Report to Congress

Device Pilot Projects

(Submitted Pursuant to
Section 708 of the FDA Reauthorization Act of 2017)

Executive Summary

Section 708 of the FDA Reauthorization Act of 2017 (FDARA) amended section 519 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360i). Section 708 of FDARA requires the Secretary of Health and Human Services to provide a report to the Committee on Energy and Commerce of the U.S. House of Representatives and to the Committee on Health, Education, Labor and Pensions of the U.S. Senate that contains a description of the pilot projects being conducted and the pilot projects being continued or expanded pursuant to that section. This is the third annual report by the U.S. Food and Drug Administration (FDA) to fulfill this requirement.

FDARA calls for, among other things, pilot projects to be designed to efficiently generate reliable and timely safety and active surveillance data for medical devices. For the pilot projects, *active surveillance* refers to actively and continuously generating information on the device's performance and on the clinical outcomes associated with the use of the device in routine clinical practice. Active surveillance of medical devices may be understood relative to FDA's traditional or "passive surveillance," which is an approach that relies on users notifying FDA of device-related events (e.g., through adverse event reporting). Active surveillance has the potential to empower stakeholders to make more timely evidence-based decisions.

The pilot projects that were initiated as required by section 708 of FDARA were designed and conducted in coordination with a comprehensive system for evaluating medical device technology. That system is the National Evaluation System for health Technology (NEST). The NEST Coordinating Center (NESTcc) operates under a governing board with an appropriate representation of stakeholders, including patient groups and device manufacturers, as set forth in the law. In coordination with FDA, the NESTcc promotes the use of electronic health data, including claims data, electronic health records (EHRs), patient survey data, registries, and other health information.

In general, the Center for Devices and Radiological Health at FDA has documented an increase in the use of real-world evidence (RWE) to support regulatory decision-making. The use of RWE in studies may be less burdensome for manufacturers because RWE is often less costly and can generate meaningful information about the safety and effectiveness of devices in a more timely manner than traditional studies.

FDARA specifies that this report should describe (1) how such pilot projects are being implemented through a contract, cooperative agreement, grant, or other appropriate agreement; (2) the number of manufacturers that have agreed to participate in such projects; (3) the data sources used to conduct such pilot projects; (4) the devices or device categories involved in the pilot projects; (5) the number of patients involved in such projects; and (6) the findings of each project in relation to device safety, including adverse events, malfunctions, and other safety information. This information is presented in the report and summarized in the Appendix.

This report features 10 device pilot studies, including six that have been completed and four that are ongoing. Of note, five of the 10 reported studies were initiated in 2020, and three of the five new studies were also completed in the same year. The pilot projects reported are at various stages of development and include several device types. This report includes two groups of

projects: (1) pilot projects completed in 2020 and (2) pilot projects that were ongoing as of October 2020. The data sources leveraged in the presented pilot projects are both national- and state-based, and they include EHRs, registries, and claims. The devices studied include orthopedic joint implants, implantable cardioverter defibrillators, vascular implants, prostate ablation devices, and ventral hernia mesh devices. A cumulative summary of all completed projects from previous reports is included in the Appendix.

Several of these pilot projects are already producing RWE for device evaluation by various stakeholders, including FDA and industry. These projects have helped and will continue to inform the development and practical applications of active surveillance in real-world settings. These efforts are important to the further development of the NEST and other RWE capabilities, and the future work outlined here will increase the scale and impact of these capabilities.

Contents

Acronyms Used in This Report

AAA	Abdominal Aortic Aneurysm
AHSQC	Americas Hernia Society Quality Collaborative
AJRR	American Joint Replacement Registry
CDRH	Center for Devices and Radiological Health
CI	Confidence Interval
CRN	Coordinated Registry Network
CRT	Cardiac Re-Synchronization Therapy
DCB	Drug Coated Balloon
DES	Drug-Eluting Stent
DELTA	Data Extraction and Longitudinal Trend Analysis
EHR	Electronic Health Record
EP PASSION	Electrophysiology Predictable and Sustainable Implementation of National Registries
EQ-5D	EuroQol-5D
EVAR	EndoVascular Aneurysm Repair
FDA	Food and Drug Administration
FDARA	FDA Reauthorization Act of 2017
FORCE TJR Registry	Function and Outcomes Research for Comparative Effectiveness in Total Joint Replacement Registry
HHS	Harris Hip Score
HOOS	Hip disability and Osteoarthritis Outcome Score
HR	Hazard Ratio
ICD	Implantable Cardioverter Defibrillator
ICOR	International Consortium of Orthopedic Registries
ICU	Intensive Care Unit
KOOS	Knee disability and Osteoarthritis Outcome Score
KP	Kaiser Permanente
KPR	Kaiser Permanente Registry
KSS	Knee Society Score
MARCQI	Michigan Arthroplasty Registry Collaborative Quality Initiative
MDEpiNet	Medical Device Epidemiology Network
NCDR	National Cardiovascular Data Registry
NEST	National Evaluation System for health Technology
NESTcc	National Evaluation System for health Technology Coordinating Center
NLP	Natural Language Processing
OPC	Objective Performance Criteria
Ortho CRN	Orthopedics Coordinated Registry Network
OSHPD	Office of Statewide Health Planning and Development
PAD	Peripheral Artery Disease
PAS	Postapproval Study
PCS	Physical Component Score
POP	Pelvic Organ Prolapse

PROM	Patient Reported Outcome Measure
PTX	Paclitaxel
PVI	Peripheral Vascular Initiative
ORC	Open Radical Cystectomy
RWD	Real-World Data
RWE	Real-World Evidence
SEER	Surveillance, Epidemiology, and End Results
SF	Short Form
SPARCS	Statewide Planning and Research Cooperative System
SPARED	Study of Prostate Ablation Related Energy Devices
SUI	Stress Urinary Incontinence
SVS	Society of Vascular Surgeons
TAVR	Transcatheter Aortic Valve Replacement
TKA	Total Knee Arthroplasty
THA	Total Hip Arthroplasty
TJR	Total Joint Replacement
TURP	TransUrethral device based Resection of the Prostate
VISION	Vascular Implants Surveillance Intervention and Outcomes Network
VQI	Vascular Quality Initiative
WHT	Women's Health Technology

I. Purpose

Section 708 of the FDA Reauthorization Act of 2017 (FDARA) amended section 519 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360i). Section 708 of FDARA requires the Secretary of Health and Human Services to provide a report to the Committee on Energy and Commerce of the U.S. House of Representatives and the Committee on Health, Education, Labor and Pensions of the U.S. Senate that contains a description of the pilot projects being conducted and the pilot projects being continued or expanded pursuant to that section.

II. Background on Section 708

Section 708 of FDARA calls for, among other things, the pilot projects to be designed to efficiently generate reliable and timely safety and active surveillance data for medical devices. For the pilot projects, *active surveillance* refers to actively and continuously generating information on the device's performance and the clinical outcomes associated with the use of the device in routine clinical practice. Active surveillance of medical devices may be understood relative to the U.S. Food and Drug Administration's (FDA's) traditional or "passive surveillance," which is an approach that relies on users notifying FDA of device-related events (e.g., through adverse event reporting). Active surveillance has the potential to empower stakeholders to make more timely evidence-based decisions.

Some of the ways in which FDA has used active surveillance strategies for monitoring medical device safety include the following:

- Conducting ongoing systematic monitoring of an existing high-quality granular data source with a system that provided regular feedback regarding safety alerts to the manufacturer and regulators.

- Collecting postmarket safety information as evidenced in real-world data (RWD) sources (typically electronic health records (EHRs) or registry data sources), extending to monitoring the overall performance of medical devices, including the effectiveness and durability of them.

- Using a pre-defined algorithm to detect potential safety signals instead of data mining or ad-hoc queries of existing data sources.

The pilot projects were designed and conducted in coordination with a comprehensive system for evaluating medical device technology, as specified by FDARA. That comprehensive system is the National Evaluation System for health Technology (NEST). The NEST Coordinating Center (NESTcc) operates under a governing board with appropriate representation of multiple stakeholders, including patient groups and device manufacturers. In coordination with FDA, the NESTcc promotes the use of real-world electronic health data, including claims data, patient survey data, EHRs, registry data, and other digital health information. The Medical Device Epidemiology Network (MDEpiNet) is one of the NEST data collaborators and is primarily

involved in advancing the strategically Coordinated Registry Networks (CRNs) featured in the pilot studies.

As intended by the law, this report has been prepared to contribute to an independent third-party's evaluation of the strengths, limitations, and appropriate uses of evidence collected pursuant to the real-world evidence (RWE) pilot projects of the Medical Device User Fee Amendments of 2017, authorized as part of FDARA.

The law calls for the voluntary participation by device manufacturers in these pilot projects. Accordingly, all the pilot projects reported here are voluntary. These pilots involve the use of multiple different RWD sources.

In general, the Center for Devices and Radiological Health (CDRH) at FDA has documented an increase in the use of RWE to support regulatory decision-making. The use of RWE in studies may be less burdensome for manufacturers because RWE is often less costly and can generate meaningful information about the safety and effectiveness of devices in a more timely manner than traditional studies.

III. Selection of Pilot Projects

The selection of pilot projects described in this report was guided by the law's requirement that such projects inform the development of methods, systems, data criteria, and programs that could be used to support safety and active surveillance activities for devices. The devices and device types in these pilot projects are widely used, and failure of any of these device types may be associated with significant health consequences. Therefore, the pilot projects involve devices and device types for which the collection and analysis of RWE regarding the devices' safety and effectiveness is likely to advance public health.

The pilot projects reported here are at various stages of development and include several device types. The data sources are both national- and state-based, and they include EHRs, registries, and claims. The devices studied include orthopedic joint implants, implantable cardioverter defibrillators (ICDs), vascular implants, prostate ablation devices, robotic-assisted devices, and ventral hernia mesh devices.

Several of these projects are already producing RWE for device evaluation (premarket and postmarket) by various stakeholders, including FDA and industry. In addition, these projects provide FDA and industry with tools and methods for the development of active surveillance and practical applications of active surveillance in real-world settings. These efforts are important to the further development of NEST and other RWE capabilities, and the future work outlined here will increase the scale and impact of these capabilities.

All pilot projects comply with the law's requirements to have established security measures to maintain confidentiality and privacy.

The persons or organizations conducting these pilot projects have high levels of research, statistical, epidemiologic, data science, informatics, and/or clinical capability and expertise to conduct and complete the activities. As applicable, pilot projects are conducted under contracts, cooperative agreements, grants, or similar arrangements in compliance with all U.S. laws and regulations.

IV. Description of the Pilot Projects

FDARA specifies that this report must describe (1) how such pilot projects are being implemented through a contract, cooperative agreement, grant, or other appropriate agreement; (2) the number of manufacturers that have agreed to participate in such projects; (3) the data sources used to conduct such pilot projects; (4) the devices or device categories involved in the pilot projects; (5) the number of patients involved in such projects; and (6) the findings of each project in relation to device safety, including adverse events, malfunctions, and other safety information. Each pilot project is described herein by providing the following information:

- Pilot project's name
- Description of the project and devices involved
- Party conducting the pilot project
- Agreement type (e.g., contract, cooperative agreement, grant)
- Specific aim(s) of the project
- Data source(s) involved
- Safety outcome(s) of interest
- Numbers and names of manufacturers involved
- Number of patients
- Findings of the project
- Status (as of October 2020)

The manufacturer's involvement in a project is defined broadly for this report. For example, some of the projects have a financial contribution from one or more device manufacturers while others do not. Additionally, some of the projects have industry representation on an oversight committee; other projects are in the process of forming those committees.

A narrative describing each pilot project is found in sections V and VI of this report. The narrative descriptions are followed by a short description of the status of each pilot project. The descriptions of the pilot projects are also summarized in the Appendix of this document. The Appendix also includes the cumulative list of all the projects previously reported.

A total of 10 studies were conducted in fiscal year 2020. The following five studies were initiated in 2020:

1. Project Name: Safety and Effectiveness of Outpatient Surgical Procedures for the Treatment of Benign Prostatic Enlargement in New York State and California (Page 10,

Number 4)

2. Project Name: Evidence-Based Objective Performance Criteria for the Evaluation of Hip and Knee Replacement Devices and Technologies (Page 11, Number 5)

3. Project Name: Mortality After PTX-Coated Balloon Angioplasty and Stenting of Superficial Femoral and Popliteal Artery in the Vascular Quality Initiative (Page 18, Number 9)

4. Project Name: Active Surveillance of Medical Device Safety and Outcomes Using EHRs: Prostate Cancer Partial Gland Ablation Technologies (Page 19, Number 10)

5. Project Name: Endovascular Treatment of Abdominal Aortic Aneurysms (EVAR) Conversion (Page 14, Number 6)

Three of the five new studies were completed in 2020, and two are ongoing. The status of these five studies is captured in sections V and VI of this report, along with the pilot projects that were ongoing in the previous fiscal year. Specifically, section V presents the findings from six pilot projects completed in 2020 (including the three that were initiated and completed in 2020). Section VI provides updates for four ongoing pilot projects (including two that were initiated in 2020).

A note about CRNs, which are frequently mentioned: Typically, CRNs are partnered, registry-based RWD sources that include registry data linked to other sources, such as claims, EHRs, and patient-generated data to enable studies of long-term outcomes via longitudinal patient healthcare profiles.

V. Completed Pilot Projects

1. Project Name: Vascular Implants Surveillance Intervention and Outcomes Network (VISION)

Description:

The devices involved in this pilot project were stents, stent-grafts, and other devices used in the treatment of diseases of the peripheral circulatory system. The VISION pilot project aimed to improve evidence generation on the safety and performance of vascular devices and procedures by linking medical device registry data with state and national claims datasets in a distributed data model. These linkages were used to monitor the long-term outcomes of patients treated with vascular devices, improve the follow-up rates and validations of complications and support the risk adjustment of outcomes. The VISION infrastructure is suitable for nesting specific pilot studies (see pilot project no. 6 in section V).

Party conducting the pilot project and agreement type:

The VISION pilot project was led by Weill Cornell Medicine under a cooperative agreement with FDA.

Specific aim(s):

The aims of the pilot project were to (1) develop a U.S. national device surveillance network in the vascular device space, (2) bring together registries in a systematic way and obtain longer, more complete patient follow-up information via data linkages, (3) provide a resource for all stakeholders to evaluate the safety and effectiveness of new devices as they enter routine usage, and (4) facilitate and conduct comparative effectiveness studies within a short period after device market entry. The pilot project also studied the validity of CRN data sources as compared to data derived from clinical trials.

Data source(s):

The data sources for this pilot project included (1) the Society for Vascular Surgery (SVS) Vascular Quality Initiative (VQI) registry, (2) Medicare claims, (3) the New York State Department of Health's Statewide Planning and Research Cooperative System (SPARCS), and (4) the clinical trial datasets of the device's manufacturer.

Safety outcome(s) of interest:

The primary outcomes identified in the linked datasets included death, procedure-specific adverse events (stroke, rupture, and amputation), reinterventions, readmissions, surveillance, imaging, and cost.

Numbers and names of manufacturers involved:

Four manufacturers collaborated on the study: Cook Medical, Endologic, W. L. Gore & Associates, and Medtronic. Additional manufacturers were approached to participate in this pilot project.

Number of patients:

Over 300,000 patients participated in this pilot project.

Findings of project:

The initial VISION efforts focused on the validation of claims data to capture the outcomes of interest. For example, in one of the studies involving endovascular aortic repair, a medical record review demonstrated a 6 percent 1-year and 16 percent 3-year reintervention rate, and

almost all (92 percent) of these events were accurately captured by the linked claims data.[1]

A related study focused on matching registry patients and procedures to these patients' Medicare claims based on an algorithm using indirect identifiers. Such algorithms will help identify and categorize late events after repairs and may serve as a means to enhance the follow up of patient outcomes.[2]

Building on these efforts, a propensity-matched study was conducted comparing the long-term survival of carotid artery stenting and carotid endarterectomy. In contrast to randomized clinical trial findings, this CRN study demonstrated a survival advantage of stenting over endarterectomy in real-world practice.[3]

Registry-linked datasets have been created for nine procedures. New devices are being added as they are approved or cleared for market in the United States.

Status:

Completed. The study was published in a peer-reviewed journal.[4]

2. Project Name: Ortho CRN (Formerly Named *ICOR-USA*)

Description:

The Ortho CRN (formerly named *ICOR-USA*) pilot project sought to apply lessons learned from the International Consortium of Orthopedic Registries (ICOR) to improve clinical evidence generation and safety evaluations for orthopedic implants in the United States via the creation of a strategically coordinated registry network.

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[1] Columbo JA, Kang R, Hoel AW, et. al. A Comparison of Reintervention Rates After Endovascular Aneurysm Repair Between the Vascular Quality Initiative Registry, Medicare Claims, and Chart Review. J Vasc Surg. 2019; 69(1):74-76.

[2] Hoel AW, Faerber AE, Moore KO, et. al. A Pilot Study for Long-Term Outcome Assessment After Aortic Aneurysm Repair Using Vascular Quality Initiative Data Matched to Medicare Claims. J Vasc Surg. 2017;66(3):751-759.

[3] Columbo JA, Marinez-Camblor P, MacKenzie TA, et. al. A Comparative Analysis of Long-Term Mortality After Carotid Endarterectomy and Carotid Stenting. J Vasc Surg. 2019;69(1):104-109.

[4] Tsougranis G, Eldrup-Jorgensen J, Bertges D, Schermerhorn M, Morales P, Williams S, Bloss R, Simons J, Deery SE, Scali S, Roche-Nagle G, Mureebe L, Mell M, Malas M, Pullin B, Stone DH, Malone M, Beck AW, Wang G, Marinac-Dabic D, Sedrakyan A, Goodney PP. The Vascular Implant Surveillance and Interventional Outcomes (VISION) Coordinated Registry Network: An effort to advance evidence evaluation for vascular devices. J Vasc Surg. 2020 Dec;72(6):2153-2160. doi: 10.1016/j.jvs.2020.04.507. Epub 2020 May 20. PMID: 32442604.

Party conducting the pilot project and agreement type:

The study was conducted by the Ortho CRN partners with in-kind support from various stakeholders.

Specific aim(s):

The aim of this pilot project was to develop surveillance infrastructure and methods to evaluate the safety of arthroplasty devices via the creation of a strategically coordinated network of orthopedic registries, called Ortho CRN.

Data source(s):

This pilot project prospectively collected data from the following U.S.-based data sources: Kaiser Permanente, the Function and Outcomes Research for Comparative Effectiveness in Total Joint Replacement (FORCE TJR) Registry, and the Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI).

Safety outcome(s) of interest:

The primary outcomes of interest for this pilot project were benchmarking performance metrics for hip and knee replacements.

Number and names of manufacturers involved:

Three manufacturers were involved as members of the steering committee: Johnson & Johnson, Zimmer Biomet, and Smith & Nephew.

Number of patients involved:

The pilot included over 600,000 patients with total joint replacement procedures.

Findings of project:

The infrastructure and methods developed under this study were used to initiate the project focusing on the development of Objective Performance Criteria (see pilot project no. 5 below).

Status:

Completed.

3. Project Name: VQI-Data Extraction and Longitudinal Trend Analysis (DELTA) Paclitaxel (PTX) Study

Description:

In 2018, a published meta-analysis identified an association between the use of PTX-drug coated balloons (DCBs) or drug-eluting stents (DESs) used to treat peripheral arterial disease (PAD) with increased mortality at 2 and 5 years after treatment, when compared to patients treated with non-PTX-coated or eluting devices.[5] Consequently, FDA has issued safety communications,[6, 7, 8] initiated additional review of the mortality signal, and convened an advisory panel.[9] This pilot project further evaluated the findings from the 2018 meta-analysis.

Party conducting the pilot project and agreement type:

The pilot project was led by the Lahey Hospital and Medical Center under a cooperative agreement with FDA in communication with the MDEpiNet Registry Assessment of Peripheral Devices effort, a private-public partnership of academia, industry, and governmental regulatory agencies dedicated to improving the national evaluation of peripheral arterial devices throughout these devices' total product lifecycle.

Specific aim(s):

This study assessed the comparative safety of PTX DCBs and PTX DESs in the treatment of PAD through analysis of the VQI Peripheral Vascular Intervention (PVI) registry module using the DELTA system.

This project evaluated the relative safety of PTX when used as an antiproliferative agent in the treatment of symptomatic PAD, analyzing PTX DCBs and PTX DESs, both together and as unique exposures, using propensity score-matched survival analysis. The VQI PVI dataset was used to maximize the consistency of outcome and clinical covariate definitions.

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[5] Katsanos,K, Spiliopoulos,S , Kitrou, P, Krokidis, M, Karnabatidis,D. Risk of Death Following Application of Paclitaxel-Coated Balloons and Stents in the Femoropopliteal Artery of the Leg: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Am Heart Assoc. 2018; 7(24):e011245.

[6] See https://www.fda.gov/medical-devices/letters-health-care-providers/treatment-peripheral-arterial-disease-paclitaxel-coated-balloons-and-paclitaxel-eluting-stents.

[7] See https://www.fda.gov/medical-devices/letters-health-care-providers/update-treatment-peripheral-arterial-disease-paclitaxel-coated-balloons-and-paclitaxel-eluting.

[8] See https://www.fda.gov/medical-devices/letters-health-care-providers/august-7-2019-update-treatment-peripheral-arterial-disease-paclitaxel-coated-balloons-and-paclitaxel.

[9] See https://www.fda.gov/advisory-committees/advisory-committee-calendar/june-19-20-2019-circulatory-system-devices-panel-medical-devices-advisory-committee-meeting.

Data sources(s):

This study leveraged clinical data regarding the treatment of PAD through the VQI data collected by the SVS. Since 2004, the SVS has collected detailed clinical data regarding the treatment of PAD through the VQI in over 550 hospitals in North America and maintains data on over 575,000 patients. VQI also includes data linkage with the Global Unique Device Identification Database to identify devices and data linkage with the Social Security Death Index to ascertain vital status over time. The DELTA surveillance system was developed to assess potential medical device safety concerns. DELTA has been previously validated for the prospective monitoring of clinical registries and clinical datasets and is available as an open-source software tool with associated technical documentation.

Safety outcome(s) of interest:

The primary safety outcome of interest was survival (i.e., freedom from death from any cause) at 2 years post intervention in the following three cohorts of patients: (1) patients treated with PTX-DCB compared to percutaneous transluminal angioplasty, (2) patients treated with PTX-DES compared to bare metal stents, and (3) patients treated with either PTX-DCB or PTX-DES analyzed together compared to non-PTX devices.

Numbers and names of manufacturers involved:

Five manufacturers were involved: Bard, Medtronic, Philips, Cook, and Boston Scientific.

Number of patients:

Among the 16,462 patients who underwent a femoral-popliteal endovascular treatment and were captured in the VQI registry during the study period, 7,814 met the inclusion and exclusion criteria for the study and were included in the analysis.

Findings of project:

Propensity scores were generated for all cases, incorporating 21 clinical and procedural factors. Of the 7,814 patients that met the study inclusion and exclusion criteria, 2,456 were successfully matched, in a 1:1 fashion with propensity-matched patients receiving non-drug containing devices. The PTX treatment group was comprised of 1,769 patients treated with a PTX-DCB and 687 patients treated with a PTX-DES.

Treatment with any PTX device was associated with an increased 2-year survival rate (89.5 percent vs. 86.7 percent; hazard ratio (HR)= 0.79, 95 percent confidence interval (CI) 0.72-0.87, p=0.004), improved interventional success (81.6 percent vs. 77.6 percent; HR= 0.82, 95 percent CI=0.74-0.91, p<0.001), and higher rates of independent ambulation at 1 year (86.0% vs. 83.4 percent; HR= 0.85, 95 percent CI 0.79-0.91, p=0.008) when compared with non-PTX devices. Treatment with a PTX-DCB was associated with improved survival at 2 years (88.9 percent vs. 85.7 percent; HR= 0.77, 95 percent CI 0.70-0.86, p=0.005) while PTX-DES therapy was

associated with similar survival compared with bare metal stents (91.3 percent vs. 89.6 percent; HR= 0.84, 95 percent CI=0.70-1.01, p=0.36).

The results of this study suggest that PTX-containing devices are associated with improved survival at 2 years and improved clinical outcomes at 1 year, as compared with non-PTX devices used for femoral-popliteal procedures. However, it's important to note that this study included patients with worsened disease as compared to the clinical trials from which the signal was initially identified. Additionally, this study followed patients for 2 years as compared to 4 to 5 years in other studies that identified a safety signal.

FDA is considering data from the VQI-DELTA PTX study and others to assess the safety of PTX-coated devices.

Status:

Completed. A manuscript of this study is in progress.

4. Project Name: Safety and Effectiveness of Outpatient Surgical Procedures for the Treatment of Benign Prostatic Enlargement in New York State and California

Description:

In this project, the short- and long-term safety and efficacy of transurethral device-based resection of the prostate (TURP), compared to laser, was studied in a generalized population in an outpatient setting. This pilot explored the utility of state databases for device safety surveillance.

Party conducting the pilot project and agreement type:

The project was conducted by Weill Cornell Medicine under a cooperative agreement with FDA.

Specific aim(s):

The specific aim of this project was to compare outcomes following laser device prostatectomy against the more commonly used TURP in a real-world setting.

Data source(s):

The data sources for this project included the New York State Department of Health's SPARCS and the California Office of Statewide Health Planning and Development (OSHPD) health databases from January 2005 to December 2016.

Safety outcome(s) of interest:

The primary outcome of this project was reoperation rates. Secondary outcomes included 30-day and 90-day readmission and emergency department visits, 90-day complications, and the development of urethral stricture.

Numbers and names of manufacturers involved:

None.

Number of patients involved:

85,682 men with benign prostatic enlargement in New York State and California who received transurethral prostatectomy or laser prostatectomy in outpatient and ambulatory surgery settings were included in this project.

Findings of project:

Laser prostatectomy for benign prostatic enlargement was associated with a lower risk of short- and long-term complications but a higher rate of long-term reoperation than TURP.

Status:

Completed. This project was published in a peer-reviewed journal.[10]

5. Project Name: Evidence-Based Objective Performance Criteria for the Evaluation of Hip and Knee Replacement Devices and Technologies

Description:

Objective performance criteria (OPC) are numerical performance targets derived from clinical studies and/or RWD used to determine the safety and effectiveness of devices. OPC can be a valuable tool for active surveillance. This project aimed to develop OPC to assess the safety and effectiveness of hip and knee replacement devices. Despite the high prevalence of hip and knee replacements,[11] no OPC currently exist for these devices.

[10] Stoddard MD, Zheng X, Mao J, Te A, Sedrakyan A, Chughtai B. Safety and Efficacy of Outpatient Surgical Procedures for the Treatment of Benign Prostatic Enlargement in New York State and California (2005-2016). J Urol. 2021 Mar;205(3):848-854. doi: 10.1097/JU.0000000000001401. Epub 2020 Oct 7. PMID: 33026907.

[11] Singh JA, Yu S, Chen L, Cleveland JD. Rates of Total Joint Replacement in the United States: Future Projections to 2020-2040 Using the National Inpatient Sample. *The Journal of rheumatology.* 2019;46(9):1134-1140.

Party conducting the pilot project and agreement type:

The pilot project was led by Weill Cornell Medicine under a cooperative agreement with FDA.

Specific aim(s):

The objective of this study was to develop 2-year dynamic OPC for the safety and effectiveness of total hip arthroplasty (THA) and total knee arthroplasty (TKA) using RWD. The OPC were constructed using data from (1) a systematic review and meta-analysis of clinical studies, (2) a direct analysis of registries, and (3) an assessment of claims databases.

Data sources(s):

The OPC were constructed using combined data from three different data sources, including (1) a systematic literature review (January 2010 through January 2020 from PubMed, MedLine, EMBASE, Web of Science, Cochrane Library, CINAHL, and Academic Search Premier), (2) a direct analysis from the FORCE-TJR Registry [12] and Kaiser Permanente Registries (KPR)[13], and (3) a direct analyses from claims data from the New York State Department of Health's SPARCS and the California OSHPD.

Safety outcome(s) of interest:

The primary OPC for safety was the 2-year all-cause *revision rate*, which was defined as the extraction, replacement, or addition (alteration) of any implant. All-cause revision is a well-recognized metric used globally for device benchmarking. Revision due to infection was included as a secondary safety OPC to aid the evaluation of devices aimed at reducing septic revision.

Effectiveness measures used to generate OPC were also considered for most widely used patient-reported outcome measures (PROMs) and focused on 2-year postoperative outcomes. Disease-specific PROMs used for the construction of OPC include the Hip disability and Osteoarthritis Outcome Score (HOOS)[14], Oxford Hip Score, Knee disability and Osteoarthritis Outcome Score (KOOS)[15], and Oxford Knee Score.[16] For general Health-Related Quality of Life, EuroQol-5D

[12] Franklin PD, Allison JJ, Ayers DC. Beyond joint implant registries: a patient-centered research consortium for comparative effectiveness in total joint replacement. *JAMA.* 2012;308(12):1217-1218.

[13] Koebnick C, Langer-Gould AM, Gould MK, et al. Sociodemographic characteristics of members of a large, integrated health care system: comparison with US Census Bureau data. *Perm J.* 2012;16(3):37-41.

[14] Nilsdotter AK, Lohmander LS, Klassbo M, Roos EM. Hip disability and osteoarthritis outcome score (HOOS)--validity and responsiveness in total hip replacement. *BMC Musculoskelet Disord.* 2003;4:10.

[15] Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *J Orthop Sports Phys Ther.* 1998;28(2):88-96.

[16] Dawson J, Fitzpatrick R, Murray D, Carr A. Questionnaire on the perceptions of patients about total knee replacement. *J Bone Joint Surg Br.* 1998;80(1):63-69.

(EQ-5D)[17], Short Form (SF)-12,[18] and SF-36 were used.[19] Global Physical Health was measured using the SF-36 Physical Component Score (PCS), and Global Emotional Health was measured using the SF-36 Mental Component Score. =OPC for the physician-evaluated Harris Hip Score(HHS)[20] and Knee Society Score (KSS)[21] were also developed.

Number and names of manufacturers involved:

None.

Number of patients:

Data were available and extracted for 653,662 patients. Within the systematic literature review, 39 studies comprising 36,557 patients were identified and contributed to the evidence. A direct data analysis of FORCE-TJR contributed 9,223 patients, KPR contributed 262,044 patients, and claims database analysis contributed 345,828 patients to the construction of THA and TKA OPC.

Findings of project:

Two-year OPC for effectiveness among THAs and TKAs were constructed based on the most commonly used PROMs. Among THAs, the identified OPC using the HOOS were 87.1, using the HHS function were 94.4, using the SF-12/SF-36 PCS were 46.5, and using the EQ-5D were 0.88. All-cause and septic 2-year revision rates for THAs were 2.0 percent and 0.5 percent, respectively. Among TKAs, the identified OPC using the KOOS were 80.6, using the KSS function were 90.6, using the SF-12/SF-36 PCS were 41.9, and using the EQ-5D were 0.84. All-cause and septic 2-year revision rates for TKAs were 1.7 percent and 0.7 percent, respectively.

Status:

Completed. A manuscript of this project is in progress.

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6. Project Name: Endovascular Treatment of Abdominal Aortic Aneurysms (EVAR) Conversion

Description:

This pilot project, which involved collaboration between the VISION CRN and the SVS, VQI, used a VQI registry and Medicare-linked dataset to study open aortic repair conversions after an unsuccessful EVAR, and compared temporal and regional variations in the VQI registry.

Party conducting the pilot project and agreement type:

This project was led by Weill Cornell Medicine and MDEpiNet's VISION CRN under a cooperative agreement with FDA.

Specific aim(s):

The first specific aim of the study was to study temporal trends and geographical variations in the VQI registry. Associated rates of open aortic repair after an unsuccessful EVAR were determined with an analysis to identify temporal, as well as regional, variations. Identification of periprocedural (related to the index EVAR procedure) predictors of subsequent open aortic conversion for a failed EVAR were determined. The second specific aim was to determine the rates of outcomes including periprocedural, 30-day, and 1-year mortality. Associated rates of cardiac and neurologic complications, including spinal cord ischemic complications and stroke, were assessed for the above procedures. In addition, associated rates for mesenteric ischemia, renal failure with dialysis requirement, bleeding complications, pulmonary complications, total length of stay, and intensive care unit (ICU) length of stay were measured.

Data source(s):

The data source for this project included the VQI-Medicare linked dataset for EVARs from 2003 to 2016.

Safety outcome(s) of interest:

The outcomes of interest for this project were temporal and regional variations in the VQI for the open abdominal aortic aneurysm (AAA) procedure after an initial EVAR: in-hospital mortality, 30-day mortality, 1-year mortality, length of stay, ICU length of stay, hospital readmission within 30 days, and discharge destination.

Numbers and names of manufacturers involved:

None.

Number of patients involved:

This project included 15,937 EVAR patients that underwent a conversion to open surgery during follow up.

Findings of project:

Approximately 2 percent of EVAR patients underwent a conversion within 5 years. There was no geographical variation in conversion rates. Patients undergoing non-elective EVAR were more likely to have a conversion than those undergoing elective EVAR. Patients who were females, who had an aneurysm diameter >60 mm, and who had a ruptured AAA were more likely to undergo conversion than those who were males, who had a small aneurysm, and who had an intact AAA. Thirty-day mortality after converted open procedures was 8.5 percent and 28.0 percent for elective and non-elective procedures, respectively.

Status:

Complete. A manuscript of this project is in progress.

VI. Progress on Ongoing Pilot Projects

7. Project Name: Electrophysiology Predictable and Sustainable Implementation of National (EP PASSION) Registries - Methods to Replace Traditional Postapproval Studies (PASs)

Description:

EP PASSION is an ongoing pilot project that is developing methods to replace traditional, mandated PASs with sustainable, reliable, and timely real-world methodology. ICD leads and cardiac re-synchronization therapy (CRT) device leads are involved in this pilot project. Current PASs of high-voltage ICD and CRT leads are conducted in prospective new patient enrollment studies. This current approach is costly, requires years to complete enrollment, and does not always maintain enough patients for follow up or provide timely answers to postmarket questions. Therefore, this project aims to reduce the cost, duration, and attrition of the PAS through leveraging RWD sources. This pilot is intended to generate more efficient and timely safety and effectiveness data and more quickly identify poorly performing devices.

Party conducting the pilot project and agreement type:

The pilot project is being executed by a consortium of voluntary stakeholders, including academia, FDA, medical device manufacturers, and professional societies and requires no funding from FDA. The funds for the conduct of the pilot have come from the manufacturers

that are conducting the pilot.

Specific aim(s):

The aims for the five phases of this pilot project are as follows:

- Phase 1 (Completed): Identify the minimal set of core data elements for an assessment of the pacing and defibrillation leads.

- Phase 2: (Completed): Determine existing sources of data, which may require formation of several working groups.

- Phase 3 (Completed): Develop a method to collect core data elements not available from existing data sources.

- Phase 4 (Completed): Develop a linked approach to combine data elements from sources identified or created in Phases 2 and 3.

- Phase 5 (Ongoing) : Compare the linked data source approach to conventional PAS findings.

Data source(s):

This pilot project includes administrative claims, device remote monitoring data, manufacturer-device tracking, and complaint handling databases.

Safety outcome(s) of interest:

The safety outcomes of interest include cardiac tamponade, cardiac perforation, and lead adverse events that require surgical intervention (such as an insulation breach or lead/conductor fracture).

Numbers and names of manufacturers involved:

The four manufacturers involved in the pilot include Abbott, BIOTRONIK, Boston Scientific, and Medtronic.

Number of patients:

The number of patients involved in this project has not yet been determined.

Findings of project:

The technical work completed to date includes an agreement on core minimum data sets, standards for data quality, and methods for linking the registry with outcomes data (such as administrative claims). Validation of the evidence methodologies with the linked data sources,

outlined above, is being conducted by the manufacturers involved in this project.

Status:

Ongoing.

8. Project Name: Creating a National Surveillance Infrastructure for Devices Used in Hernia Repairs

Description:

The Abdominal Core Health CRN aims to address the long-term surveillance of techniques and devices commonly used in the care of abdominal core health, which includes improving the data infrastructure through a linkage of registry data with administrative and clinical data; this linkage may improve longitudinal and cross-facility follow-up rates as well as validations of complications and devices.

Party conducting the pilot project and agreement type:

The pilot project is being led by Weill Cornell Medicine under a cooperative agreement with FDA. Weill Cornell Medicine has also contracted with the Americas Hernia Society Quality Collaborative (AHSQC).

Specific aim(s):

The primary aims of this pilot study are to link registry and state claims data to (1) examine data completeness and to determine the feasibility of an effective linkage model in the abdominal core health space (successfully executed), (2) assess long-term follow-up rates, and (3) determine long-term catastrophic complications following ventral hernia repair.

Data source(s):

The data sources for this pilot project include (1) the New York State Department of Health's SPARCS claims data and (2) the AHSQC hernia patient registry data.

Safety outcome(s) of interest:

The primary outcomes to be identified in linked datasets include hernia recurrences, hospital readmissions, reoperations, surgical site infections, and mesh-related complications.

Numbers and names of manufacturers involved:

None.

Number of patients involved:

There were 737 registry patients that were identified in the AHSQC registry who had undergone hernia repair in New York State from 2015 to 2016.

Findings of project:

A total of 737 New York State patients were originally identified from the AHSQC registry for linkage. SPARCS data were available through 2016, and therefore, 577 registry patients whose date of repair occurred in 2017 or later were excluded. Of the remaining 160 registry patients qualified for linkage, 88.1 percent (N=141) were successfully linked to SPARCS claims data using a sequential matching algorithm. Additional SPARCS data for 2017 and 2018 were recently acquired, and these data will support the project's aims of assessing long-term outcomes and determining follow-up and complication rates.

Status:

Ongoing.

9. Project Name: Mortality After PTX-Coated Balloon Angioplasty and Stenting of Superficial Femoral and Popliteal Artery (VISION CRN)

Description:

The MDEpiNet's VISION CRN uses RWD for tracking outcomes, such as late mortality, after approval of PADs. This project involves a large, observational, registry linked with Medicare to study PTX-related mortality in the treatment of PAD that will inform the development of methods and systems for active surveillance.

Party conducting the pilot project and agreement type:

This project is led by Weill Cornell Medicine and MDEpiNet's VISION CRN under a cooperative agreement with FDA.

Specific aim(s):

The objective of this study is to compare mortality rates after treatment of superficial femoral-popliteal artery disease with PTX and non-PTX devices using a multicenter vascular registry.

Data source(s):

The data sources for the project include the VISION CRN, which consists of the VQI registry linked to Medicare claims data for long-term surveillance evaluation.

Safety outcome(s) of interest:

The outcome of interest for this project is the mortality rate after treatment of superficial femoral-popliteal artery disease with PTX- and non-PTX devices.

Numbers and names of manufacturers involved:

Some of the manufacturers of these devices are engaged.

Number of patients involved:

A total of 8376 patients that underwent endovascular treatment of superficial femoral-popliteal artery disease from October 2016 to December 2017 were identified in the SVS VQI and included in this pilot project. Linkage with Medicare data is ongoing.

Findings of project:

One-year mortality rates were compared among the following three groups: (1) plain balloon angioplasty, (2) PTX-coated balloon angioplasty, bare-metal stenting, and (3) PTX-eluting stents. The combined PTX versus non-PTX devices were also compared. The study found that mortality was similar, if not lower, after treatment of femoral-popliteal occlusive disease with PTX devices versus non-PTX devices.

Status:

Ongoing.

10. Project Name: Active Surveillance of Medical Device Safety and Outcomes Using EHRs: Prostate Cancer Partial Gland Ablation Technologies

Description:

The primary objective of this project is to develop Natural Language Processing (NLP) methodologies using EHR data to perform active surveillance of medical device safety and outcomes for prostate cancer therapies, including partial gland ablation. The project also aims to integrate the data into the Study of Prostate Ablation Related Energy Devices (SPARED) CRN registry with the help of HIVE technologies at the MDEpiNet Coordinating Center and Weill Cornell Medicine.

Party conducting the pilot project and agreement type:

Weill Cornell Medicine has subcontracts with Johns Hopkins University under a Center for Excellence in Research Science and Innovation grant to conduct this project as part of a

cooperative agreement with FDA.

Specific aim(s):

The specific aims of this project are as follows: (1) collect data from EHRs with manual data extraction of cancer characteristics from pathology and radiology reports, (2) develop and validate NLP tools by developing sustainable and scalable strategies to supplement the existing NLP infrastructure to support active surveillance of partial gland ablation, and (3) develop and add active surveillance statistical methodology to the data ecosystem.

Data source(s):

The data sources for this project include the EHRs at Weill Cornell Medicine.

Safety outcome(s) of interest:

The specific outcomes of interest are the data elements harvested from EHRs into the NLP and HIVE repository that are integrated into the SPARED registry.

Numbers and names of manufacturers involved:

None. Outreach to manufacturers is planned for the next phase of the project.

Number of patients involved:

A minimum of 100 patients will be targeted for this study.

Findings of project:

Pending.

Status:

Ongoing.

VII. Conclusion

A variety of active surveillance pilot projects are currently underway, several of which are already producing RWE for device evaluation by various stakeholders, including FDA and industry. In addition, the voluntary pilot projects have and will continue to help inform the development of active surveillance and practical applications of active surveillance in real-world settings. These efforts are important to the further development of the NEST and other RWE capabilities, and the future work outlined here will increase the scale and impact

of these capabilities.

Appendix: Summary Table of Device Pilot Projects Under Section 708 of FDARA

#	Pilot name	Device(s) Involved	Data Source(s) Involved	Safety Outcome(s) of Interest	Manufacturers Involved	Status	# of Patients	Agreement Type
Pilot Projects for Current Reporting Period								
1	VISION	Stents, stent-grafts, and other devices used in the treatment of diseases of the peripheral circulatory system	SVS VQI Registry, Medicare claims, New York State Department of Health's SPARCS, device manufacturer clinical trial databases	Death, procedure-specific adverse events (stroke, rupture, and amputation), reinterventions, readmissions, surveillance, imaging, cost	Cook Medical, Endologic, W. L. Gore & Assoc., and Medtronic	Completed	>300,000 patients	Cooperative agreement with FDA
2	Ortho CRN (formerly named *ICOR-USA*)	Joint replacements	Ortho CRN members: KP, AJRR, FORCE TJR, and MARCQI	Revision rates	Zimmer Biomet, Smith & Nephew, and Johnson & Johnson	Completed	>600,000 patients	Cooperative agreement with FDA
3	VQI-DELTA PTX Study	PTX DCBs and PTX DESs	VQI data collected by the SVS	Survival (i.e., freedom of death from any cause)	Medtronic, Bard, Philips, Cook, and Boston Scientific	Completed.	7,814 patients	Cooperative agreement with FDA
4	Outpatient Surgical Procedures for the Treatment of Benign Prostatic Enlargement in New York State and California	Transurethral prostatectomy and laser prostatectomy	New York State and California statewide databases	Reoperation rates	None	Completed	85,682 men	Cooperative agreement with FDA

#	Pilot name	Device(s) Involved	Data Source(s) Involved	Safety Outcome(s) of Interest	Manufacturers Involved	Status	# of Patients	Agreement Type
5	Evidence-Based OPC for the Evaluation of Hip and Knee Replacement Devices and Technologies	THA and TKA devices	Literature, FORCE-TJR, KPR, the New York State Department of Health's SPARCS, and the California OSHPD	PROMs and cumulative joint revision rates at 2 years	None	Completed	653,662 patients	Cooperative agreement with FDA
6	EVAR Conversion	Endovascular Treatment Devices	VQI-Medicare linked dataset for EVAR	In-hospital mortality, 30-day mortality, 1-year mortality, length of Stay, ICU length of stay, hospital readmission within 30 days, and discharge destination	None	Completed	15,937 EVAR patients	Cooperative agreement with FDA

#	Pilot name	Device(s) Involved	Data Source(s) Involved	Safety Outcome(s) of Interest	Manufacturers Involved	Status	# of Patients	Agreement Type
7	EP PASSION	ICD leads and CRT device leads	Administrative claims, device remote monitoring data, manufacturer-device tracking, and complaint handling databases	Cardiac tamponade and perforation, lead adverse events that require surgical intervention	Abbott, BIOTRONIK, Boston Scientific, and Medtronic	Ongoing	Not yet determined	No funding for phase 1, but funding from industry for subsequent phases
8	Creating a National Surveillance Infrastructure for Devices Used in Hernia Repairs	Mesh for ventral hernia repair	New York State's Department of Health's SPARCS and AHSQC	Hernia recurrences, hospital readmissions, reoperations, surgical site infections, and mesh-related complications	None	Ongoing	737 registry patients	Cooperative agreement with FDA
9	Mortality After PTX-Coated Balloon Angioplasty and Stenting of Superficial Femoral and Popliteal Artery in the Vascular Quality Initiative	PTX devices and non-PTX devices	VQI-Medicare data	Mortality	All major manufactures of PTX devices and non-PTX devices	Ongoing	8,376 patients	Cooperative agreement with FDA

#	Pilot name	Device(s) Involved	Data Source(s) Involved	Safety Outcome(s) of Interest	Manufacturers Involved	Status	# of Patients	Agreement Type
10	Active Surveillance of Medical Device Safety and Outcomes Using EHRs: Prostate Cancer Partial Gland Ablation Technologies	Prostate Cancer Partial Gland Ablation Technologies	Weill Cornell Medicine Urology Department and related EHRs.	Data elements harvested from EHRs into NLP and HIVE repository that are integrated into SPARED registry	None	Ongoing	100+ Patients	Cooperative agreement with FDA
Completed/Terminated/Discontinued Projects from Previous Reports								
	Signal detection: Opioid use and risk of joint revision surgery	Total knee and total hip	KP's TJR Registry and EHRs	Risk of revision surgery	Johnson & Johnson, Smith & Nephew, and Zimmer Biomet	Completed	24,105 (knees) 12,895 (hips)	Cooperative agreement with FDA
	DELTA-ICD leads	ICD leads	ICD Registry in the NCDR	Survival (freedom from failure)	None	Completed	374,132	Cooperative agreement with FDA and funding from the William M. Wood Found.
	SPARED robot-assisted cystectomy	Robotic devices	SEER-Medicare data	Benign ureter stricture and stricture diagnoses	None	Completed	1,781 patients	Cooperative agreement with FDA

#	Pilot name	Device(s) Involved	Data Source(s) Involved	Safety Outcome(s) of Interest	Manufacturers Involved	Status	# of Patients	Agreement Type
	WHT-CRN mesh for POP repairs	Mesh implants used in POP repairs	New York State's Department of Health's SPARCS	Reoperation risk	None	Completed	54,194 patients	Cooperative agreement with FDA
	WHT-CRN slight mesh for SUI	Sling mesh implants for SUI	New York State's Department of Health's SPARCS	Reoperation and erosion	None	Completed	36,195 patients	Cooperative agreement with FDA
	DELTA-TAVR	Aortic and mitral valves	NCDR's Transcatheter Valve Therapy Registry	Survival (i.e., freedom from a composite of death, stroke, or repeat valve operations)	Medtronic, Abbott, and Edwards	Discontinued	> 150,000 patients	Cooperative agreement with FDA
	WHT-CRN Urogynecological Mesh and Risk of Cancer	Mesh	New York State's Department of Health's SPARCS	Cancer	None	Discontinued	59,117 patients	Cooperative agreement with FDA