Independent Adjudication, Registries and Streamlining Device Evaluation

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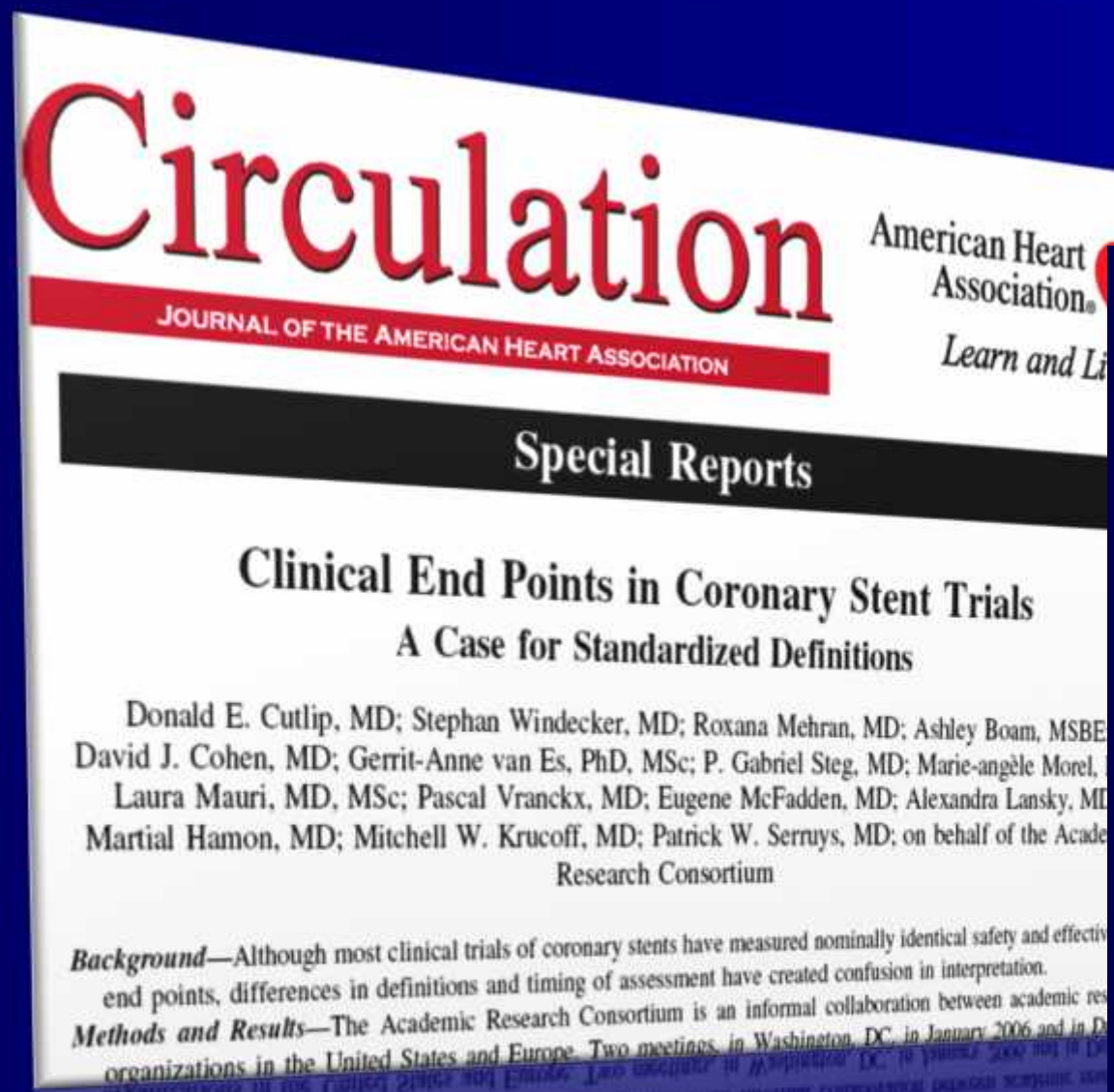
The Role of CEC Adjudication*:*
Better Clinical Trials Science
Better Regulatory Science

- **Value of consistency:**
  - Consistent endpoint definitions
  - Consistent operational processes
- **Minimizing bias:**
  - Independent committee
  - Blinding where feasible

The Role of Registries & Structured Data*:*
Better Clinical Trials Science
Better Regulatory Science

- **Value of consistency:**
  - Consistent endpoint definitions
  - Consistent operational processes
- **Minimizing bias: *Generalizability***
  - Selection bias:
    - *RCT vs Real world populations*
    - *Experience centers vs real world*

Structured data & definitions: Academic Research Consortium (ARC): *Pragmatic consensus definitions for device evaluation*

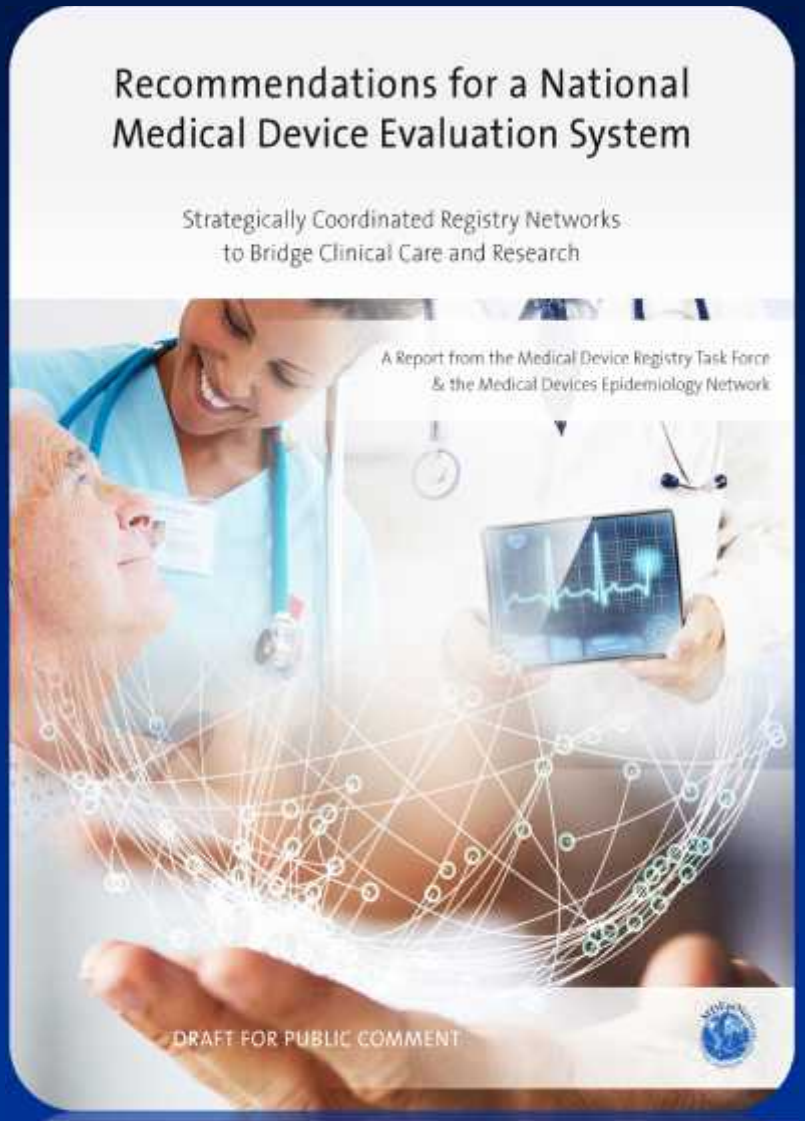


ARC LAST:

- **>500 reported trials**
- **Cypher**
- **Cypher Select**
- **Taxus**
- **Taxus Liberte**
- **Xience**
- **Endeavor**
- **Resolute**
- **Costar**
- **Nevo**
- **Biomatrix**
- **Biofreedom**
- **Absorb**
- **Combo**

Cutlip D et al. Circulation. 2007;115:2344-2351

MDRTF Report: August 24, 2015



BRIDGING UNMET CLINICAL CARE AND CLINICAL RESEARCH NEEDS WITH STRATEGICALLY COORDINATED REGISTRY NETWORKS

Report from the National Medical Device Registry Task Force & The Medical Devices Epidemiology Network

Mitchell W. Krucoff, Sharon Lise Normand, Fred Edwards, Theodore Lystig, Eve Ross, Elise Berliner, Kristi Mitchell, James Tcheng, David Blaser, Ralph Brindis, Jack Cronenwett, Pamela Gavin, Linda Harrington, Amy Helwig, Kevin Larsen, William Maloney, Matthew McMahon, Bray Patrick Lake, John Rumsfeld, Julia Skapik, Art Sedrakyan, Danica Marinac-Dabic


VIEWPOINT

Bridging Unmet Medical Device Ecosystem Needs With Strategically Coordinated Registries Networks

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In June 2014, the Medical Device Epidemiology Network (MDEpiNet) Public Private Partnership,[1] on behalf of the US Food and Drug Administration Center for Devices and Radiologic Health (CDRH), convened the Medical Device Registries Task Force (MDRTF) (see eAppendix in the Supplement). The task force was launched to address the CDRH's commitments[2,3] to strengthen the medical device postmarket surveillance system using existing resources and under current authorities and to develop an integrated system that efficiently and effectively achieves its basic functions, from timely identification of postmarket signals to facilitating premarket device clearance and approval.

The MDRTF included broad stakeholder representation and was mandated to examine the objectives and logistics of leveraging existing electronic registries and information repositories in support of a national system. This work was done in parallel with efforts at the Engelberg Center at the Brookings Institution, which in 2015 reported recommendations from their planning board for a "national medical devices surveillance system." These recommendations depicted a system that "supports optimal patient care by leveraging the experiences of pa-

The MDRTF recognized that most existing registries, electronic health records (EHRs), and data sources do not contain all the elements necessary for device evaluations, including device and procedural details, patient descriptors, or long-term outcomes. However, the MDRTF recognized that such limitations could be mitigated through interoperability solutions that strategically link complementary registries and data sources to produce networks for which the data composite could support robust device evaluation. The MDRTF termed this structure the strategically coordinated registries network, or CRN—with the recognition that many key elements in such networks (such as EHRs, administrative claims data, or mobile device outputs) are not registries per se. The MDRTF recommends strategic CRNs as the foundational architectural construct for the national system that will augment national registry development and unique device identifier implementation rather than replace them.

The proposed CRN structure could provide novel, important attributes to the national system. Creation of CRNs could encourage efficient "dual-purpose" leveraging of existing registries, EHRs, administrative data resources, and lessons learned from existing linked-registry models such

www.mdepinet.org

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Krucoff MW, Normand SL et al, JAMA 2015

MDRTF Functional Objective for National System:
Transforming Heterogeneity to Dimensionality

Current Model:
Idiosyncratic heterogeneity

- Disparate data sources
- Disparate data quality
- Disparate data elements
- Disparate definitions

Analytic Methodologies:
- ***Signals vs. Noise***
- ***Build stand alone RCTs***
  - ***"Vanilla" populations***
  - ***Expensive & slow***
- ***Pre- vs Post-market gaps***

National System Model:
True heterogeneity of clinical practice

- Data sharing infrastructure across existing e-health systems
- Implement structured data sets
  - Core minimum data elements
  - Common definitions
  - Device-specific applications

Assignable dimensionality of outcomes:
- Benefit/risk
- Signal detection & mitigation
- Clinical practice = research data

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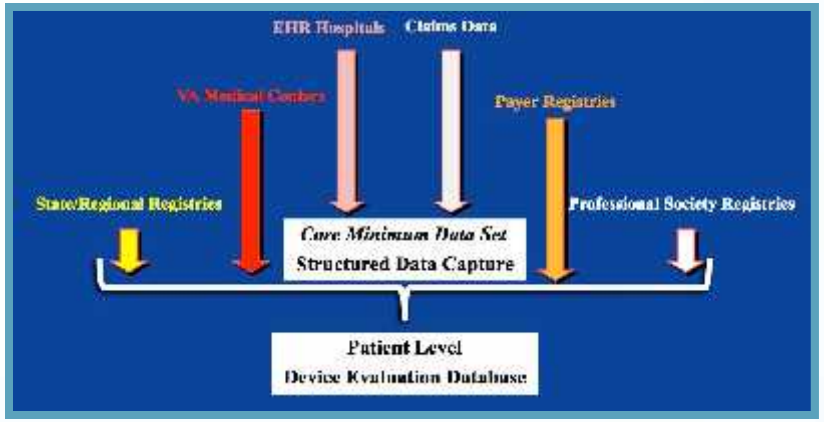
CRI Duke Clinical Research Institute

MDRTF: Foundational constructs & CRNs

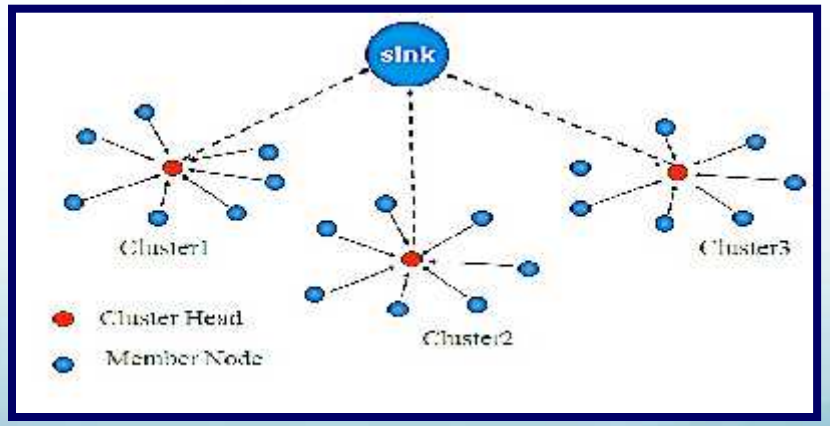
- **Of current & emerging e-health information sources (registries, EHRs, administrative, moblie apps, etc)** ***registries provide most robust content & operational predicates***
- ***No single registry suffices*** **for benefit/risk & safety for all devices**
- ***Data sharing interoperability*** ***(linking) complementary e-health sources could mitigate single source deficiencies: CRNs***

Strategically Coordinated Registry Networks (CRNs)
Existing Predicates of Data Sharing Solutions

A. Linked complementary registries



B. Multiple source structured data extraction



C. Distributed data networks

The Randomized Registry Trial — The Next Disruptive Technology in Clinical Research?

Michael S. Lauer, M.D., and Ralph B. D'Agostino, Sr., Ph.D.

The NEW ENGLAND JOURNAL of MEDICINE

September 2013

Embedding a randomized clinical trial into an ongoing registry infrastructure: Unique opportunities for efficiency in design of the Study of Access site For Enhancement of Percutaneous Coronary Intervention for Women (SAFE-PCI for Women)

Connie N. Hess, MD, MHS,[a] Sunil V. Rao, MD,[a] David F. Kong, MD,[a] Laura H. Aberle, BSPH,[a] Kevin J. Anstrom, PhD,[a] C. Michael Gibson, MD,[b] Ian C. Gilchrist, MD,[c] Alice K. Jacobs, MD,[d] Sanjit S. Jolly, MD,[e] Roxana Mehran, MD,[f] John C. Messenger, MD,[g] L. Kristin Newby, MD, MHS,[a] Ron Waksman, MD,[h] and Mitchell W. Krucoff, MD[a] *Durham, NC; Boston, MA; Hershey, PA; Ontario, Canada; New York, NY;*

A Registry-Based Randomized Trial Comparing Radial and Femoral Approaches in Women Undergoing Percutaneous Coronary Intervention

The SAFE-PCI for Women (Study of Access Site for Enhancement of PCI for Women) Trial

Sunil V. Rao, MD,* Connie N. Hess, MD, MHS,* Britt Barham, BA,* Laura H. Aberle, BSPH,* Kevin J. Anstrom, PhD,* Tejan B. Patel, MD,† Jesse P. Jorgensen, MD,‡ Ernest L. Mazzaferri Jr., MD,§ Sanjit S. Jolly, MD,‖ Alice Jacobs, MD,¶ L. Kristin Newby, MD,* C. Michael Gibson, MD,# David F. Kong, MD,* Roxana Mehran, MD,** Ron Waksman, MD,†† Ian C. Gilchrist, MD,‡‡ Brian J. McCourt,* John C. Messenger, MD,§§ Eric D. Peterson, MD, MPH,* Robert A. Harrington, MD,‖‖ Mitchell W. Krucoff, MD*

Lauer M et al, NEJM 2013

Hess C et al, Am Heart J 2013

Rao S et al JACC Cardiovascular Int 7(8)2014

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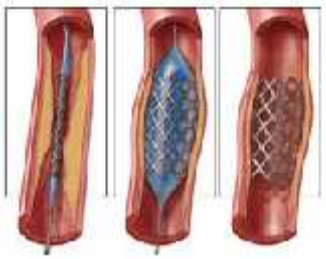
SAFE-PCI for Women workflow

Randomization



Demographics

Medical Hx

Procedural data

Index Hosp MACE

NCDR® National Cardiovascular Data Registry CathPCI Registry®

Autopopulate

Part 11 Compliant

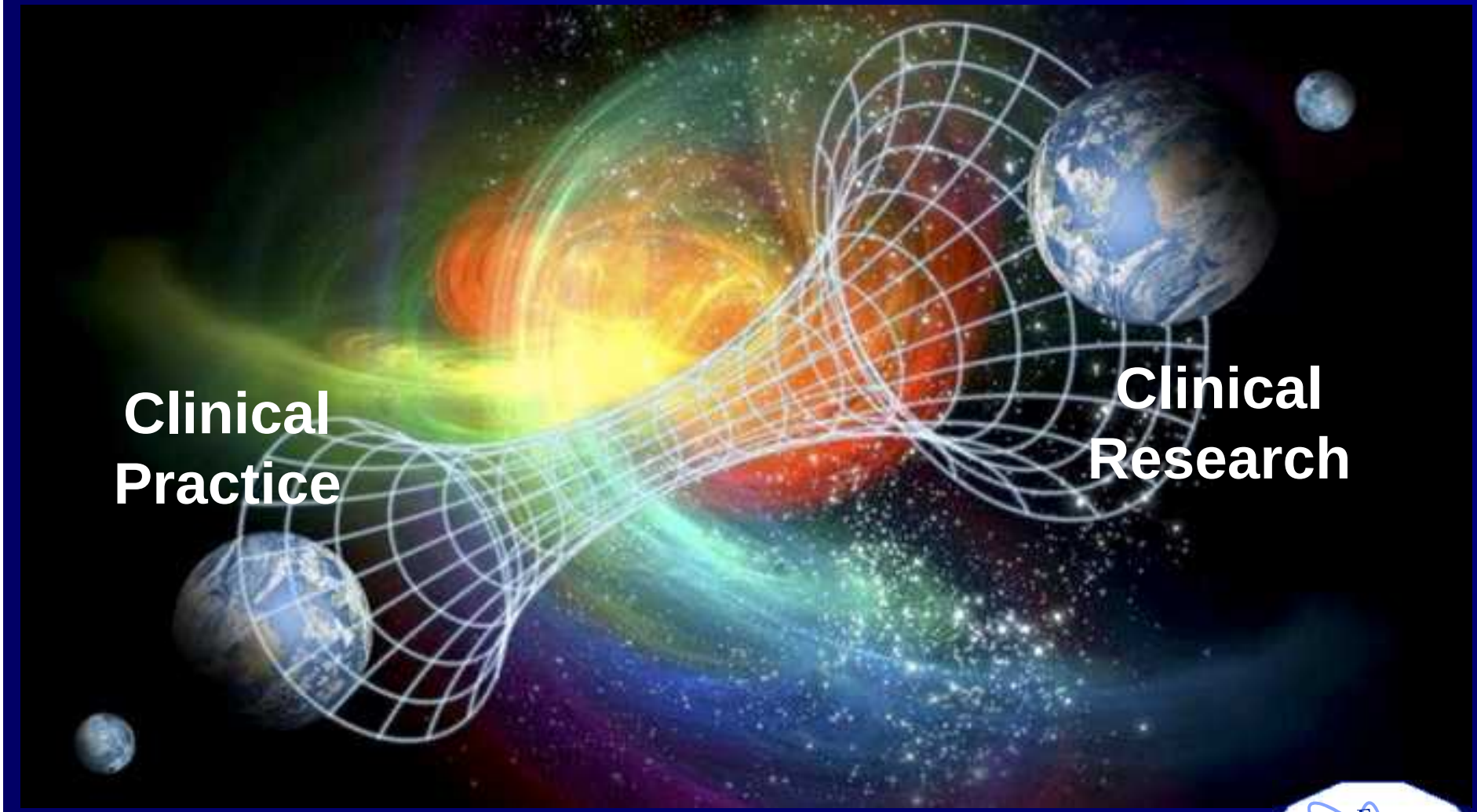
65% site coordinator workload reduction

Unique pages for trial

ORACLE®

Analytic Database

2.5 Decades:
Paying for The “Parallel Universe” Model



2016 FDA CDRH Regulatory Science Top 10 Priorities

U.S. Food and Drug Administration
Center for Devices and Radiological Health

REGULATORY SCIENCE PRIORITIES

(FY2016)

- Leverage "Big Data" for regulatory decision making
- Leverage evidence from clinical experience and employ evidence synthesis across multiple domains in regulatory decision making
- Improve the quality and effectiveness of reprocessing reusable medical devices
- Develop computational modeling technologies to support regulatory decision making
- Enhance performance of Digital Health and medical device cybersecurity
- Incorporate human factors engineering principles into device design
- Modernize biocompatibility / biological risk evaluation of device materials
- Advance methods to predict clinical performance of medical devices and their materials
- Advance the use of patient reported outcome measures (PROMs) in regulatory decision making
- Collect and use patient experience/preference in regulatory decision making

http://**www.fda.gov/MedicalDevices/ScienceandResearch/ucm467550.htm**

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  - Consistent endpoint definitions
  - Consistent operational processes
- **Minimizing bias**
- **Registries (esp linked CRNs):**
  - Implement structured data
  - Enhance generalizability
  - Leverage existing work flow

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