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National Evaluation System for health Technology Coordinating Center (NESTcc)

NESTcc Round 1 Real-World Evidence Test-Cases

NESTcc has selected 8 initial Real-World Evidence (RWE) Test-Cases. These Test-Cases were submitted in January 2018 through a public call and will address two primary objectives. First, they will explore the feasibility for the medical device industry to work with Real-World Data (RWD) sources and NESTcc's initial set of Network Collaborators. Second, the Test-Cases will help identify areas where NESTcc could play a role in reducing transaction costs (e.g., contracting, IRB, data sharing agreements, publication policies).

The projects below will be executed through collaborations with Abbott, Adhesys Medical, Johnson & Johnson Medical Devices Companies, and W.L. Gore & Associates, Inc. as industry partners. In addition to the industry groups working through independent collaborations, the American Academy of Orthopaedic Surgeons (AAOS) is serving as a neutral convener, bringing together DJO Global, DePuy Synthes, Smith & Nephew, Stryker, and Zimmer Biomet for a Test-Case that will bring together NESTcc Network Collaborators with the American Joint Replacement Registry (AJRR) which is housed at AAOS.

The first round of Test-Cases includes projects along the 510(k) and premarket approval regulatory pathways, across five disease areas, and throughout the medical device total product lifecycle.

The second round of Test-Cases is scheduled to be awarded in February 2019. The second round of Test-Cases included two calls for concepts that were posted in July 2018: a broad announcement and a targeted announcement seeking concepts to utilize patient-generated health data (PGD). Both announcements were open to concepts from stakeholders across the ecosystem, including health systems, government organizations, non-profit patient organizations, and medical device manufacturers.

Round 1 Test-Case Abstracts

Comparative Effectiveness of Alternative Approaches for Wound Closure

Technology of Interest: Wound Closure

Disease Area: Dermatology

Duration: 9 months

Network Collaborator(s): PEDSnet; OneFlorida

There are three methods for closure of wounds that result from surgeries or trauma: sutures, staples, and skin adhesives. The purpose of this project is to compare each of these skin closure approaches in terms of the types of skin wounds and the patient populations they are used for, along with short-term outcomes, such as need for additional procedures, wound dehiscence, and health services use. A scientific team of physicians, patients, informaticians, and researchers will: define a set of surgical procedures and trauma-related lacerations in order to characterize a study cohort; specify a set of clinical features to describe the cohort; define each of the wound closure comparator methods; and, specify the clinical features for the outcomes.

Once these scientific specifications are developed, the PEDSnet data science team will craft a statistical query based on the PCORnet common data model to evaluate as many of the clinical criteria as possible. The query will then be executed in the PEDSnet and OneFlorida data networks that include analysis-ready electronic health records (EHR), and results will be evaluated by the scientific team. Case abstraction forms will then be developed that will be used for chart reviews of samples of adults and children from the overall cohort. It is expected that chart review will be necessary to define the type of skin closure and details for some of the outcomes. Results of this study will provide novel information on the effects of alternative skin closure methods for different types of procedures.

Developing Capacity to Conduct Proactive Post Marketing Safety Surveillance of Craniomaxillofacial Distractors Using Electronic Health Record Data

Technology of Interest: Craniomaxillofacial Distractors

Disease Area: Orthopedics

Duration: 9 months

Network Collaborator(s): PEDSnet

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 with devices used in pediatric populations.

The European Union (EU) issued new Medical Device Regulations (MDR) in May 2017 that includes requirements for "proactive surveillance" for recertification of medical devices to remain on the market in the EU by May 2020. Companies that develop and manufacture medical devices will therefore need to develop methodology and approaches for proactive surveillance of medical devices that meets the EU's MDR standards in order to keep medical devices accessible to patients in the EU.

The use of implantable devices is generally rare in pediatrics, and therefore the study of devices such as craniomaxillofacial (CMF) distractors requires multi-site collaboration. The low patient density, combined with significant per-site start-up costs, have made pediatric device studies difficult to execute.
This test-case seeks to determine the feasibility of using RWD captured through PEDSnet, a NESTcc Data Network Collaborator, to conduct proactive post-market surveillance for safety and effectiveness for CMF distractors.

Developing Capacity to Conduct Proactive Post Marketing Safety Surveillance of Intervertebral Body Fusion Devices Using Electronic Health Record Data

Title: Developing Capacity to Conduct Proactive Post Marketing Safety Surveillance of Intervertebral Body Fusion Devices Using Electronic Health Record Data

Technology of Interest: Intervertebral Body Fusion Devices

Disease Area: Orthopedics

Duration: 9 months

Network Collaborator(s): Lahey; PEDSnet

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. The project efforts will be completed in collaboration with PEDSnet Coordinating Center at the Children's Hospital of Philadelphia.

Intervertebral body fusion devices are used in the treatment of a variety of spine pathologies such as degenerative disc disease or fractures at one or more levels to aid in spinal fusion and may be combined with autogenous and/or allogenic bone, and with supplemental fixation such as posterior pedicle systems. Post-market surveillance across various indications, populations, and hardware configurations becomes challenging. Test-case execution will provide information not only about performance of specific devices, but about ways to effectively support research in collaboration with manufacturers and regulators.

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Feasibility of Using Real-World Data to Evaluate Thermal Ablation of Liver Tumors

Technology of Interest: Ablation Device

Disease Area: Surgery

Duration: 9 months

Network Collaborator(s): Duke University Health System; Vanderbilt; Mayo Clinic; Weill-Cornell

This test-case assesses the ability of the NESTcc Data Network to reliably and validly capture Real-World Data (RWD) on class II surgical devices with a general indication for use to study the safety and effectiveness to support a more specific indication.

The Device of Interest is intended for the ablation (coagulation) of soft tissue via percutaneous, open surgical, and laparoscopic techniques. The product is a class II medical device and entered the market through the 510(k) pathway. FDA has not required clinical data to clear any thermal ablation products with a general soft tissue indication. The product is used in real-world medical practice to ablate several types of soft tissue lesions, including cancers; especially in the liver. The use of thermal ablation to treat unresectable liver tumors is supported by multiple national and international treatment guidelines and standards of care. However, no thermal ablation device currently has an indication that includes the treatment of benign and malignant non-resectable liver tumors.

This test-case will explore the feasibility of generating evidence on the use of this product for the ablation of non-resectable liver tumors, either benign or malignant. The feasibility assessment will examine if the NESTcc Data Network Collaborators capture the necessary data elements, if the data are of appropriate quality (e.g., reliability and relevance) and there is a sufficient population for a representative sample to support future regulatory submissions to expand the indications for use and be used to inform physicians about treatment options for patients.

Real-World Clinical Outcomes in Patients with Mechanical Heart Valve Replacement and Anticoagulation Variability

Technology of Interest: Mechanical Aortic Heart Valves

Disease Area: Cardiology

Duration: 12 months

Network Collaborator(s): Vanderbilt; Weill-Cornell

Valvular heart disease affects tens of millions of patients worldwide and is associated with high morbidity and mortality. Symptoms such as fatigue, shortness of breath, and chest pain can also contribute to significant quality-of-life limitations. Treatment for severe aortic valve disease often includes surgical replacement with a prosthetic heart valve. Mechanical heart valves (MHV) are a type of prosthetic heart valve constructed of durable materials such as titanium or carbon that can potentially last a patient's lifetime. Despite their high durability, MHV are associated with an increased risk of developing blood clots that may interrupt blood flow and travel to various organs (thromboembolism).

Oral anticoagulation therapy with a vitamin K antagonist (warfarin) is a class I recommendation for patients implanted with a MHV based on the 2014 AHA/ACC Guidelines. The potential protective benefit of anticoagulation therapy against blood clots must be weighed against an increased risk of bleeding in patients with an MHV and adjusting the warfarin dose is necessary to reduce the risk of these complications. The efficacy of warfarin is monitored by measuring how fast the blood clots using a standardized measure called the International Normalized Ratio (INR). Clinical guidelines currently

recommend a target INR of 2.0 – 3.0 for patients implanted with a MHV in the aortic position. However, recent data suggest that a lower target INR maintains the anticoagulation benefit while decreasing the risk of bleeding in patients implanted with an MHV in the aortic position.

This test-case will explore the safety of a reduced target INR in patients implanted with the mechanical valve prosthesis of interest in the aortic position. Retrospective data will be drawn from the electronic health records (EHR) and other data sources of participating NESTcc Data Network Collaborators. Longitudinal outcomes such as hemorrhage, stroke, and mortality will be collected to understand the feasibility to determine the risks and benefits of various anticoagulation strategies for MHV patients. Insights drawn from this test-case have the potential to impact long-term clinical care and outcomes for patients implanted with an MHV. In addition, this test-case will assess the feasibility of linking various sources of existing Real-World Data (RWD) to study longitudinal patient outcomes.

Testing the Feasibility of Registry and Claims Data Linkages

Technology of Interest: Total Joint Arthroplasty (TJA), Primary Total Knee Arthroplasty

Disease Area: Orthopedics

Duration: 12 months

Network Collaborator(s): HealthCore; Mayo Clinic

Medical device manufacturers are obligated to perform post-market surveillance. However, standard post-market reporting mechanisms do not always ensure patient safety (Hauser, 2012). The American Joint Replacement Registry (AJRR) provides a resource to track device usage, adverse events, complications, device survivorship, and clinical measures for total joint arthroplasty (TJA) outcomes. AJRR currently has over 1,100 participating institutions with annual submissions representing 28-30% of U.S. TJA volume. While data collection efforts are extensive, there are limitations and resulting bias if there remain non-participating providers nationally. As complications and device failure management may occur at institutions outside the Registry network, data pertaining to failures may be missed. Furthermore, patients entered in AJRR prior to 2017 (≥1,000,000) do not have Level II elements (post-operative complications or comorbidity data) included, limiting the Registry's ability to risk-adjust outcomes. Also, while participants are "required" to submit Level II data, not all are doing so, or are unable to submit all Level II data.

This project aims to conduct anonymous data linkages of Registry data with Real-World Data (RWD) sources, including private claims databases within the NESTcc Network Collaborators, from Mayo Clinic (Optum Labs) and HealthCore. A data linkage, supported by Weill-Cornell Medical College as an honest broker, will be put in place between AJRR and HealthCore, which has longitudinal data through private payer claims on ~350,000 TKA patients. In addition, data will be collected through OptumLabs, with data on over 121,000 total knee arthroplasty (TKA) patients and analyzed through Mayo Clinic.

Linkages provide a valuable resource for determining more accurate device performance, survivorship, and surgical outcomes, thereby supporting standardized post-market surveillance reporting mechanisms. The specific aim is to conduct a descriptive study to evaluate the clinical outcomes of TKA implant survivorship, mortality, revision/reoperation, readmission, and Emergency Department visit following TKA 2012-2017 for private health plan members. This study has implications for future anonymous data linkages with additional private payer claims sources and for additional orthopedic procedures.

1. Hauser RG. Here we go again–another failure of postmarketing device surveillance. N Engl J Med. 2012; 366(10):873-5. doi: 10.1056/NEJMp1114695.

Testing the Use of Real-World Data from Three Unique Sources to Expand Indications

Technology of Interest: Endovascular Therapies

Disease Area: Vascular

Duration: 12 months

Network Collaborator(s): MDEpiNet; Duke University Health System; OneFlorida

This project will design, collect, and examine Real-World Data (RWD) about the novel application of an endovascular stent graft for patients with complex abdominal aortic aneurysms. Stent grafts are a flexible metal wire structure covered with an impermeable material used to treat aneurysms or weakening in the walls of blood vessels. Stent grafts prevent aneurysms from rupturing and potentially causing death.

This project will use three unique data sources and a specific case identification algorithm to study new ways surgeons have adapted an existing stent graft. The device of interest is made of two components: a main body implanted in the common iliac artery and an iliac stent that extends into the internal iliac artery. Data will be collected from three Real-World Data sources: the Vascular Quality Initiative (a Coordinated Registry Network that is part of MDEpiNet), a statewide clinical research network (OneFlorida), and a regional quaternary health system (DukeHealth).

This test-case will study how specific endovascular graft cases using the two components can be identified from these data sources and evaluate clinical outcomes for cases using the device of interest. Information collected from these RWD sources will be used to guide decisions by physicians, payers, and regulatory agencies about potential FDA approval of the main body device in conjunction with the iliac stent, a new device as a component of a larger system. Additionally, this project will help researchers learn about the utility of these new approaches both in the treatment of different aneurysms as well as how this type of data can be applied to regulatory submissions.

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The Feasibility of Using Real-World Data in the Evaluation of Cardiac Ablation Catheters

Technology of Interest: Ablation Catheters

Disease Area: Cardiology

Duration: 8 months

Network Collaborator(s): Mercy; Mayo Clinic; Yale-New Haven Hospital

This test-case will assess the ability of the NESTcc Data Network to reliably and validly capture data on class III surgical devices to study the safety and effectiveness outcomes for an indication expansion.

Currently, the standard treatment for cardiac arrhythmias includes cardiac ablation with a catheter to destroy a small area of heart tissue that is causing rapid and irregular heartbeats. Catheters have been generally approved by the FDA for use in the treatment of specific cardiac arrhythmias, such as paroxysmal atrial fibrillation and ischemic ventricular tachycardia. Catheters vary in which of these cardiac arrhythmias the FDA has approved their use. There are currently no catheters that are indicated for the treatment of persistent atrial fibrillation.

This test-case will explore the feasibility of generating evidence for label expansions on the use of cardiac ablation catheters to treat cardiac arrhythmias. The feasibility assessment will examine if the NESTcc Data Network Collaborators capture the necessary data elements, and if the data are of appropriate quality (e.g., reliability and relevance) and there is a sufficient population for a representative sample to support a robust and rigorous study for label extensions.