ENGELBERG CENTER for Health Care Reform at BROOKINGS

Developing the Capabilities for Device Surveillance through the Medical Device Epidemiology Network

Danica Marinac-Dabic, U.S. Food and Drug Administration

Mary Beth Ritchey, U.S. Food and Drug Administration

Benjamin Eloff, U.S. Food and Drug Administration

Fred Resnic, Brigham and Women's Hospital and Harvard Medical School

Art Sedrakyan, Weill Cornell Medical College

April 9, 2012

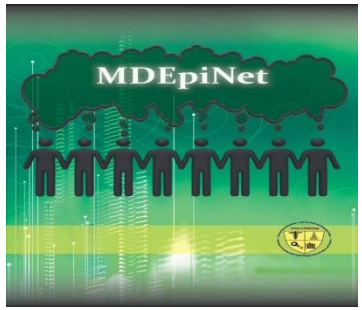
Brookings Roundtable on Active Medical Product Surveillance

Some Initial Housekeeping

- To minimize feedback, please confirm that the microphone on your telephone is muted.
- To mute your phone, press the mute button or '*6'. (To unmute, press '*7' as well.)
- **There will be several opportunities for questions and discussion throughout today's session. Please use the Q&A tab at the top of your screen to submit your questions into the queue at any point and we will call upon you to state your question.**
- We will open up the lines for questions from those participating only by phone at the end of each Q&A session.
- Call the Brookings IT Help Desk at 202-797-6193 with technical problems.

FDA Medical Device Epidemiology Network (MDEpiNet) Initiative

Danica Marinac-Dabic, MD, PhD
Mary Beth Ritchey, RN, PhD
Benjamin Eloff, PhD
Fred Resnic, MD, MS
Art Sedrakyan, MD, PhD



Outline

- **FDA MDEpiNet Core:**
  - Postmarket context, mission, objectives, strategies: Danica Marinac-Dabic
  - Contracts and Work Streams: Mary Beth Ritchey
  - Public Private Partnership: Benjamin Eloff
- **MDEpiNet Methodology Center** : Fred Resnic
- **MDEpiNet Infrastructure Center**: Art Sedrakyan
- **MDEpiNet Public Private Partnership:** Benjamin Eloff
- **Next steps:** Danica Marinac Dabic

Evaluation of Medical Device Postmarket Landscape

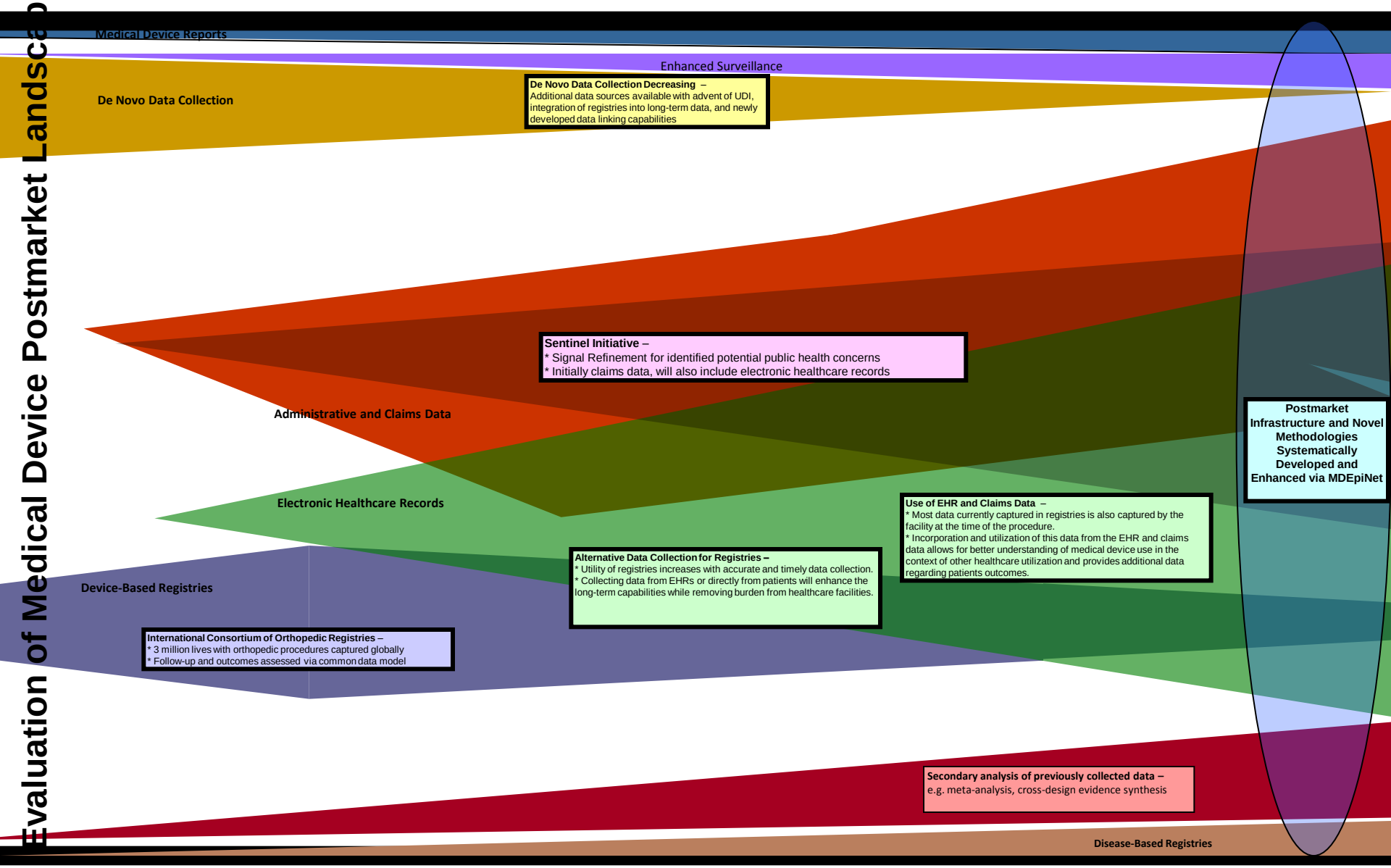
2009-2014
ARRA, HITECH Acts.
125 million lives captured in mini-Sentinel.
Establishment of MDEpiNet.
Final Rule for UDI.

2014-2019
Evaluation of UDI within claims and EHR.
Linkage of device registries with other healthcare data sources.
Use of distributed data networks for surveillance.

2019-2024
Device registries and UDI fully integrated into patient healthcare dataset.
Patient info able to be tracked across datasets via "hashing" or "fuzzy logic" linking.

2024-2029
Postmarket infrastructure allows most evaluation via automatic data collection.
In rare instances where additional data needed, patient surveys and disease-based registries created.

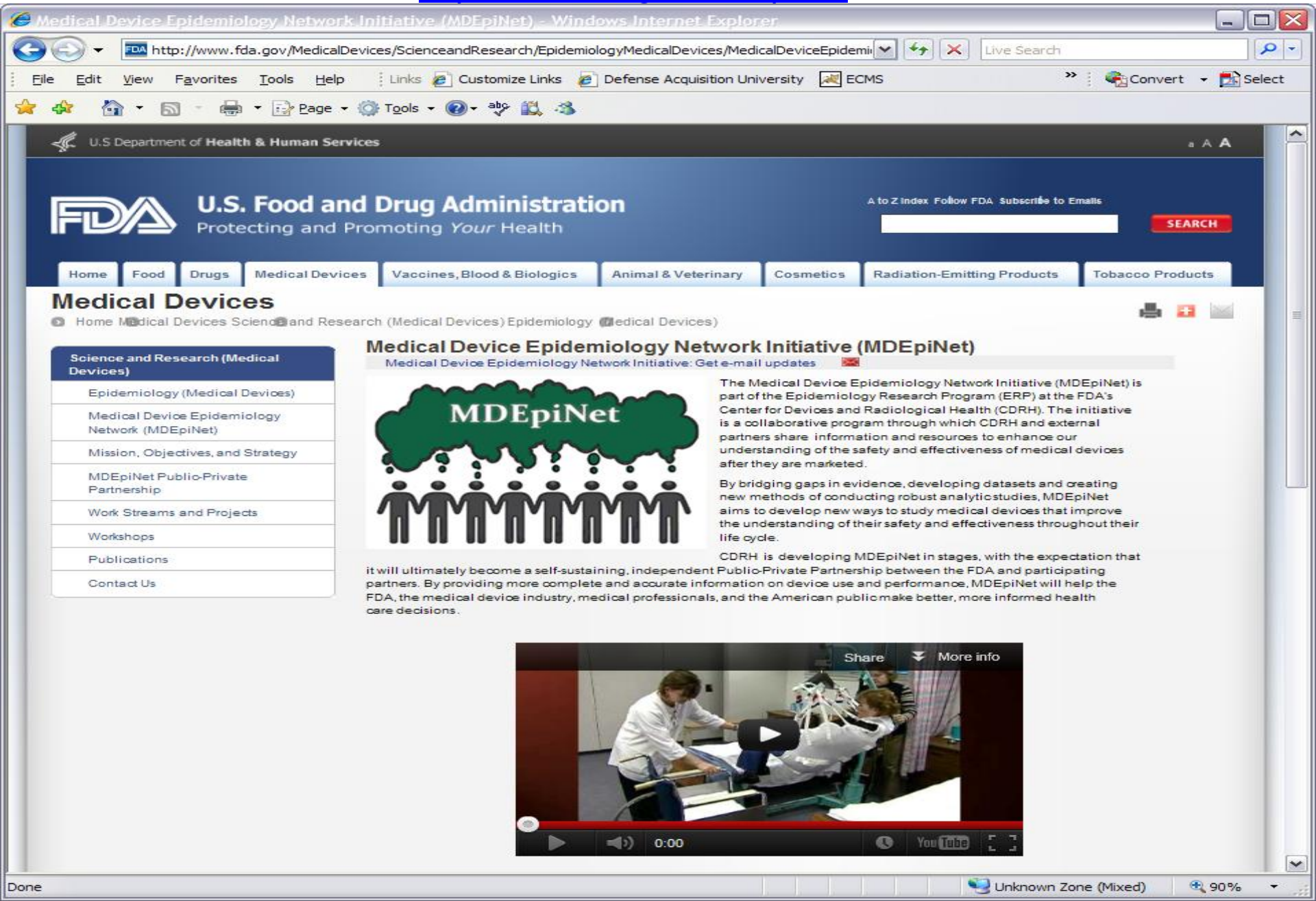
2029-future
Continue to innovate and utilize novel methodologies and new technologies to better understand performance and clinical outcomes of medical devices in the postmarket.
Ongoing evaluation of postmarket landscape used to provide context for benefit-risk balance for newly developed devices.



Devices ≠ Drugs

- **Put what know about drug regulation aside**
  - Drugs and devices, and the way they are used, are very different
    - A minor drug change can alter its properties – not always true for devices
    - Implanted devices may remain in the body for extended time
    - Discontinuing exposure to a device may be difficult/impossible
    - Devices are very susceptible to manufacturing tolerances and mechanical failures
    - Device use is more dependent on the skills of the operator
    - It is very difficult to blind a patient or user to device exposure
  - The laws governing drug regulation (premarket and postmarket processes/requirements) are very different than those for devices.
    - Multiple RCTs are not the norm in the world of devices
    - Device law allows for a broader interpretation of “valid scientific evidence”
    - Many devices can reach market by bench comparison testing to a predicate

http://www/fda/gov/MDEpiNet



MDEpiNet Initiative

MISSION

✓To develop infrastructure and innovative methodological approaches for conducting robust studies to improve medical device safety and effectiveness understanding throughout the device life cycle.

MDEpiNet Initiative

OBJECTIVES

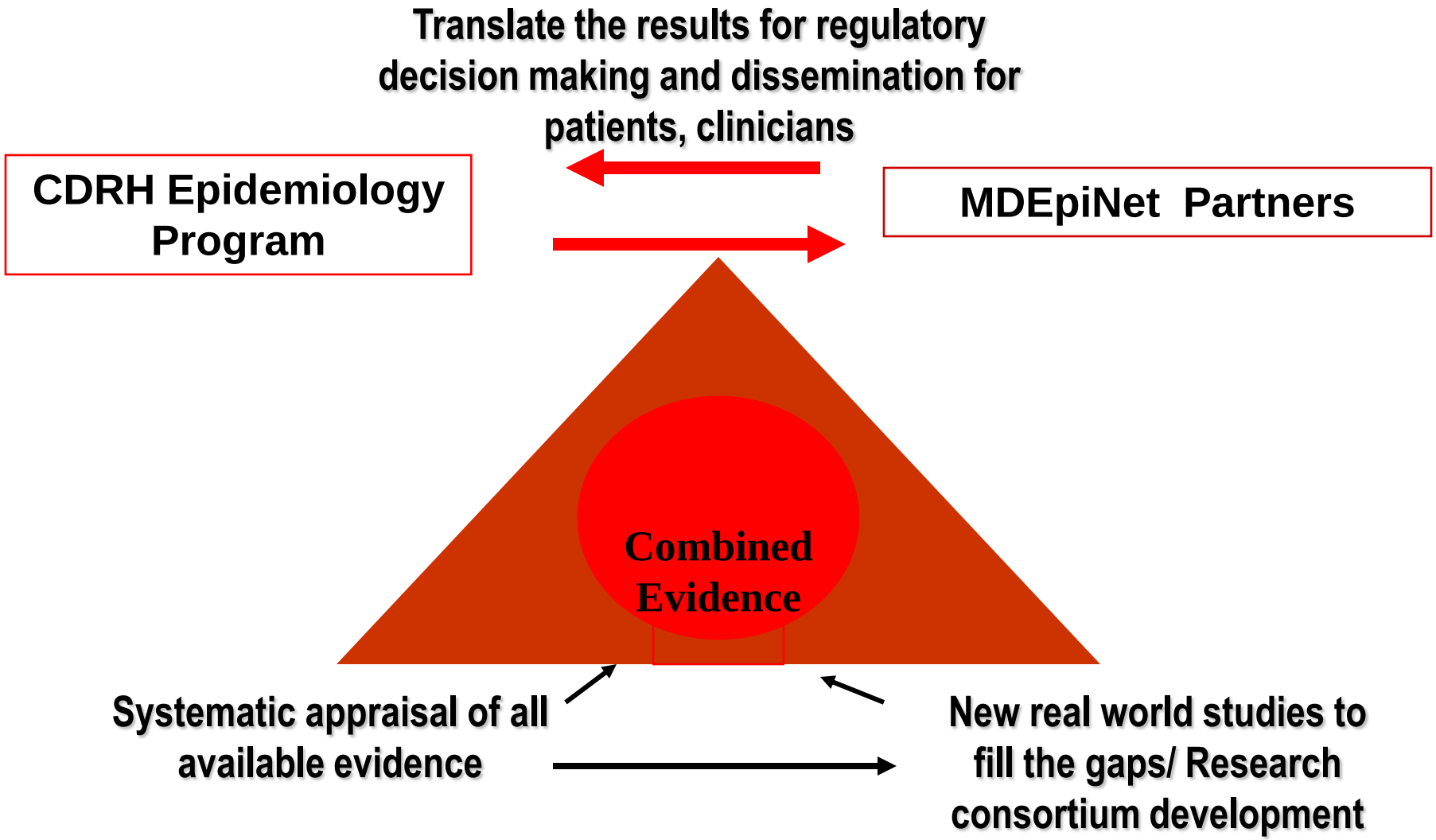
- ✓Improve the paradigm of how medical device knowledge is utilized throughout device life cycle
- ✓Leverage partner resources and expertise to create a sustainable, robust infrastructure through which stakeholders will continue to gain valuable knowledge about medical devices
- ✓Become fully integrated in the systematic evaluation of medical devices and CDRH decision making

MDEpiNet Initiative

APPROACHES

- ✓Systematically evaluate evidence of risks and benefits associated with medical devices
- ✓ Collaborate with external parties with relevant expertise to determine evidence gaps, study questions, methodologies and best practices
- ✓ Develop and test innovative methodological approaches for medical device research and regulatory science
- ✓ Disseminate the findings to all stakeholders

MDEpiNet Conceptual Framework



Methodology Work Stream

MDEpiNet Methodology Center: Harvard University

Evidence Synthesis

- Obtain safety and effectiveness estimates, develop and apply modeling techniques, translate results

Patient-Centered Outcomes

- Compare adverse events between groups, accounting for important device, operator, and patient characteristics

Existing Gaps

- Identify gaps in existing data sources and develop sustainable infrastructure and methods for addressing gaps to better evaluate medical devices

Infrastructure Work Stream

MDEpiNet Science and Infrastructure Center:

Cornell Weill Medical College

ICOR

- International Consortium of Orthopedic Registries

- Classification and harmonization with UDI
- Demonstration projects: bearing surface, femoral head size, fixed vs. mobile knees, pediatric joints

UDI Work Stream

Incorporated within Methodology Center and Science and Infrastructure Center

UDI

- Identify challenges and opportunities with UDI; demonstrate capabilities for use within EHR and registries
  - Roadmap of potential hurdles and best practices
  - 2 EHR cardiovascular demonstration projects
  - 3 orthopedic registry demonstration projects

The MDEpiNET Methodology Center

Co-Principal Investigators:

Sharon-Lise Normand, PhD
Harvard Medical School & Harvard School of Public Health

Frederic S. Resnic, MD MSc
Brigham and Women's Hospital & Harvard Medical School

Harvard Medical School

Brigham & Women's Hospital

Harvard School of Public Health

No Medical Device is Perfectly Safe

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The New York Times

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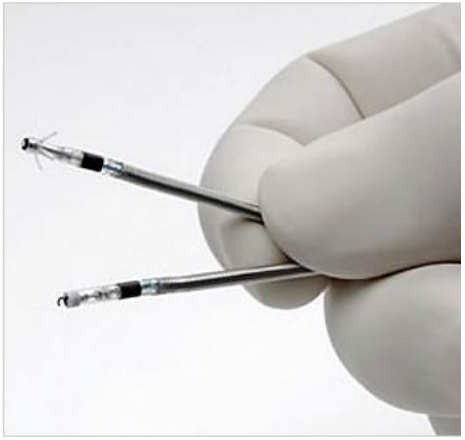
In Data for Heart Devices, Parts



Experts say there is a dearth of information about the performance of th

By BARRY MEIER
Published: October 16, 2007

Medtronic's decision to stop selling a widely used pa heart devices underscores the dearth of safety monit products, as well as a design trend that may make th prone to failure, several experts said yesterday.

Remedy Is Elusive as Metallic Hips Fail at a Fast Rate

An orthopedic surgeon, Dr. Young- Hospital.

By BARRY MEIER
Published: September 30, 2011

BOSTON — As surgeons h failed artificial hip in a 53 like a biological dead zon stained gray and black; a contracted.

The New York Times

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Doctors Rethink Widespread Use of Heart Stents

Librado Romero/The New York Times

Key Differences in Safety Monitoring

Medications:

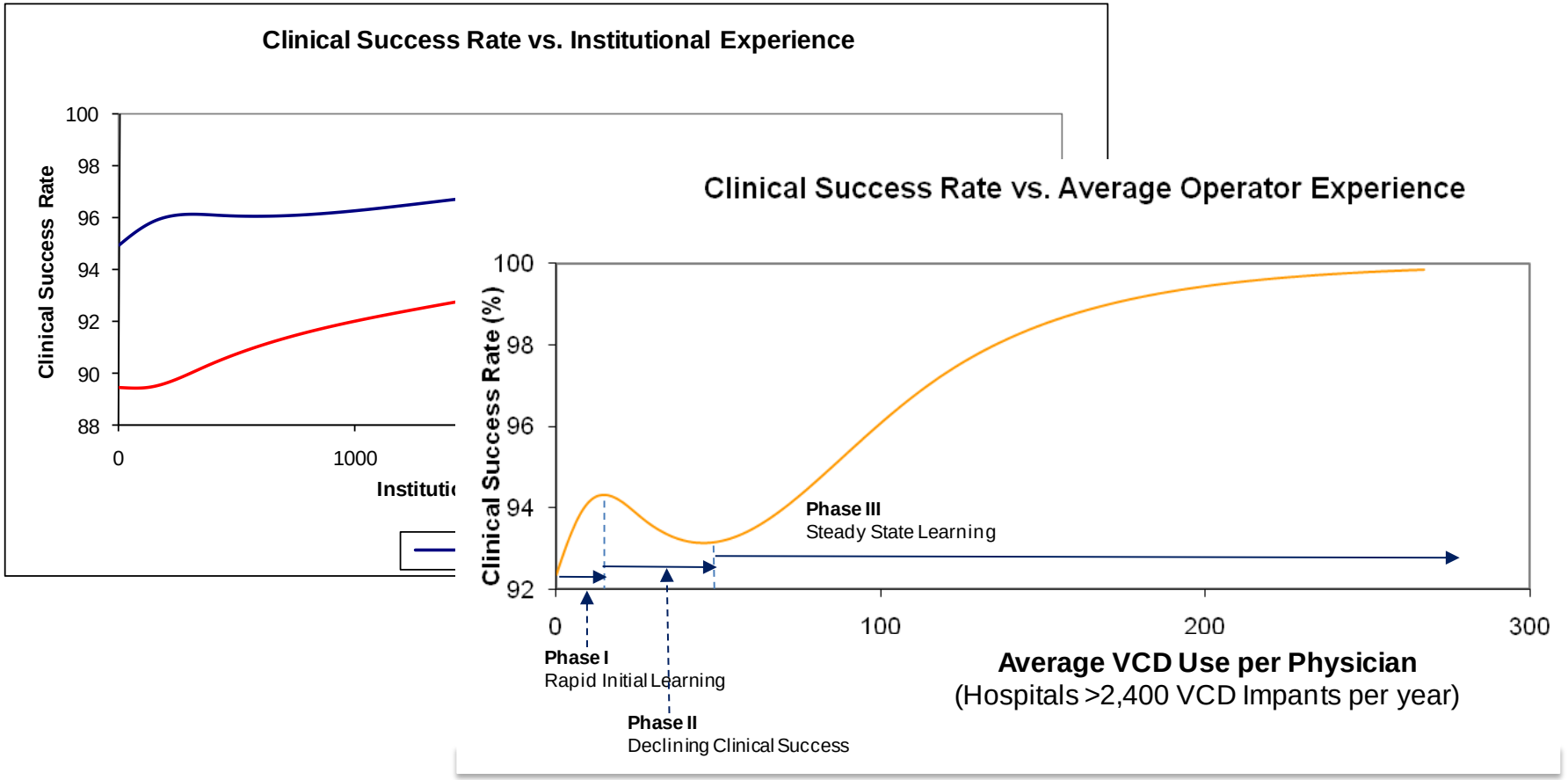
- Exposure: NDI uniform documentation; available in claims records
- Outcomes: general clinical conditions, rare diagnoses
- Often suitable for population based surveillance

Devices:

- Exposure: No existent uniform identification. Initial UDI efforts underway; ? claims requirement for UDI.
- Variable documentation of implant procedure
- Multiple failure modes of interest
- Learning curve; procedural quality

Learning Curve with Novel Device

An evaluation of 107,000 consecutive new VCD deployments in the national NCDR CathPCI dataset demonstrates a clear learning curve in the use of these devices.



Source: Resnic FS et al. JACC Interventions Jan 2012

Methodology Center Project Goals

1. Developing evidence-based regulatory science
   - Novel approaches for combining information
   - Identification of methodological gaps
   - Comparative effectiveness and safety studies

2. Implementation of a Unique Device Identifier Demonstration Project
   - Development of an end-to-end (purchaser to point of consumption) UDI tracking system
   - Utilize electronic health records and clinical registries to assess the continued safety and effectiveness of medical devices after they have reached the marketplace

Investigators

- **Statisticians**:
  - Sharon-Lise Normand (HMS & HSPH)
  - Laura Hatfield (HMS)
- **Epidemiologists**:
  - Miguel Hernan (HSPH)
  - Sebastian Schneeweiss (HMS & HSPH)
- **Clinicians**:
  - Frederic Resnic (Brigham & HMS)
  - Joe Drozda (Mercy Healthcare System)

Developing Evidence-Based Regulatory Science and Surveillance

Combining Information

- Selection of Medical Device Area & Data Sources
- Protocol Development of Evidence Abstraction
  - From published literature
  - From virtual data bases
- Development of Methodology to Combine Information
  - New measures of evidence
  - Comparison groups
- Proof of Concept: apply to selected devices

Existing Resources for Evaluation of Medical Devices

- Identification of Classes of Medical Devices and Data Sources
  - diagnostic, therapeutic, aesthetic, combination
- Evaluation of Gaps in Analytical Approaches
- Identification of Databases & Development of New Methodology
- Proof of Concept: apply to selected devices

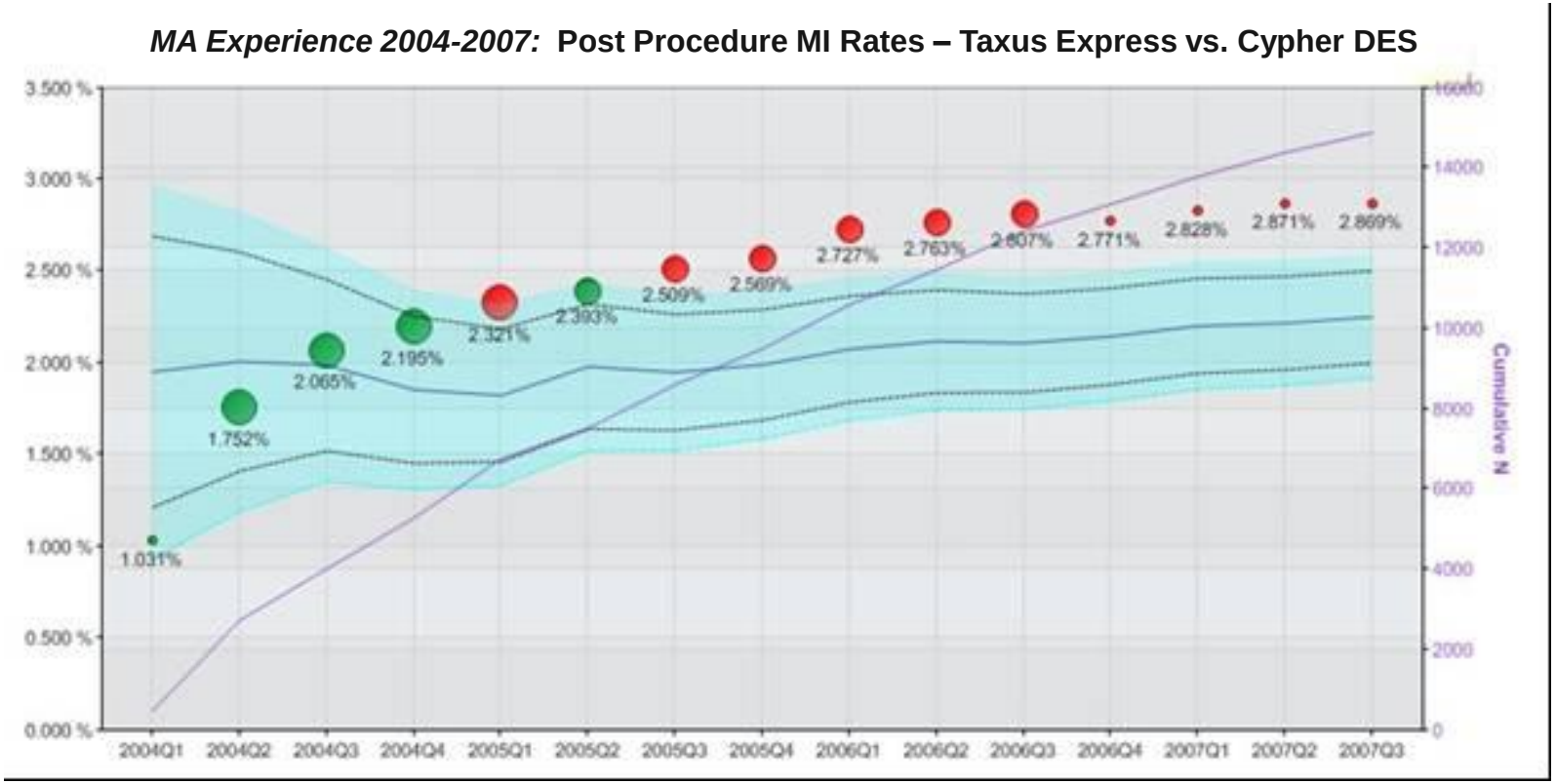
Going Forward

- **Tools**: statistical methodologies to use retrospectively and prospectively data (1) to infer cause and effect and (2) validity of assumptions to infer cause and effect
- **Collaborators**: network of multidisciplinary investigators interested in assessing devices
- **Data Sources**: virtual warehouse of post-approval surveillance information

Example Analysis: Retrospective Surveillance Demo

Using the MA state-wide PCI device dataset, we explored the ***cumulative*** post-procedure myocardial infarction rate for new drug eluting stent as compared with propensity matched control DES.

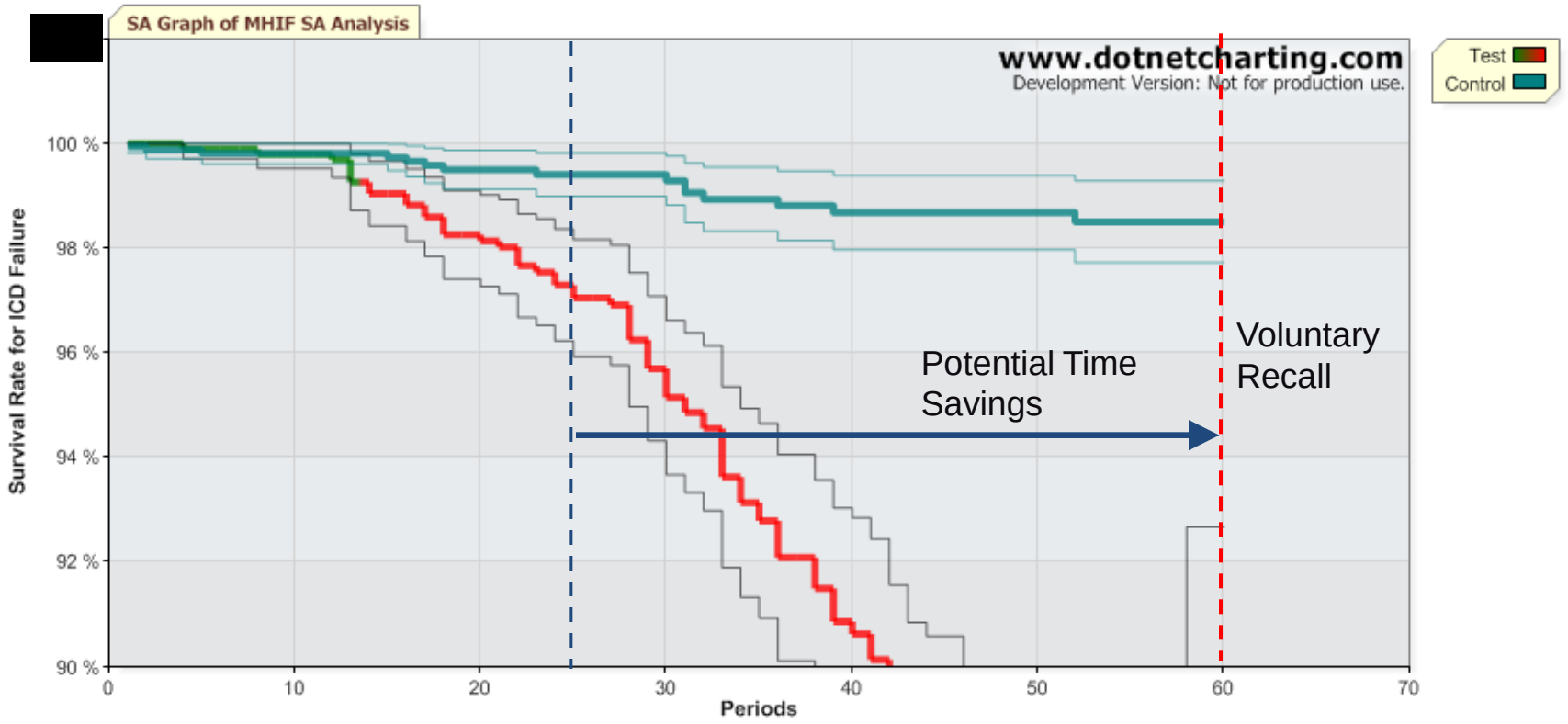
Using 38 clinical variables in propensity match a total of 81.5% of 18,277 new stents were analyzed.



Adapted from: Resnic F et al. JAMA November 2010

Example: Potential Time Savings

Using pooled data from *three* high volume centers, DELTA performed a propensity matched analysis 0f 859 Fidelis lead implants versus traditional leads. By 25 months of analysis (dashed line) 3% of Fidelis leads had fractured (red line) whereas only 0.1% (1 of 859) alternative ICD leads had fractured.

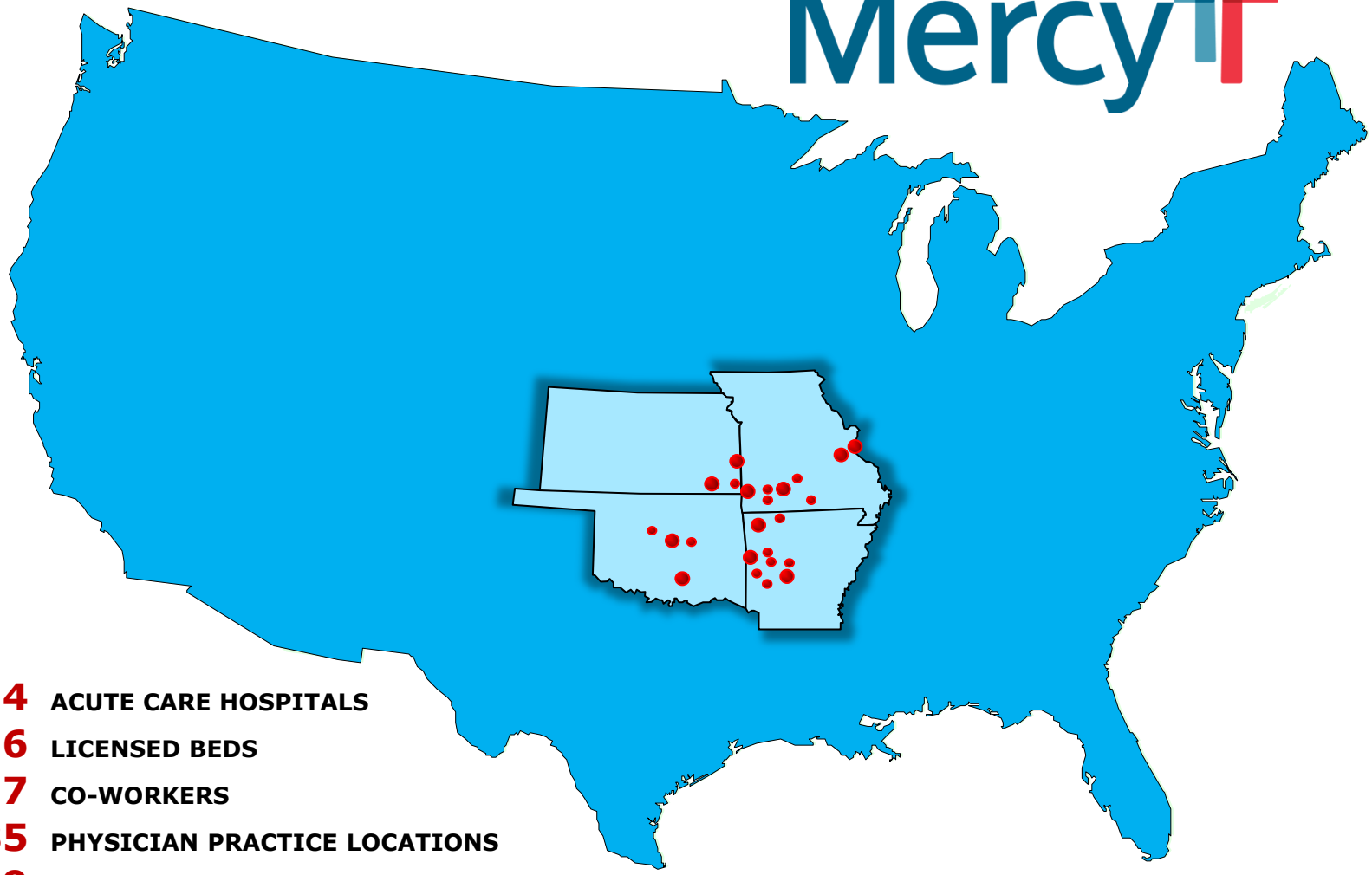


Hauser et al. *Circ Cardiovasc Qual Outcomes*. 2012

Unique Device Identifier Demonstration Project

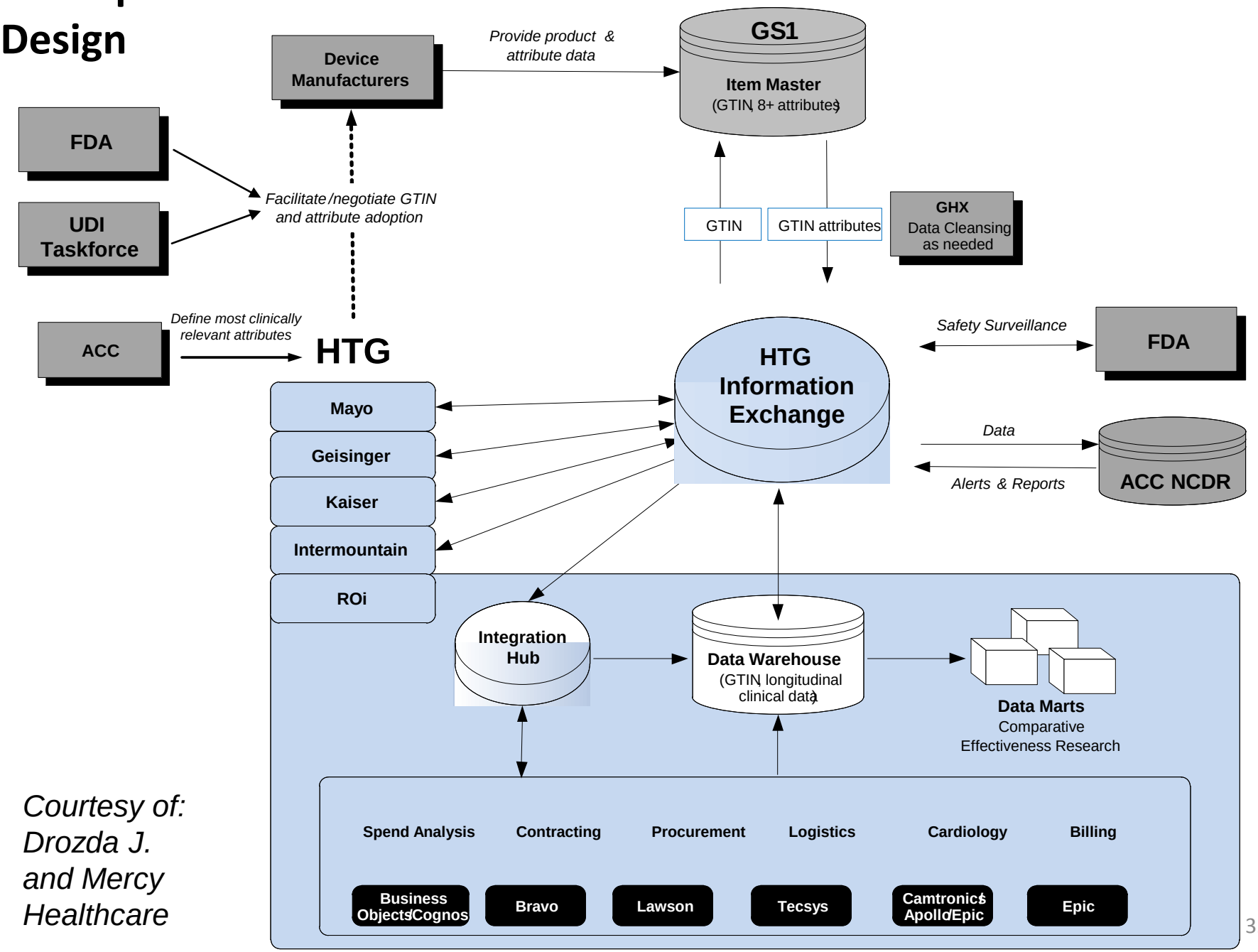
- Dr. Joe Drozda (PI)
- Site: Mercy Health System
  - 34 acute care hospitals
  - 2 heart hospitals, outpatient care facilities
  - Over 1200 integrated physicians
  - skilled nursing and long-term residential care facilities, clinics, and other health-related services
  - one of the nation's "Most Wired" health care organizations in the U.S. (Hospitals and Health Networks)
- Professional Society Advisors: ACC and SCA&I

- Implement a coronary artery stent UDI-based surveillance system in the EHR in a multi-hospital system
- Identify obstacles to implementation of the UDI Roadmap & to characterize the effectiveness of interventions to overcome them;
- Assess the validity and utility of data obtained from the EHR and incorporated UDIs for purposes of post-market surveillance

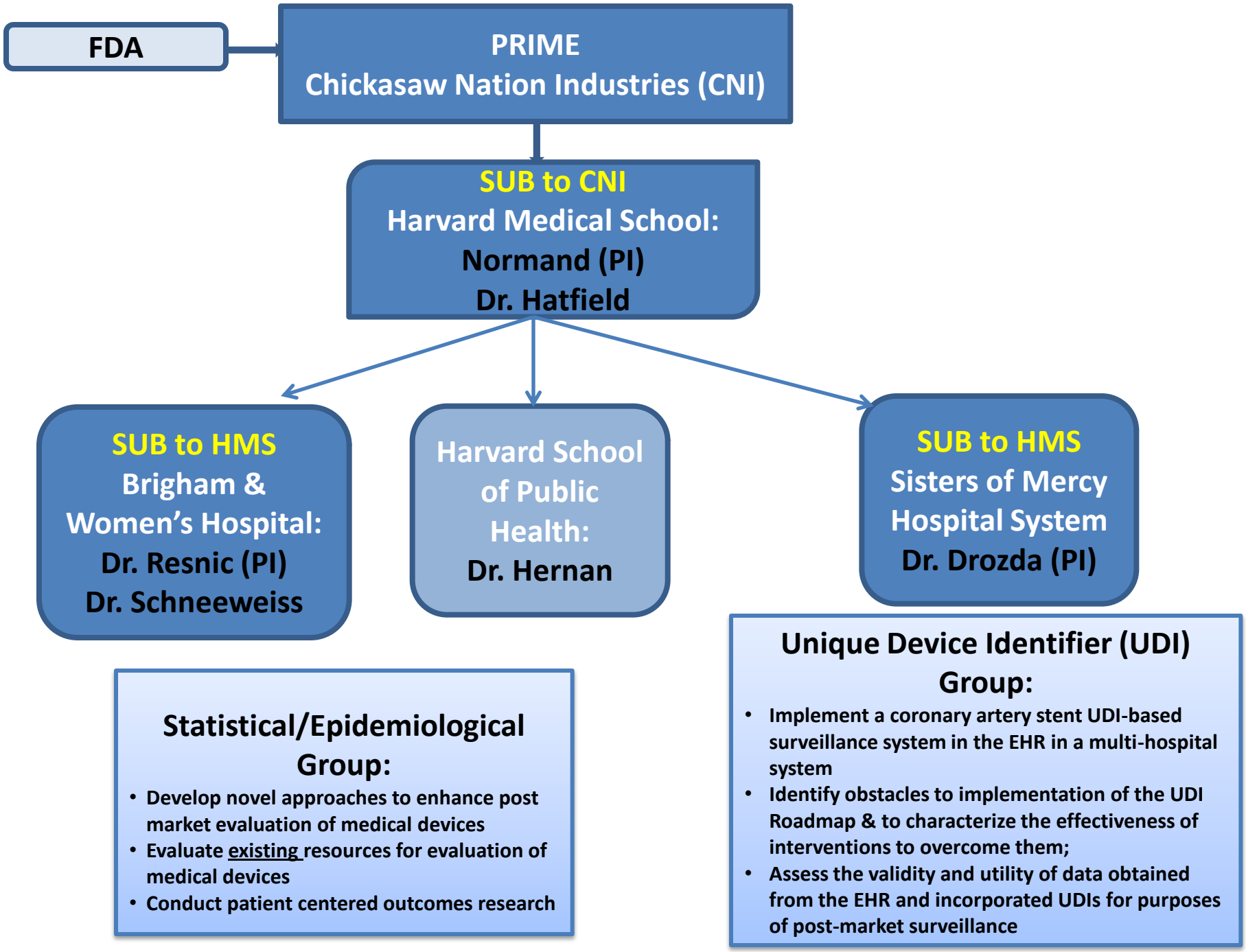


34 ACUTE CARE HOSPITALS
4,396 LICENSED BEDS
36,917 CO-WORKERS
185 PHYSICIAN PRACTICE LOCATIONS
4,659 MEDICAL STAFF MEMBERS
1,235 INTEGRATED PHYSICIANS
$4.05 OPERATING REVENUE (Billions USD)

Conceptual Design



Courtesy of: Drozda J. and Mercy Healthcare


FDA
PRIME
Chickasaw Nation Industries (CNI)
SUB to CNI
Harvard Medical School:
Normand (PI)
Dr. Hatfield
SUB to HMS
Brigham &
Women's Hospital:
Dr. Resnic (PI)
Dr. Schneeweiss
Harvard School
of Public
Health:
Dr. Hernan
SUB to HMS
Sisters of Mercy
Hospital System
Dr. Drozda (PI)
Statistical/Epidemiological Group:
• Develop novel approaches to enhance post market evaluation of medical devices
• Evaluate existing resources for evaluation of medical devices
• Conduct patient centered outcomes research
Unique Device Identifier (UDI) Group:
• Implement a coronary artery stent UDI-based surveillance system in the EHR in a multi-hospital system
• Identify obstacles to implementation of the UDI Roadmap & to characterize the effectiveness of interventions to overcome them;
• Assess the validity and utility of data obtained from the EHR and incorporated UDIs for purposes of post-market surveillance

The MDEpiNET Science and Infrastructure Center

Principal Investigator:

Art Sedrakyan, MD, PhD
Associate Professor
Weill Cornell Medical College
Director of Comparative Effectiveness Research Program

Co-investigator:
Elizabeth Paxton, MA
Director of Surgical Outcomes and Analysis
Kaiser Permanente

Weill Cornell Medical College

NewYork-Presbyterian Hospital
Weill Cornell Medical Center

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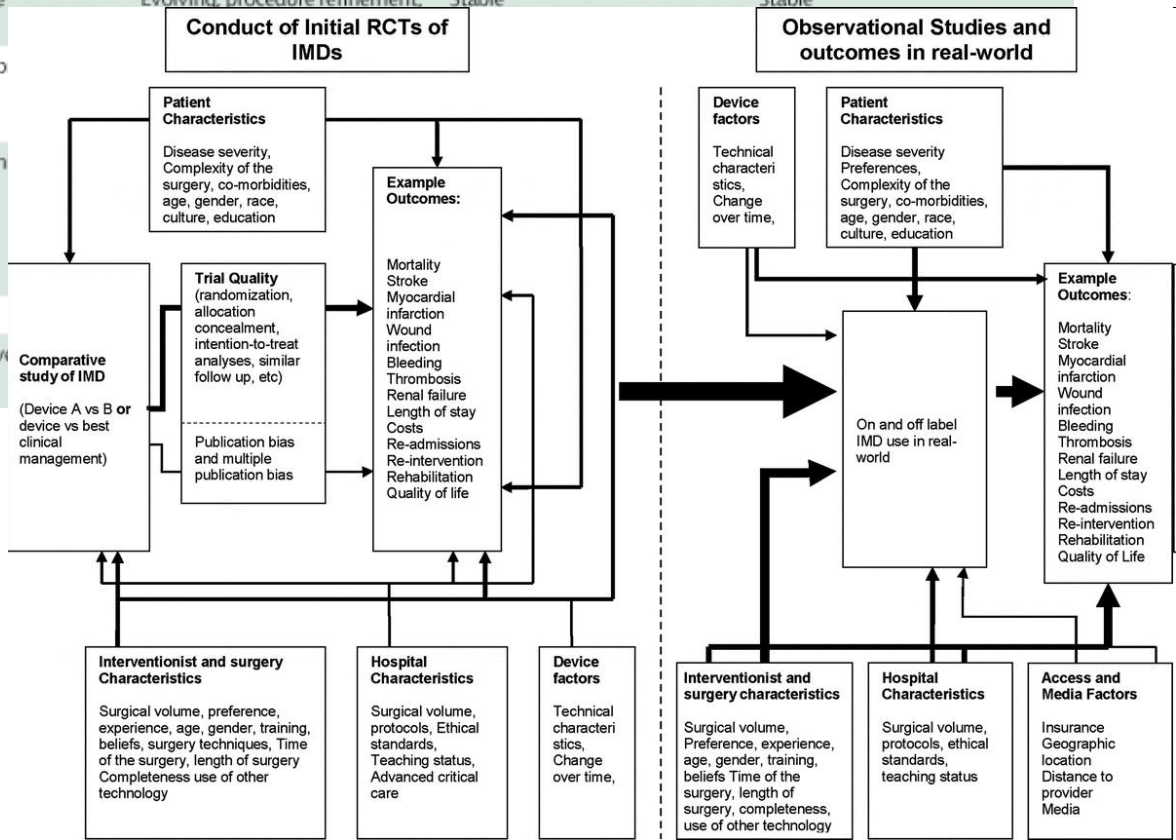
Science and Infrastructure Center

- Developing Conceptual Frameworks for Device evaluation

	1 Idea	2a Development	2b Exploration	3 Assessment	4 Long-term study
Purpose	Proof of concept	Development	Learning	Assessment	Surveillance
Number and types of patients	Single digit; highly selected	Few; selected	Many; may expand to mixed; broadening indication	Many; expanded indications (well defined)	All eligible
Number and types of surgeons	Very few; innovators	Few; innovators and some early adopters	Many; innovators, early adopters, early majority	Many; early majority	All eligible
Output	Description	Description	Measurement; comparison	Comparison; complete information for non-RCT participants	Description; audit, regional variation; quality assurance; risk adjustment
Intervention	Evolving; procedure inception	Evolving; procedure development	Evolving; procedure refinement;	Stable	Stable
Method	Structured case reports	Prospective develop studies			
Outcomes	Proof of concept; technical achievement; disasters; dramatic successes	Mainly safety; techn procedural success			
Ethical approval	Sometimes	Yes			
Examples	NOTES video[6]	Tissue engineered v			

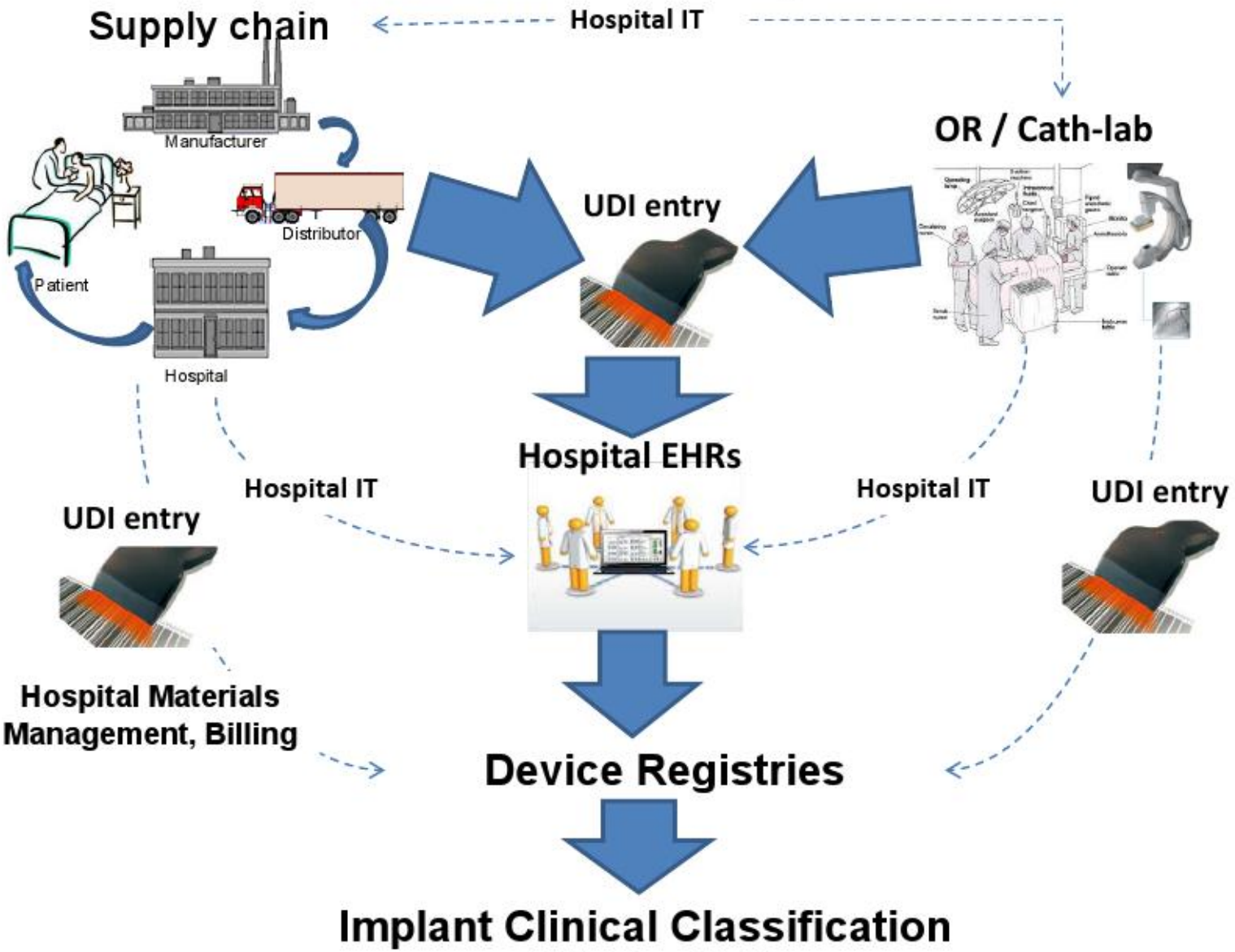
Sedrakyan et al. A framework for evidence evaluation in implantable device studies. Med Care 2010



Registry: a key infrastructure

- 'A *patient registry* is an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes' *AHRQ handbook*
- Critical discussion issues:
  - Hypothesis driven?
  - Comprehensive, all inclusive, mandatory
    - National or nationally representative?

Building UDI based device registries: Various models of Implementation



Art Sedrakyan, Md, PhD

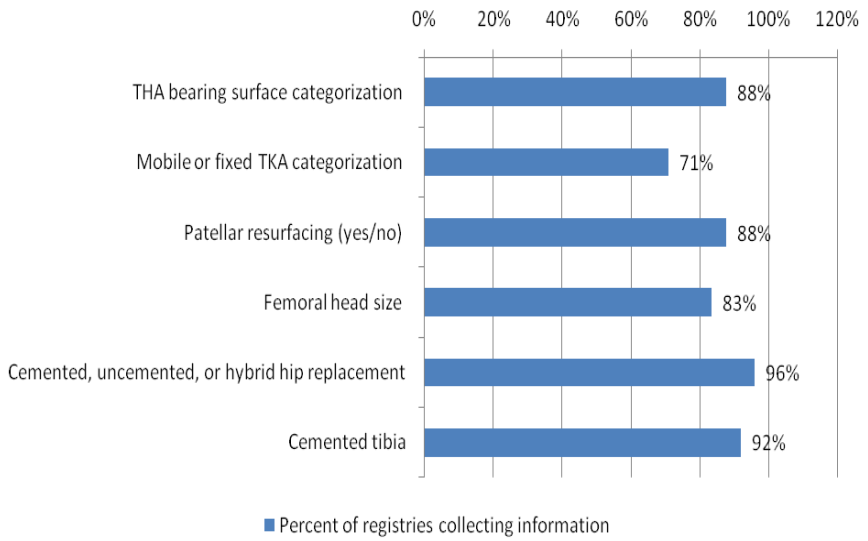
The ICOR: Mission and Goals

- Contract Awarded to Cornell-Kaiser
- To advance the research and improve evidence for the safety and effectiveness of orthopedic devices and procedures
  - Harmonize the data among US based and international orthopedic registries
  - Implement a distributed data analysis system and conduct studies to monitor the safety and effectiveness of orthopedic devices
- First study: bearing surface

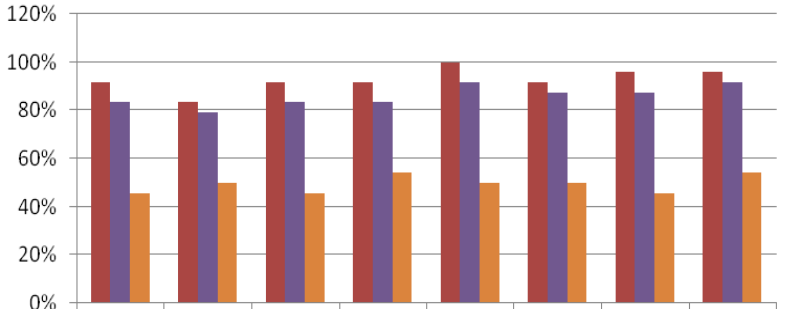
American Joint Replacement Registry
Australian Orthopaedic Assoc. Registry
Austrian Arthroplasty Register
California Joint Replacement Registry
Hospital for Special Surgery
Italian Register of Orthopaedic Implants
Kaiser Permanente
Massachusetts General Hospital
Mayo Clinic
New England Baptist Hospital Registry
New Zealand Joint Register
Norwegian Arthroplasty Register
OrthoCarolina
Portuguese Arthroplasty Register
Rush University Med. Ctr. Joint Registry
Slovakian Arthroplasty Register
ScFCOT THA Registry
Swedish Hip and Knee Registers
Scottish Arthroplasty Project
UMass FORCE Registry
Virginia State Registry
Western Slope Study Group

>3,000,000 Patients Worldwide

Fixation and Implant Characteristics



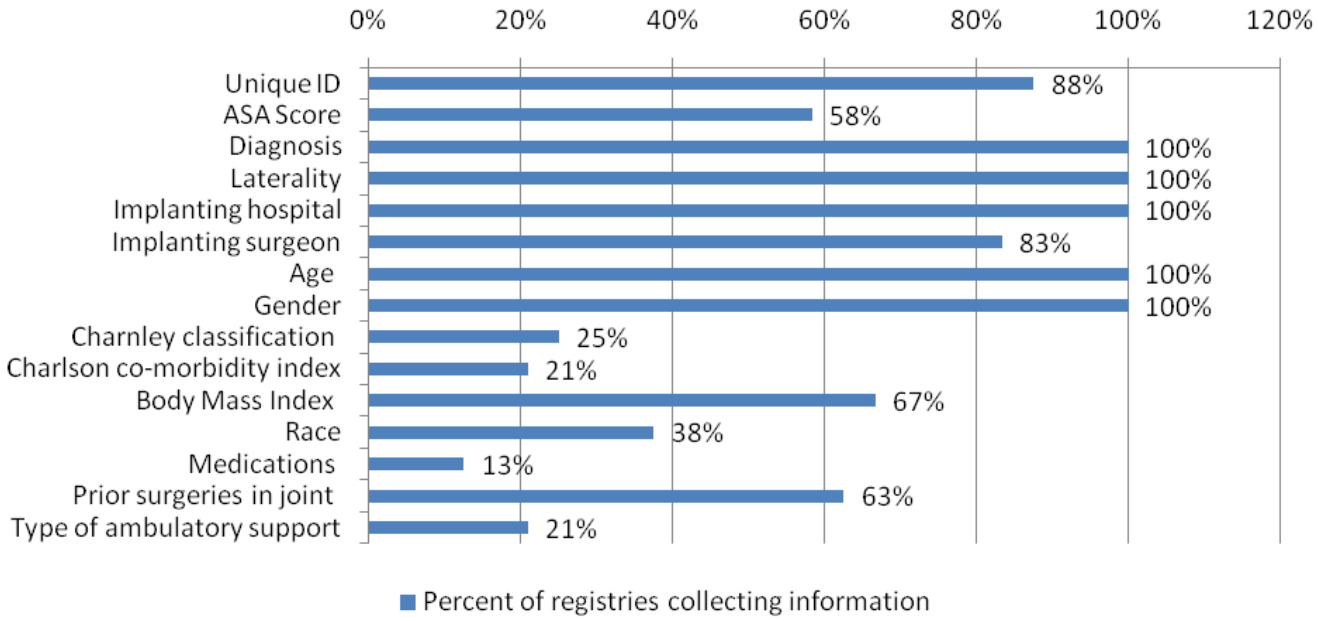
Implant Components



	Femur	Patella	Tibia	Cement	Stem	Femoral head	Cup	Insert
Vendor/manufacturer name	92%	83%	92%	92%	100%	92%	96%	96%
Catalog number	83%	79%	83%	83%	92%	88%	88%	92%
Short description of implant	46%	50%	46%	54%	50%	50%	46%	54%

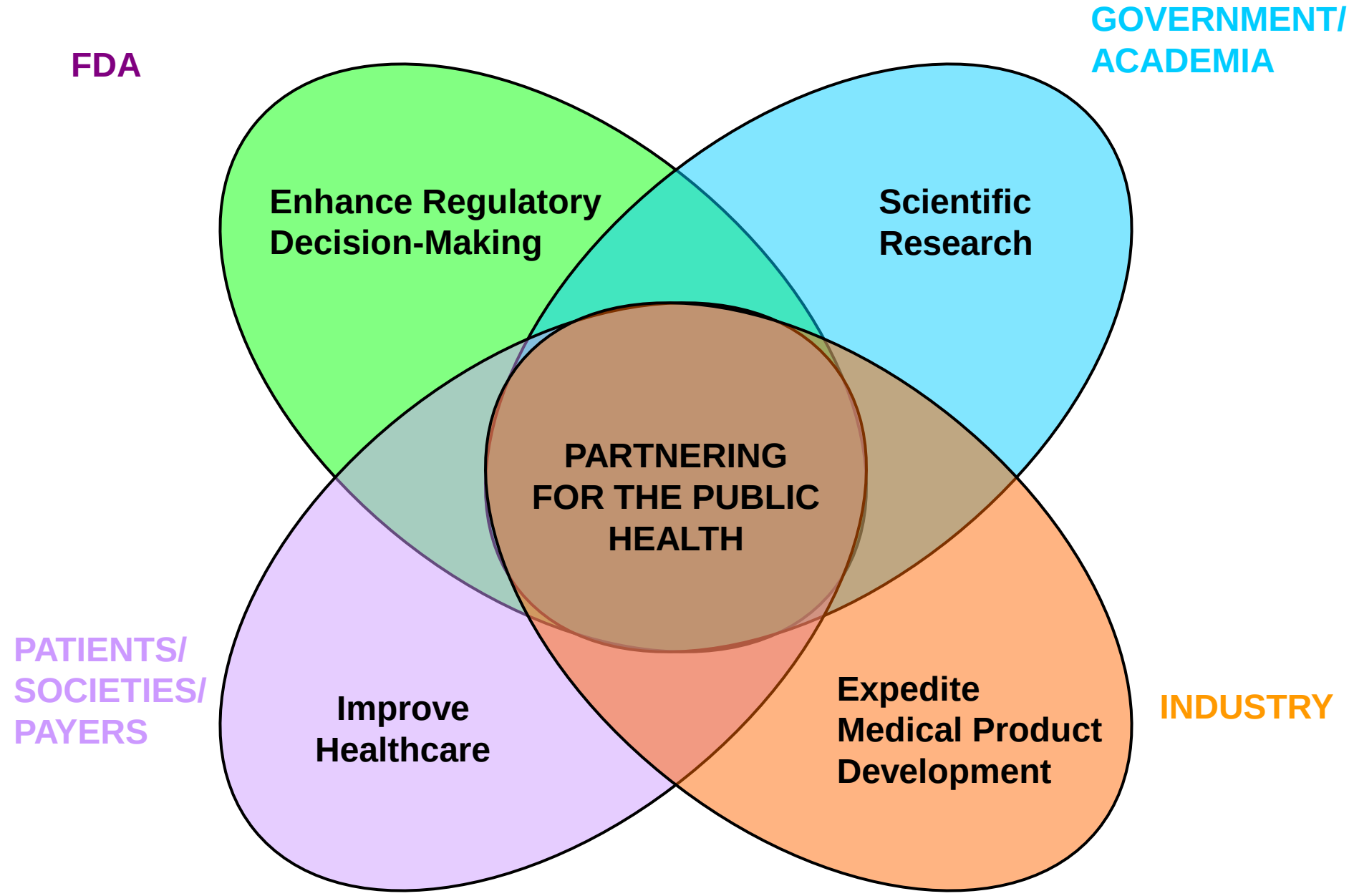
Vendor/manufacturer name Catalog number Short description of implant

Patient Characteristics and Diagnosis



Why Public-Private Partnerships?

- FDA and stakeholders have limited resources, time & expertise
- Leverage resources and expertise among stakeholders to minimize costs (time and money)
- Open new lines of communication among partners
- Create "value added" for all stakeholders: *optimizing economies of scale . . . advancing public health mission*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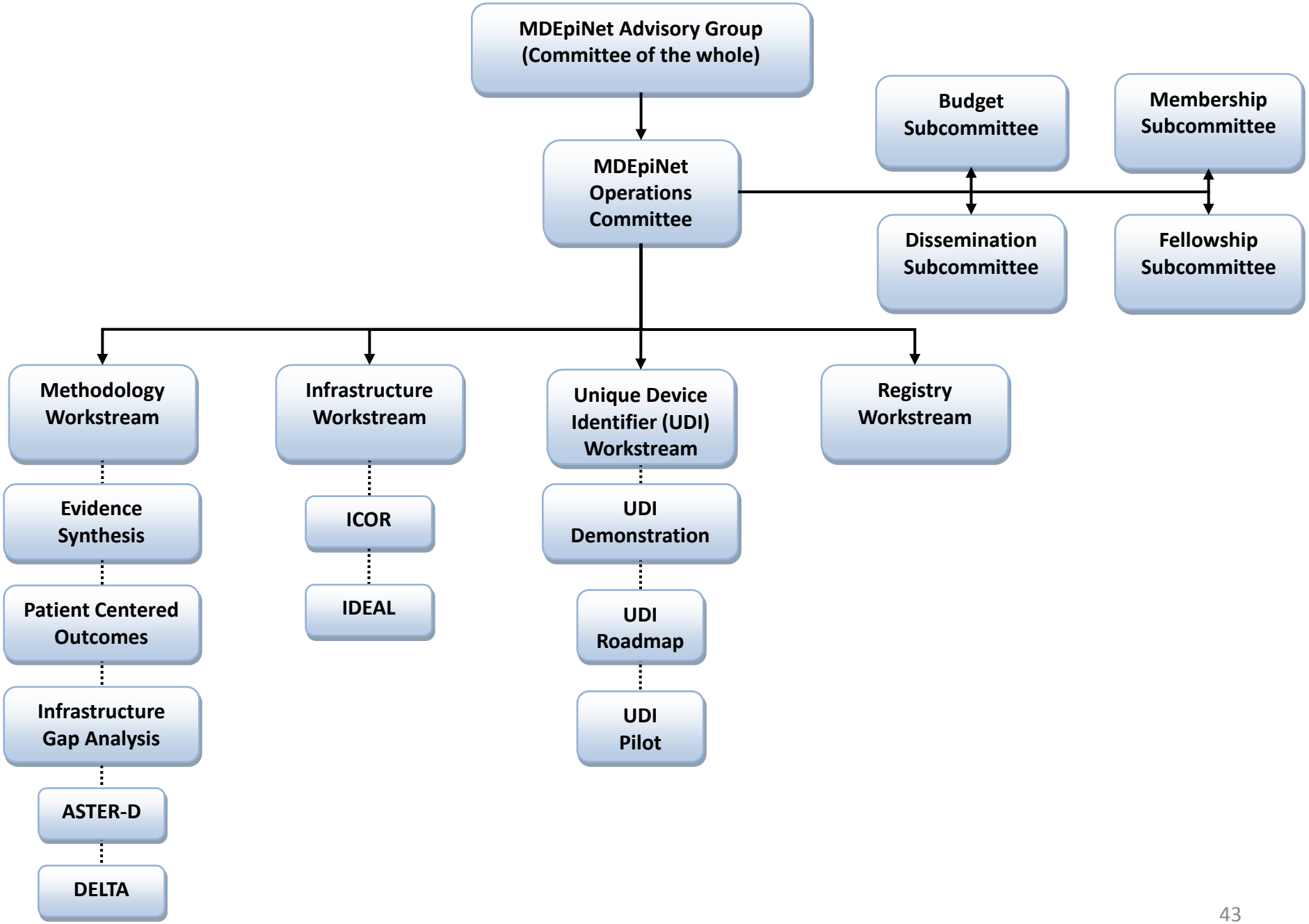
Expedite
Medical Product
Development
INDUSTRY


MDEpiNet Advisory Group (Committee of the whole)
MDEpiNet Operations Committee
Budget Subcommittee
Membership Subcommittee
Dissemination Subcommittee
Fellowship Subcommittee
Methodology Workstream
Evidence Synthesis
Patient Centered Outcomes
Infrastructure Gap Analysis
ASTER-D
DELTA
Infrastructure Workstream
ICOR
IDEAL
Unique Device Identifier (UDI) Workstream
UDI Demonstration
UDI Roadmap
UDI Pilot
Registry Workstream

Who are our Partners?

Other Federal Agencies (*"public-public"* partnerships)
Academia
Public & Patient Advocates
Professional Societies
Industry
3rd Party Payers & Hospitals

So long as . . . *The Partnership is:*

- Science Driven & Rigorous
- Fair & Inclusive
- Compliant with Federal law, regulation & policy
- Priority to the agency and stakeholders

Alignment of Missions

Alignment of Missions & Goals -- *relatively easy*
Alignment of cultures is *not* so easy

- Different timelines
- Different concepts of time
- Different internal processes
- Different decision points
- Different vocabularies

Difficulty is in the details!

Keys to Successful Collaborations

- Collaboration and Stakeholder involvement…early
- Shared risks and benefits
- Develop infrastructure (e.g. registries/databases) that may serve many needs
- Collaboratively identify and address gaps in knowledge
- Leverage resources, expertise, best practices, and know how
- Communicate outcomes/findings: timely, inform future efforts
- Translate findings into medical product development, labeling, and guidelines for public health benefit

Next Steps

- May 14-17, 2012 – Series of FDA Public meetings (FR Notices going out next week) focusing on:
  - National postmarket surveillance system for devices
  - MDEpiNet
  - Registries
- RFA – opportunity
- Public Private Partnership development

ENGELBERG CENTER for Health Care Reform at BROOKINGS

Roundtable Discussion and Questions

View this and past Active Medical Product Surveillance webinars at:

http://www.brookings.edu/health/Projects/surveillance/roundtables.aspx