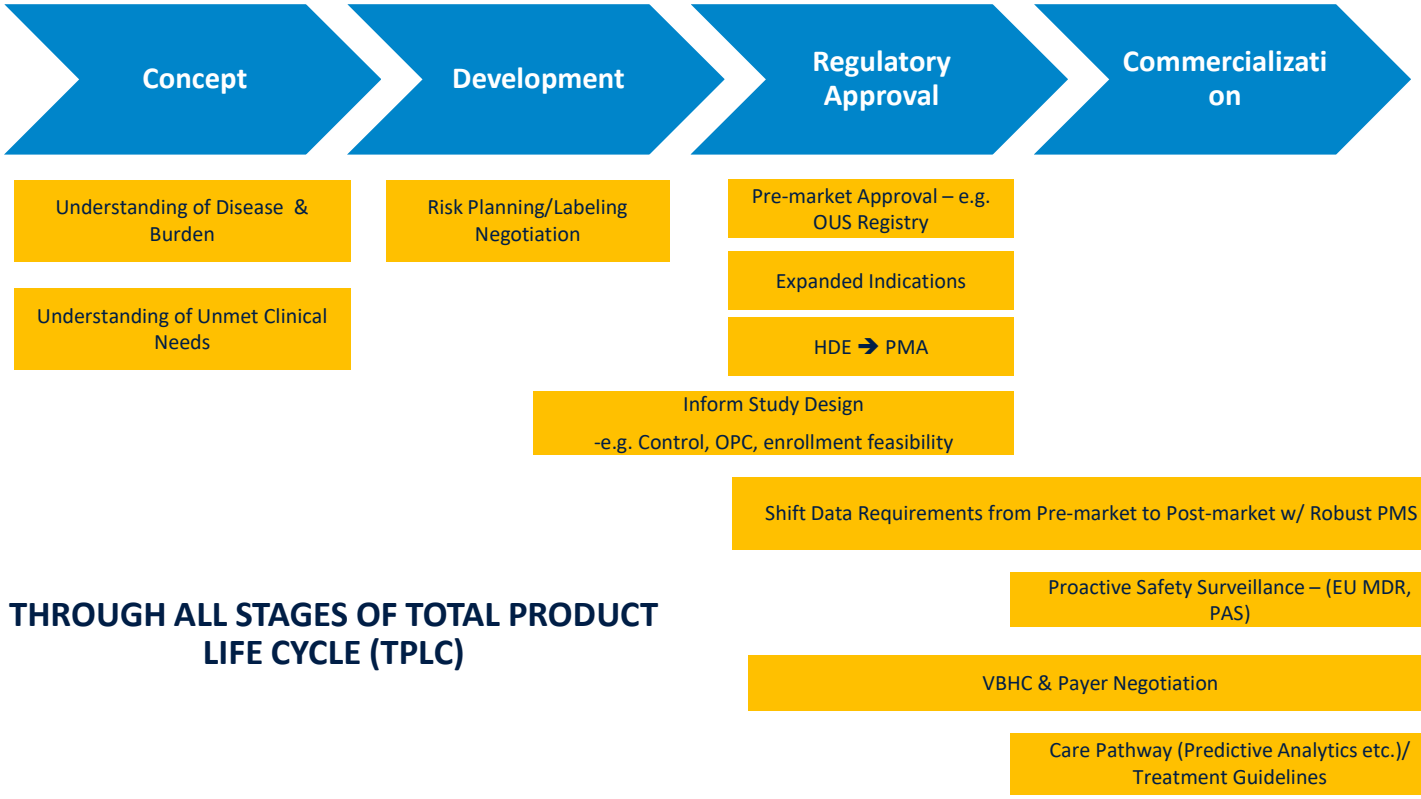
- **Different patient populations –age, race, ethnicity and gender distribution**
- **Variation in severity level of concomitant diseases**
- **Different (Unstudied) concomitant therapies**
- **Variation in care pathways**
- **Different indications/Off-label use**



RWD/RWE PROVIDES <u>INSIGHTS NOT POSSIBLE SOLELY</u> FROM CLINICAL STUDIES

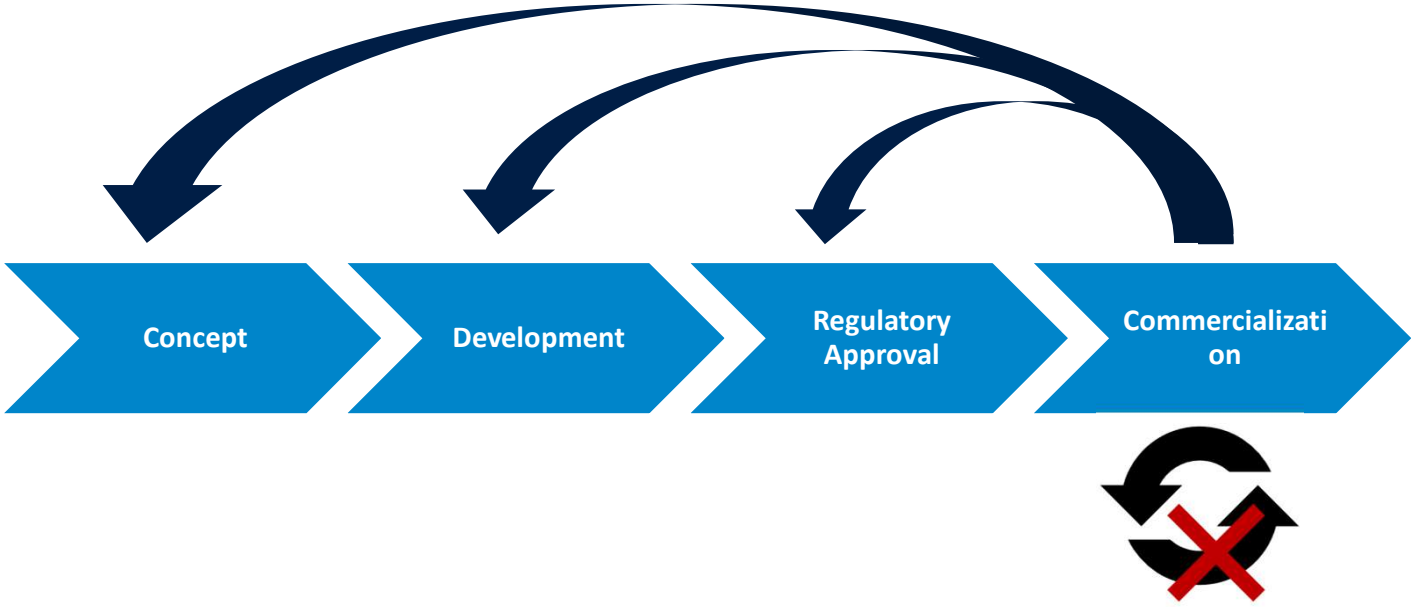
**https://sites.duke.edu/diss2017/files/2017/09/S2B_MitchDeKoven_DISS2017.pptx*

APPLICATIONS OF RWD AND RWE



THROUGH ALL STAGES OF TOTAL PRODUCT LIFE CYCLE (TPLC)

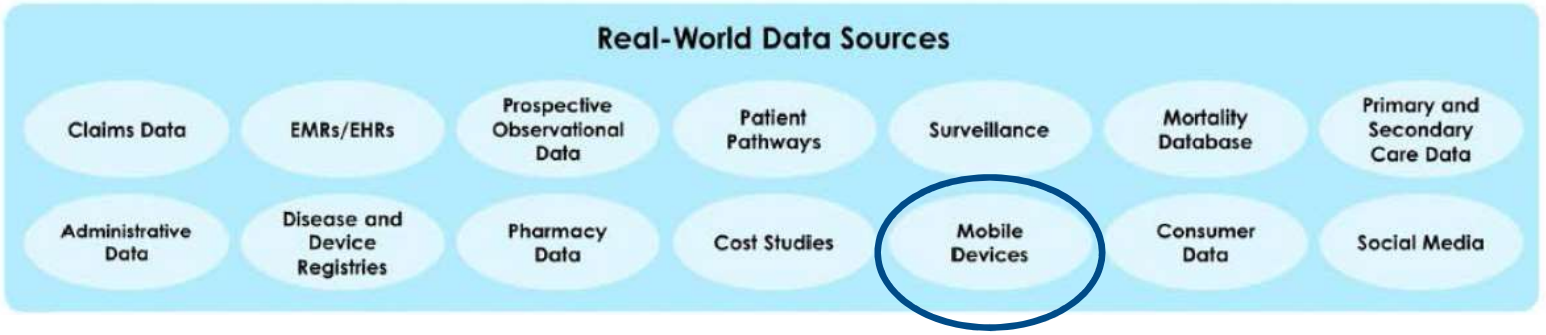
APPLICATIONS OF RWD AND RWE



FACILITATE CONTINUUM OF EVIDENCE GENERATION AND LEARNING

IMPROVE DECISION MAKING AND OUTCOMES THROUGH ALL STAGES OF TPLC

MOBILIZING RWD/RWE GENERATION



Patient-Driven/Facing

- Mobile Apps
- Wearables/Sensors

- High frequency patient data collection
- Cost effective longitudinal follow-ups
- Reduce lost-to-Follow-up
- Objective patient outcomes (Orthopaedics) in a real-world setting

OPTIMIZING EVIDENCE GENERATION

- Clinical Studies and RWD/RWE provides different aspects of evidence to support device performance and safety
- They complement each other
  - Opportunities to shift data from pre-market to post-market
  - RWD/RWE in lieu of PAS
- They do not necessarily have to be sequential
  - Our goal is to timely fill knowledge GAP (can it work ➔ does it work?)
  - Hybrid of clinical study and RWD/RWE to support regulatory decision
  - Embedded clinical studies in routine clinical practices - mimicking real-world setting
- Fit-for-Purpose approach ➔ Focus on ability to address regulatory/scientific questions based on strengths and limitations of Clinical Study and RWD/RWE

FACTORS TO SUCCESSFUL ADOPTION OF RWD/RWE

Engagement & Sustainability	• Full engagement of all stakeholders • Value Proposition that resonates with each stakeholder • Robust business models for all the required stakeholders to make this work
Data Quality & Robustness	• Don't underestimate the challenges of getting reliable / clean data for the required data models • Establish Quality criteria and understand the limitation of each type of RWD • Still requires robust Data Mining & Sampling Plan
Governance, Privacy and Legal	• Data ownership, access, usage and interpretation • Leveraging technologies in order to minimize data transfers • Fit-for-Purpose: procedural level vs aggregated
Learn by Doing	• Get Started • Multi-stakeholder engagement • Where/how to apply – Guidance and Training are critical

THANK YOU

BREAK

Real World Evidence Panel Discussion

Michelle McMurry-Heath
Josh Chetta
Rachael Fleurence
Jing Xie
Dr. Stephen Weber
Dr. Vincent Devlin

Meeting Adjournment

Don't Forget!

Please leave your
name tag
on the table.