Use of Real-World Healthcare Data for Clarifying the Scope and Occurrences of Metal Implant Complications

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Abstract

Background: With a broad number of adverse events reportedly associated with metallic implants, their clinical scope and terminology as well as underlying pathogenic background remain unclear. For this reason, a comprehensive study of metal implant-related adverse health outcomes is critical for enhancing clinical and regulatory decision-making regarding metal implants.

Purpose: Our goal is to derive real-world evidence on clinically-consequential adverse outcomes attributable to metal implants in order to outline their scope and frequency, explore their true nature, and clarify their terminology and ontology.

Methodology: The project has started in collaboration with the LoopBack Analytics, as the provider of clinical data and infrastructure support for data sourcing and management. Patient records with devices of interest are identified through standardized diagnosis and procedure codes such as CPT, HCPCS, ICD-9/ICD-10. Where possible, device information within the EMR system is matched to the Global Unique Device Identification Database (GUDID) to provide device-specific metadata. The hospitals used are chosen because of their size, high level counts of target cases, and frequency of device data occurring.

Results: The 1st phase of the project is focused on identifying and collating patient and device related data for the analysis on metal-containing orthopedic and gynecological implants in comparison with their non-metal containing counterparts. The dataset of >25000 unique patients with hip, knee and shoulder arthroplasty devices and hysteroscopic sterilization devices is collated by the LoopBack Analytics and transferred to FDA. Further data processing and analytic approaches are being developed to explore correlations between patient factors, device characteristics, and post-implantation clinical sequalae representing potential device-related adverse outcomes.

Conclusion: The deployment of big healthcare data on metal-containing implants is expected to yield real-world insights into device-patient interactions, outline the corresponding clinically relevant health outcomes and their possible pathogenetic links, and thereby enhance predictive evaluation of metal implant safety in specific patient subpopulations.

Materials and Methods

Data Requirements Span a Variety of Cases And Data Domains

Cases

Table 1. Priority List of Implanted Metal-based Devices

Metal based Orthopedic Implants (Priority 1)

Group 1	Group 2
▪ Total hip replacement	▪ Total knee arthroplasty
▪ Hip resurfacing	▪ Unicompartmental knee replacement
▪ Hemiarthroplasty	▪ Reverse total shoulder replacement
▪ Bi-polar systems	▪ Total elbow replacement
▪ Dual mobility systems	▪ Wrist joint replacement
	▪ Total ankle arthroplasty
	▪ Total toe arthroplasty

Non-orthopedic metal-based implants (Priority 2)

Group 1	Group 2
▪ Contraceptive devices	▪ Sterilization devices

Materials and Methods (cont'd)

Data Domains

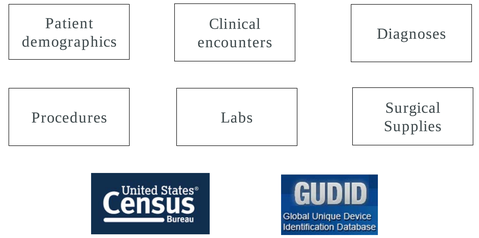

Figure 1. Data Requirements Span a Variety of Cases and Data Domains

Real-World Data (RWD) Dataset Optimization

RWD Constraints		Research Objectives
# of data sites / dataset size	⟷	Statistical significance across priorities
Coverage across years	⟷	Pre / Post implant longitudinal coverage
Breadth of clinical data domains	⟷	Analysis of comorbidities / risk factors
Changing practice patterns	⟷	Availability of implant composition data
Evolving coding standards	⟷	Consistent coding / coverage across years
Payer / Patient mix	⟷	Representative demographics

Figure 2. Real-World Data (RWD) Dataset Optimization

Case Identification Methodology

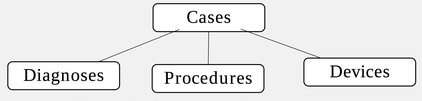

Figure 3. Case Identification

- Diagnoses – The primary method for patient identification was using diagnosis codes which consisted of 163 ICD-10 diagnosis codes.
- Procedures – The secondary method for patient identification was using procedure codes which consisted of 22 CPT codes, 2 HCPCS codes, and 164 ICD-10 procedure codes.
- Devices – Manufacturers catalog numbers in the device data and the GUDID database can be used to identify specific devices and their material properties that have been implanted into a patient. Device information can provide specific metal composition data for the devices. Fifty-nine product codes were chosen for the orthopedic devices as the priority group for this investigation; one permanent sterilization device was evaluated with no additional product codes.

Connection to Device-related Characteristics

The Global Unique Device Identifier database (GUDID) provides a connection to Global Medical Device Nomenclature (GMDN) terms and the FDA Submission Number. The submission number can be used to look up the summary of safety and effectiveness data (SSED) sheets which will provide insights into the composition of the device. The figure below illustrates how the RWD and the device data objects are related.

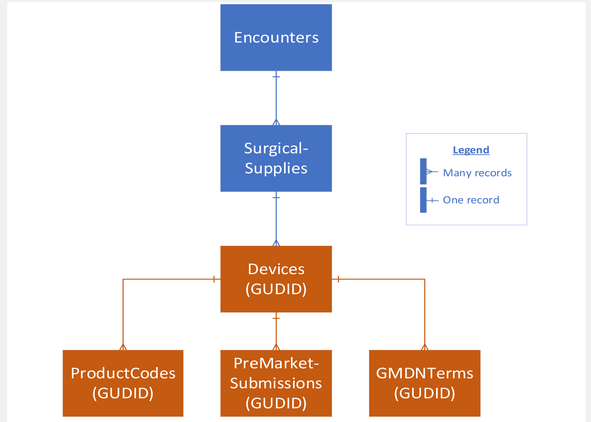

Figure 4. Data Relationship to GUDID

Table 2. Categories for Material/Alloy for Metal based Orthopedic Implants

Bearing Surface	Alloy
▪ Metal-on-metal (MoM)	▪ CoCr
▪ Metal-on-polyethylene (MoP)	▪ SS
▪ Ceramic-on-metal (CoM)	▪ Ti
▪ Ceramic-on-polyethylene (CoP)	▪ NiTi
	▪ Other

Preliminary Results

Source Data Demographics

Table 3. Race and Sex Demographics Across All Source Data

Race	Male	Female	Grand Total	% of Total
Asian	7,851	5,687	**13,538**	**2%**
Black	133,993	106,593	**246,586**	**29%**
White	279,856	223,916	**503,772**	**58%**
Other	53,846	43,589	**97,435**	**11%**
Grand Total	**481,546**	**379,785**	**861,331**	**100%**

Target Case Demographics

After all the filtering was completed, the target population showed demographic characteristics as described in Tables 4 and 5. Since some patients can be part of multiple study groups, the sum of totals for each priority/ group (P-G) is expected to exceed the total number of unique patients across all target subpopulations.

Table 4. Sex by Research Priority Across Target Population

Sex	P1-G1		P1-G2		P2-G2		Grand Total
Female	6,230	60%	11,685	62%	324	100%	**16,535**
Male	4,117	40%	7,183	38%	0	0%	**10,356**
Grand Total	**10,347**		**18,868**		**324**		**26,891**

Preliminary Results (cont'd)

Table 5. Race by Research Priority Across Target Population

Race	P1-G1		P1-G2		P2-G2		Grand Total
Asian	18	<1%	52	<1%	3	<1%	**70**
Black	1,941	19%	3,592	19%	115	35%	**5,175**
White	8,185	79%	14,763	78%	179	55%	**20,988**
Other	203	2%	461	2%	27	8%	**658**
Grand Total	**10,347**		**18,868**		**324**		**26,891**

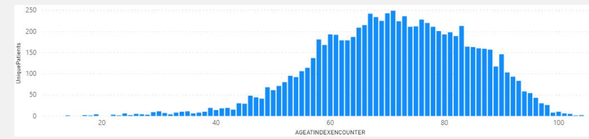

Figure 5. Age Demographics Across Target Population

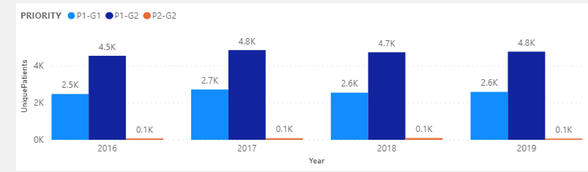

Figure 6. Unique Patients within Target Population by Priority and Year

To date we have identified target patients using a verified systematic approach. The dataset of >25000 unique patients that had an encounter with the selected facilities between January 1, 2016 and December 31, 2019 with hip, knee and shoulder arthroplasty devices and hysteroscopic sterilization devices is collated by the LoopBack Analytics and transferred to FDA. Specifically, we have completed:

- Site selection - Identify hospitals that possess data most likely to meet project objectives.
- Case selection- Identify cases using criteria most likely to accurately identify patients with implants.
- Case Identification – A full list of codes (Diagnosis Code, Procedure Code, and Product Code) have been identified specific for the case identification for this project.

Further data processing and analytic approaches are being developed to explore correlations between patient factors, device characteristics, and post-implantation clinical sequalae representing potential device-related adverse outcomes.

Conclusion

- Per our preliminary results, big healthcare RWD can be successfully deployed for regulatory research on the role of implant characteristics and patient demographics in development of adverse health outcomes;
- Our subsequent research is expected to delineate the clinical scope of implant-related adverse outcomes and their pathogenetic links, providing real-world insights and thereby enhancing predictive evaluation of real-world implant performance.