Advancing NESTcc Real-World Evidence Test-Cases

Robbert Zusterzeel, MD, PhD, MPH
Data Network Director, NESTcc

September 5, 2019
PANEL SESSION AGENDA

• 3:10 – 3:15 p.m. – Introduction and Overview of NESTcc Test-Cases
  o Robbert Zusterzeel, MD, PhD, MPH - NESTcc (Moderator)

• 3:15 – 3:25 p.m. – Test-Case: Intervertebral Body Fusion Devices
  o Fred Resnic, MD, MSc - Lahey Hospital and Medical Center

• 3:25 – 3:35 p.m. – Test-Case: mHealth for Insomnia
  o Frances Thorndike, PhD - PEAR Therapeutics

• 3:35 – 3:45 p.m. – Test-Case: Synthetic Mesh Sling
  o Ron Yustein, MD - FDA Center for Devices and Radiological Health (CDRH)

• 3:45 – 3:55 p.m. – Panel & Audience Q&A
  o Robbert Zusterzeel, MD, PhD, MPH - NESTcc (Moderator)
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

2012
- FDA proposed the development of a **national system**
- NESTcc envisioned as a **voluntary data network** of collaborators by Planning Board

2015
- NESTcc Executive Director named and Governing Committee selected

2016
- FDA awarded funding for NESTcc to **Medical Device Innovation Consortium (MDIC)**

2017
- NESTcc Strategic and Operational Plan developed

2018
- Initial NESTcc Data Network formed and testing initiated through Round 1 Test-Cases
- NESTcc Data Quality and Methods Subcommittees formed

2019
- Interim and Final Results from **Round 1 and Round 2 Test-Cases**
- NESTcc Version 1.0 is operational

2022
- NESTcc **fully launched and operational**
Establishing the NESTcc Data Network
ESTABLISHING THE NESTcc DATA NETWORK

NESTcc has established relationships with 12 Network Collaborators to advance evaluation and use of high-quality Real-World Data (RWD) from various sources. Profiles of each Network Collaborator can be found on NESTcc’s website.
NESTcc surveyed its Network Collaborators to determine current capabilities, gaps, and priority areas.

**Network Collaborators represent**
- 195 Hospitals
- 3,942+ Outpatient Clinics

**Common data models**
- I2b2
- OMOP
- PCORnet
- Sentinel

**Network Collaborators report regular data refreshes**
- 2 Daily
- 3 Monthly
- 4 Quarterly
- 3 Mixed Rates

**Most cited expertise**
- Cardiovascular and Cardiac Surgery
- Women’s Health
- Neurosurgery
- Gastroenterology
- Orthopedic

**Patient data represents**
- 494M+*

*Does not account for duplicate records

**Patient Records**

Numbers reflect data as of February 2018
Utilizing the NESTcc Data Network
PROGRESSIVE EXPANSION OF THE NESTcc CAPABILITIES AND USES

Since 2018, NESTcc has been progressively developing the capabilities of the NESTcc Data Network through Test-Cases with the NESTcc Network Collaborators.

2018
ADDRESS RETROSPECTIVE RESEARCH QUESTIONS FROM MEDICAL DEVICE MANUFACTURERS

2019
ADDRESS QUESTIONS FROM STAKEHOLDERS, INCORPORATING PATIENT-GENERATED DATA (PGD) FOR PROSPECTIVE RESEARCH QUESTIONS

2019
UTILIZE THE NETWORK TO ADDRESS ACTIVE SURVEILLANCE SAFETY SIGNAL REFINEMENT

2020
UTILIZE THE NETWORK’S CAPABILITY TO DETECT SAFETY SIGNALS
The following process outlines the Test-Case process that has taken place:

1. **Organization submits question**
2. **Network Collaborators opt-in**
3. **NESTcc matches manufacturer and collaborators**
4. **Collaborators submit project short forms**
5. **Collaborators submit full project proposal**
6. **Lessons and gaps are sent to NESTcc**
7. **Project is executed**

**NESTcc awards funding**

**Call for submissions posted**

1. **Final Selection Team project-level approval**
2. **GC slate approval**
3. **MDIC Board slate approval**
4. **FDA project-level approval**

START HERE
**NESTcc Test-Cases Address a Range of Device Questions**

NESTcc’s Test-Cases span a wide range of devices classes, regulatory pathways, TPLC stages, data sources, and disease areas.

<table>
<thead>
<tr>
<th>TPLC Alignment</th>
<th>Regulatory Pathway</th>
<th>Device Classes</th>
<th>Disease Area</th>
<th>Data Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Market</td>
<td>510(k)</td>
<td>Class I</td>
<td>Cardiology</td>
<td>Claims</td>
</tr>
<tr>
<td>Label Expansion</td>
<td>PMA</td>
<td>Class II</td>
<td>Dermatology</td>
<td>Electronic Health Records (EHR)</td>
</tr>
<tr>
<td>Post-Market</td>
<td></td>
<td>Class III</td>
<td>Ear, Nose, &amp; Throat</td>
<td>mHealth</td>
</tr>
<tr>
<td>Coverage</td>
<td></td>
<td></td>
<td>Mental Health</td>
<td>Patient-Generated health Data (PGD)</td>
</tr>
<tr>
<td>Surveillance</td>
<td>(Active)</td>
<td></td>
<td>Oncology</td>
<td>Registries</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Orthopedics</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Respiratory</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Stress Urinary Incontinence</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Surgery</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Vascular</td>
<td></td>
</tr>
<tr>
<td>TOTAL-PRODUCT LIFE CYCLE (TPLC) ALIGNMENT</td>
<td>DISEASE AREA</td>
<td>TECHNOLOGY OF INTEREST</td>
<td>DATA SOURCES</td>
<td></td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>--------------</td>
<td>---------------------------------------------------------------------------------------</td>
<td>---------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Pre-market Submission</td>
<td>Dermatology</td>
<td>Wound Closure Devices (topical skin adhesives, staples, sutures)</td>
<td>Claims; Electronic Health Records (EHR)</td>
<td></td>
</tr>
<tr>
<td>Label Expansion</td>
<td>Vascular</td>
<td>Endovascular stent</td>
<td>Registry</td>
<td></td>
</tr>
<tr>
<td>Label Expansion</td>
<td>Cardiology</td>
<td>Catheters used in Rx of Cardiac Arrhythmias</td>
<td>EHR</td>
<td></td>
</tr>
<tr>
<td>Label Expansion</td>
<td>Cardiology</td>
<td>Mechanical Aortic Heart Valves</td>
<td>EHR; Registry</td>
<td></td>
</tr>
<tr>
<td>Label from General to Specific Indication</td>
<td>Surgery</td>
<td>Microwave Ablation Device</td>
<td>EHR</td>
<td></td>
</tr>
<tr>
<td>Post-market Surveillance</td>
<td>Orthopedics</td>
<td>Total Knee Arthroplasty</td>
<td>Claims; Registry</td>
<td></td>
</tr>
<tr>
<td>Post-market Surveillance</td>
<td>Orthopedics</td>
<td>Craniomaxillofacial Bone Distractors</td>
<td>EHR</td>
<td></td>
</tr>
<tr>
<td>Post-market Surveillance</td>
<td>Orthopedics</td>
<td>Intervertebral Lumbar Body Fusion Devices</td>
<td>Claims; EHR</td>
<td></td>
</tr>
<tr>
<td>TOTAL-PRODUCT LIFE CYCLE (TPLC) ALIGNMENT</td>
<td>DISEASE AREA</td>
<td>TECHNOLOGY OF INTEREST</td>
<td>DATA SOURCES</td>
<td></td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>--------------</td>
<td>------------------------</td>
<td>--------------</td>
<td></td>
</tr>
<tr>
<td>Pre-Market Submission</td>
<td>Oncology</td>
<td>Lung Cancer Diagnostic</td>
<td>Electronic Health Records (EHR)</td>
<td></td>
</tr>
<tr>
<td>Pre-Market Submission</td>
<td>Cardiovascular</td>
<td>Electrode Renal Denervation System</td>
<td>EHR</td>
<td></td>
</tr>
<tr>
<td>Pre-Market Submission; Label Expansion</td>
<td>Cardiovascular</td>
<td>Cardiovascular Device</td>
<td>Claims</td>
<td></td>
</tr>
<tr>
<td>Pre-Market Submission; Post-Market</td>
<td>Orthopedics</td>
<td>Annular Closure Device</td>
<td>Claims</td>
<td></td>
</tr>
<tr>
<td>Pre-Market Submission; Label Expansion; Surveillance</td>
<td>Orthopedics</td>
<td>Objective Performance Criteria (OPC) for Knee and Hip Implants</td>
<td>Claims; Registry</td>
<td></td>
</tr>
<tr>
<td>Post-Market; Surveillance; Coverage</td>
<td>Cardiology</td>
<td>Apple Watch Diagnostic + mHealth</td>
<td>EHR; Patient-Generated health Data (PGD)</td>
<td></td>
</tr>
<tr>
<td>Pre-Market Submission</td>
<td>Ear, Nose, and Throat</td>
<td>Ear Tubes</td>
<td>Claims; EHR</td>
<td></td>
</tr>
<tr>
<td>Post-Market; Surveillance</td>
<td>Cardiovascular</td>
<td>Cardiac Device Leads</td>
<td>Claims; EHR</td>
<td></td>
</tr>
<tr>
<td>Surveillance</td>
<td>Stress Urinary Incontinence</td>
<td>Synthetic Mesh Sling</td>
<td>EHR; Registry</td>
<td></td>
</tr>
<tr>
<td>Surveillance</td>
<td>Stress Urinary Incontinence</td>
<td>Urinary Mesh Software mHealth</td>
<td>PGD; Registry</td>
<td></td>
</tr>
<tr>
<td>Surveillance; Coverage</td>
<td>Mental Health</td>
<td>mHealth for Insomnia</td>
<td>EHR; PGD</td>
<td></td>
</tr>
<tr>
<td>Coverage</td>
<td>Respiratory</td>
<td>Positive Air Pressure, PAP Therapy</td>
<td>Claims; EHR; PGD</td>
<td></td>
</tr>
</tbody>
</table>
LAUNCHING NEST 1.0
NEST IS PREPARING FOR A PUBLIC LAUNCH

By the end of 2019, NESTcc will be operationally capable of intaking unsolicited projects from external stakeholders to utilize the capabilities of the NESTcc Data Network.

1. ENGAGE

Engage with NESTcc to develop a project and gain access to:
- Data Network Assets
- Pricing Structures
- Terms and Conditions

2. LAUNCH

Launch through collaborations with identified Network Collaborators:
- Execute required agreements
- Communicate with the FDA point of contact

3. EXECUTE

Execute the project through collaboration with the project team of Network Collaborators while engaging with NESTcc to ensure project progress

4. COMPLETE

Complete the engagement with NESTcc through the receipt of the final report, while participating in:
- Publications and dissemination opportunities
- Engaging directly with regulators and coverage providers for product-specific discussions and submissions

@MDICAnnualForum
Lessons from Round 1 Test Case:

A Network Collaborator Perspective

September 5, 2019

Frederic S. Resnic, MD MSc
Chairman, Department of Cardiovascular Medicine
Co-Director, Comparative Effectiveness Research Institute
Lahey Clinic Medical Center
Professor of Medicine
Tufts University School of Medicine
Topics for Discussion:

- Project Process and Phases
- Challenges Encountered
- Generalizable Lessons Learned
Round 1 Test Case: Vertebral Fusion Device Performance

- One of 8 initial test cases proposed by industry partners to explore the utility of EHR derived RWE in evaluating the performance of specific vertebral fusion devices.

- Network data collaborators responded to ‘RFP’ based on data availability and interest in topic. NESTcc served as ‘match maker’ to bring collaborators together with sponsors.

- Vertebral Fusion Devices were one of several topics Lahey was interested in from among the 8 proposed test cases. Interest based on subject matter (spine surgery), case volume and opportunity to explore methods for data extraction and analysis.

- First pass feasibility – ask the chief of spine surgery how many of these operations do we perform....
NESTcc surveyed its Data Network to determine current capabilities, gaps, and priority areas.

**COMPOSITION OF LAHEY CLINIC NETWORK**

<table>
<thead>
<tr>
<th>AVAILABLE DATA SOURCES</th>
<th>AVAILABLE DATA TYPES</th>
</tr>
</thead>
<tbody>
<tr>
<td>EHR</td>
<td>Demographics</td>
</tr>
<tr>
<td></td>
<td>Encounters</td>
</tr>
<tr>
<td></td>
<td>Diagnoses</td>
</tr>
<tr>
<td></td>
<td>Procedures</td>
</tr>
<tr>
<td>Public Claims</td>
<td>Vitals</td>
</tr>
<tr>
<td></td>
<td>Labs</td>
</tr>
<tr>
<td>Private Claims</td>
<td>Death</td>
</tr>
<tr>
<td></td>
<td>PROs</td>
</tr>
</tbody>
</table>

Lahey CERI Database System

- Research Data Warehouse: de-identified OMOP v4 based on Epic Clarity (>10,000 data tables)
- Includes device UDI captured by barcode scanning at point of care.
- Formal data quality audit program
- Flexible Valueset definition management system.
- Supports PRO if captured through patient portal (or local DB).
Round 1 Test Case: Major Challenges

- **Exposure Identification**: Deep domain knowledge required to identify appropriate comparator devices from extensive list of implants used during spinal surgery.

- **Changes in EHR Documentation**: Over time, EHR system updates change where data reside. Example: Opioid equivalent dose calculation.

- **Temporal Mapping**: Defining exposure windows (pre- and post-operatively) for clinical comorbidities, medications and adverse events.

- **Valueset Changes**: Definitions of covariates and outcomes change as protocol is refined by multi-stakeholder group.
Round 1 Test Case: Lessons Learned (so far....)

• **It Takes a Village**: Expertise required in disparate disciplines including clinical domain, informatics, statistics, and medical device ecosystem.

• **Write it Down**: Clearly written protocol, with amendments for any changes is essential to valid analysis and to avoid perception of data mining.

• **Valueset Management**: Definitions of covariates and outcomes vary with purpose and change as protocol is refined. RWD systems must actively manage and implement these definitions.
Prescription Digital Therapeutics (PDTs)
A new therapeutic class that is being integrated into standard of care

“Software as therapeutic” that treat serious diseases with high unmet medical need

PDTs meet stringent regulatory requirements related to:
- Safety and effectiveness of clinical data
- Regulatory labeling
- Payers to evaluate coverage based on traditional therapeutic coverage mechanisms

---

Insomnia: A Public Health Burden

- Insomnia is a major public health problem. 1 in 3 adults complain of insomnia symptoms\(^1\). About 10% have diagnosable chronic insomnia.\(^1\)\(^-\)\(^3\)

- Insomnia imposes significant medical, psychological, and financial burden in patient lives.\(^4\)\(^-\)\(^6\)

- FDA is reviewing a PDT product candidate designed to treat adults with chronic insomnia and depression by using CBT for insomnia and sleep restriction.

- Background research:
  - 8 completed and published clinical trials\(^7\)\(^-\)\(^15\) and 14 ongoing studies in range of diseases including oncology, diabetes, depression, asthma, HIV, anxiety.
  - But no healthcare utilization data outside of self-report.

References
1. Roth J Clin Sleep Med 2008
4. Ozminkowski et al. Sleep 2007
5. Taylor et al. Behavioral Sleep Medicine 2003
6. Morin et al. Sleep Medicine Clinics 2013
7. Batterham et al. BJPsych Open. 2017
8. Hagatun et al, Behavioral Sleep Medicine, 2017
9. Ritterband et al, JAMA Psychiatry 2017
12. Ritterband et al, Psycho-Oncology, 201.
NestCC: Use of Real-World Data To Evaluate Use of a Prescription Digital Therapeutic Product Candidate for the Treatment of Insomnia and Depression

Collaborator(s):
• Yale New Haven Hospital (Lead): Joseph Ross, MD, MHS
• Mayo Clinic: Nilay Shah, PhD
• Pear Therapeutics, Inc.: Yuri Maricich, MD & Frances Thorndike, PhD

Goal: To assess the effect of a novel, mobile-delivered, pre-market digital therapeutic CBT-I intervention on improving both patient reported and clinical outcomes for real-world patients with chronic insomnia and depression ... and collect real-world healthcare utilization data to detect trends for the PDT to reduce healthcare utilization.
Specific and Exploratory Aims

Specific Aim 1:
Test the ability of the Hugo platform (Healthcare utilization metrics & HER data) to record and evaluate patient-reported outcomes of insomnia and depression, as well as clinically validated metrics for insomnia and depression. This data can then be compared to multiple conducted RCTs in the digital CBT-I space.

Specific Aim 2:
Evaluate whether the mobile-delivered CBT-I can feasibly collect real-world healthcare utilization data through Hugo and show trends for the PDT to reduce healthcare utilization, through reduction in outpatient visits, sleep or psychotropic medication refills, and any other unexpected healthcare usage. These real-world data points and trends will help inform a larger healthcare effectiveness and outcomes research study.

Exploratory Aim 1:
Within the PDT, engagement data will be collected and analyzed, including details on the utilization and completion of the 6-CBT-I Cores, total time spent engaging with the therapeutic, time spent in each Core, number of patient-reported sleep diaries, and other usage metrics.

Exploratory Aim 2:
To assess the feasibility of linking Fitbit to Hugo to collect patient activity data and sleep metrics. This can be done compared to data collected within the PDT for sleep diaries as a test of comparability of these sleep metrics.
Outcomes

• **Primary Outcomes**: (ascertained at baseline, 9-week post baseline, and 21-week post baseline)
  • Difference in the self-reported online ratings of insomnia (per the ISI) compared to control
  • Differences in self-reported depressive symptoms (per the PHQ-8) compared to control

• **Secondary Outcomes**: (ascertained at baseline, 9-week post baseline, and 21-week post baseline)
  • Rate of healthcare utilization (as reported in Hugo by outpatient visits, etc.) compared with Hugo platform only group
  • Change within individual patient-reported outcomes of sleep quality (PSQI), daytime sleepiness (ESS), health status (SF-12), and stress (PSS-10) compared to control
  • Change in sleep outcomes (sleep efficacy, number of awakenings, sleep quality and total sleep time in minutes) compared to control

• **Exploratory Outcomes**: (ascertained at 9-week post baseline and 21-week post baseline)
  • Patient and sleep activity measured using Fitbit (steps/day, total sleep time in minutes, and self reported metrics such as weight, and height)
Methods: Overall Study Design & Patient Population

- This will be a multi-center, randomized, controlled trial over a 9-week period:
  - Half of the patients with insomnia-depression will receive the Pear digital therapeutic candidate with linkage to Hugo and Fitbit and;
  - Half of the patients with insomnia-depression will **not** receive the Pear digital therapeutic candidate but will receive Hugo and Fitbit

- This project is expected to be completed no later than December 2020 with enrollment beginning in December 2019

- All patients will be evaluated at baseline, as well as prompted to complete additional assessments at weeks 9 and 21

- The Pear-003 digital therapeutic candidate is designed to deliver CBT-I via mobile devices as 6-core modules over 9 weeks

- We will enroll 70 patients (~35 at each site) from sleep clinics at Yale and the Mayo Clinic, who are:
  - Aged between 18-64 years
  - Have a diagnosis of chronic insomnia (measured by a score of 8+ on the Insomnia Severity Scale [ISI])
  - Have a diagnosis of sub-clinical depression (measured be a score of 4-20 on the Patient Health Questionnaire (PHQ)-8 scale for depressive symptoms)
NEST Postmarket Signal Management Test Case

Long-Term RWE on Transvaginal Mesh for SUI

Ron Yustein, MD
Director, Signal Management Program
FDA/CDRH/OPEQ
CDRH’s Signal Management Program

• Program led out of CDRH/OPEQ/Immediate Office
  • Safety Signal Coordinators embedded in each OPEQ/OHT
• Responsible for evaluating and acting on identified safety signals for marketed medical devices in a timely manner.
  • Signal: Represents a new potentially causal association or a new aspect of a known association between a medical device and an adverse event or set of adverse events.
Stress Urinary Incontinence (SUI)

• Unintentional loss of urine during physical activity or movement due to weakness in pelvic floor muscles and/or urinary sphincter.

• Common among women and increases with age (affects 35-50%).

• Multiple treatment options for SUI
  • Non-invasive (lifestyle changes, pelvic floor exercises, medications)
  • Surgery
    • Burch colposuspension (procedure; not regulated device)
    • Autologous pubo-vaginal sling (procedure; not regulated device)
    • Bulking agents (medical device)
    • Synthetic mid-urethral slings (medical device)
      • Open
      • Transvaginal MUS
        • Retropubic
        • Transobtrurator
        • Single Incision Sling
Transvaginal Mesh for Gynecological Indications

- Circa 2010:
  - Significant number of MDRs on chronic pain, infection, organ perforation, re-operation.

- 2011:
  - FDA Safety communication for POP repair with mesh
  - FDA Advisory Committee Meeting
    - Risk with POP mesh more concerning
    - Benefit/risk for SUI mesh was satisfactory

- Post-Panel
  - Decision to upclassify vaginal mesh for POP II → III
  - 522 studies for newer “single incision slings” used for SUI

- More recently
  - Several countries have put a ban/“pause” on use of transvaginal mesh for both POP AND SUI.
  - FDA is currently undertaking a review of data related to synthetic MUS for SUI to determine whether recent data demonstrates any new findings that should prompt further FDA action.
CDRH Focus

• Short-term outcomes (e.g., ≤ 2 years) have been well characterized.
• Considering the device is intended as a permanent implant, we are seeking to better characterize longer-term outcomes
  • MDRs and literature are of some value but have significant limitations.
  • Effectiveness:
    • Objective and/or subjective measures
    • Predictors of success/failure
  • Safety
    • Rates of concerning events including erosion, denovo LUTS, pain, infection, re-operation
    • Predictors and/or risk factor for events
• FDA sought to partner with NEST to see what RWE may be available with a particular emphasis on outcomes extending beyond 1-2 years.
Collaborators and Project Proposal

• Five collaborators were interested and signed on to the effort
  • Vanderbilt University Medical Center (Lead) Michael Matheny
  • Lahey Hospital & Medical Center Frederic Resnic
  • Mayo Clinic Nilay Shah
  • Weill-Cornell Art Sedrakyan
  • Yale-New Haven Hospital Joe Ross
Project Summary

• Objective: Assess the capacity of routinely collected EHR data to be used to evaluate longer-term (>2 yrs) adverse events following synthetic surgical mesh implantation for female SUI.

• Multi-site retrospective cohort analysis

• Duration: 12 months (anticipated Spring 2020)

• Sources: EHR and peri-operative implant registries.
Project Summary

• Outcomes – Signal Related:
  • Rates for
    • re-operation (revision, incision, excision, removal),
    • mesh erosion,
    • all-cause chronic pain, and
    • voiding symptoms (recurrence of incontinence, new retention)
  • Risk prediction model to assess a person’s risk for complications among those receiving mesh for SUI if data quality and volume sufficient
  • Obtain outcomes for MUS as well as SUI surgeries w/o mesh for comparison
  • Provide a report of additional data elements important to conduct future device post-market surveillance in implantable devices for this indication

• Outcomes – Process Related:
  • How robust is EHR data for these types of device outcome surveillance activities?
  • Report on improvements in data collection that would improve capacity for post-market surveillance
Importance for FDA (And Public Health)....

- Safety Signal Specific
  - Hopefully will further inform FDA’s understanding of the longer-term benefit-risk profile of these products.
  - Will be taken into consideration, along with other available information, in decision-making processes.

- Begin Assessing Role for NEST in Postmarket Signal Refinement
  - Test case for EHR
    - What kind useful information can we get? And what can we not get?
    - How granular (surgical route, device specific)
  - How quickly can the information be obtained, analyzed and reported?
  - How can the information be used by FDA in its toolbox of refinement sources for an identified signal?
  - How can the information be used by FDA to support public health or regulatory actions?
Thank You
Panelist & Audience Q&A
QUESTIONS FOR PANELISTS

• What has been going well with your Test-Case project?
  o What can be improved?

• How have you dealt with the potential issues of sharing data across organizations?

• What value does working with NESTcc provide to your organization, and how do you see engagement with NESTcc in the future?
Engage with NESTcc
The NESTcc Quarterly Newsletter is distributed on the first Tuesday of each quarter.

- The Newsletter is in response to feedback from NESTcc stakeholders for a high-level update on NESTcc activities.
- The Newsletter contains upcoming dates and links to news items and publications from the previous quarter.
- The newsletter is available to the public and can be subscribed to here.
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
Appendix: Test-Case Slides
ORTHOPEDIC TEST-CASE – INTERVERTEBRAL LUMBAR BODY FUSION DEVICES

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Developing Capacity to Conduct Proactive Post Marketing Safety Surveillance of Intervertebral Body Fusion Devices Using Electronic Health Record Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Available Data Sources</td>
<td>Claims; Electronic Health Records (EHR)</td>
</tr>
<tr>
<td>Project Duration</td>
<td>9 months</td>
</tr>
<tr>
<td>Disease Area</td>
<td>Orthopedic</td>
</tr>
<tr>
<td>Technology of Interest</td>
<td>Intervertebral Body Fusion Devices</td>
</tr>
</tbody>
</table>

Project Aims

- This test-case will assess the feasibility of using Real-World Data (RWD) captured through the NESTcc Data Network to conduct proactive post-market surveillance for safety for class II medical devices.
- Specifically, this test-case will conduct proactive post-market surveillance for safety and effectiveness of lumbar interbody systems captured within Lahey Hospital and Medical Center (Lahey), a NESTcc Data Network Collaborator.

Participating Network Collaborators

- PEDSnet
- Lahey Hospital & Medical Center
- MDIC Annual Public Forum

Regulatory Pathway

510(k)
<table>
<thead>
<tr>
<th>Project Title</th>
<th>Use of Real-World Data to Evaluate Clinical and Patient Outcomes by Use of a Prescription Digital Therapeutic (delivered via mobile app) for the Treatment of Insomnia and Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Available Data Sources</td>
<td>Electronic Health Records (EHR); Patient-Generated health Data (PGD); Patient-Reported Outcome Measures (PROMs)</td>
</tr>
<tr>
<td>Project Duration</td>
<td>12 months</td>
</tr>
<tr>
<td>Disease Area</td>
<td>Mental Health – Insomnia/Depression</td>
</tr>
<tr>
<td>Technology of Interest</td>
<td>mHealth for Insomnia</td>
</tr>
</tbody>
</table>

**Project Aims**

- Leveraging PGD, this project will assess the impact of a mobile-delivered, prescription digital therapeutic (PDT)* device (Pear-003) delivering Cognitive Behavioral Therapy for Insomnia (CBT-I) for real-world patients with chronic insomnia and depression.
  - *Planned; this product has not yet been reviewed and approved by the FDA.
- The goal of this Test-Case is to conduct a multi-center randomized controlled trial to collect and evaluate real-world data (RWD) alongside clinically-validated measures of insomnia and depression.

**Participating Network Collaborators**

- Yale
- Mayo Clinic

**Regulatory Pathway**

- 510(k)
Project Title | Synthetic Mid-Urethral Slings for Stress Urinary Incontinence in Women
---|---
Available Data Sources | Electronic Health Records (EHR); Research Dataset
Project Duration | 12 months
Disease Area | Stress Urinary Incontinence (SUI)
Technology of Interest | Synthetic Mesh Sling

**Project Aims**

- The objectives of this project are to assess the capacity of routinely collected EHR data to be used to evaluate long-term (>2 years) adverse events following synthetic surgical mesh implantation (mid-urethral slings) for female SUI.
- NESTcc was approached by the U.S. Food and Drug Administration (FDA) to engage in a collaborative consortium to pursue concerns around the risk of mesh use for SUI. This study has the potential to increase medical knowledge regarding the safety of SUI devices.

**Participating Network Collaborators**

[Logos of participating institutions]