Using Real-World Evidence (RWE) for Regulatory Decision Making and Pracatice

Danica Marinac-Dabic, MD, PhD
Director, Division of Epidemiology

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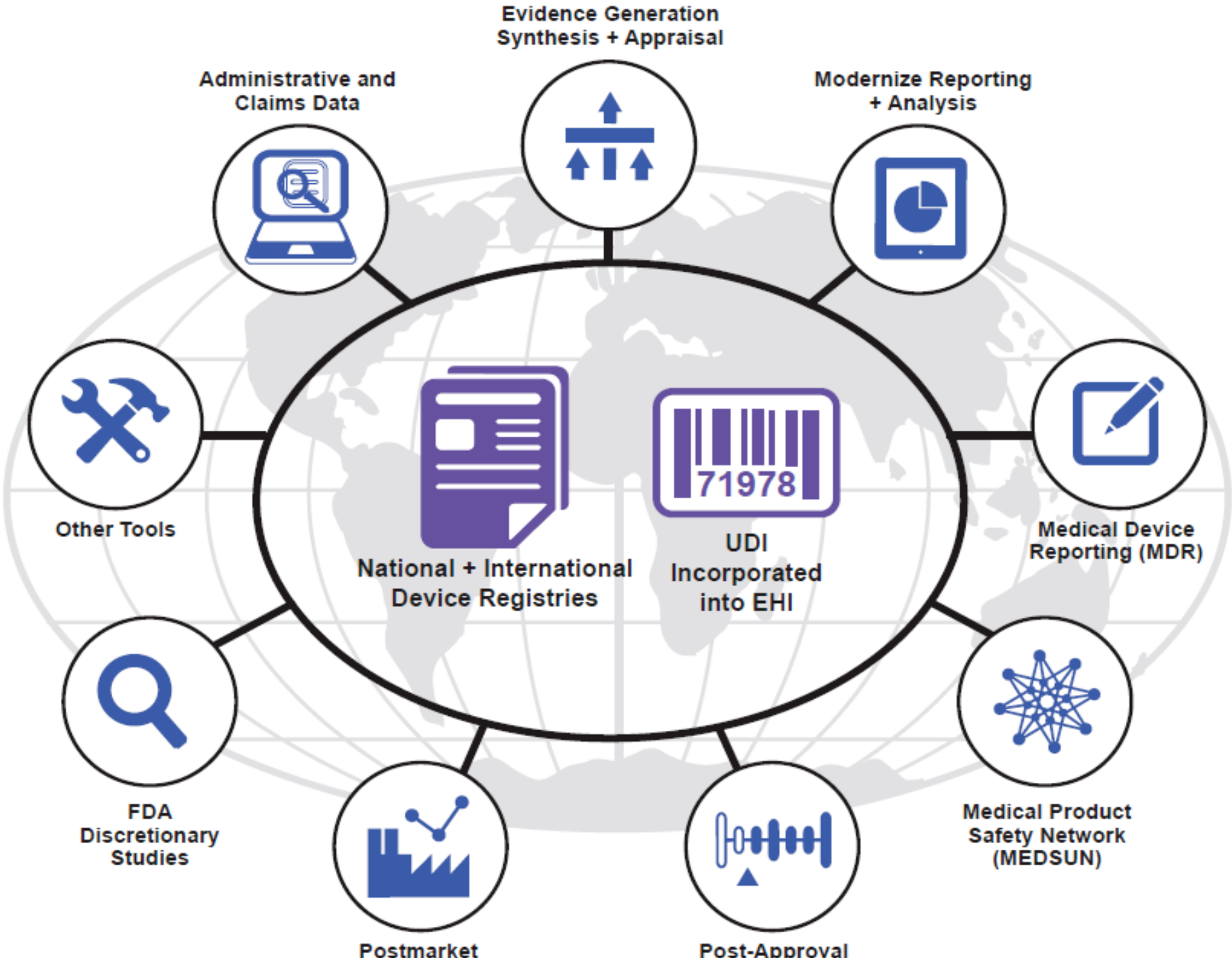
Summary

- RWE – context
- Selected Examples of Early Successes and Impact
- Moving Forward


Evidence Generation
Synthesis + Appraisal
Administrative and
Claims Data
Modernize Reporting
+ Analysis
Other Tools
National + International
Device Registries
71978
UDI
Incorporated
into EHI
Medical Device
Reporting (MDR)
FDA
Discretionary
Studies
Medical Product
Safety Network
(MEDSUN)
Postmarket
Post-Approval

Why Are We Talking about RWE ?

- Standalone clinical trials are lengthy, expensive and redundant of clinical care
- The health care delivery systems and government are making huge investments in electronic record systems
- Current approaches to studies for regulatory decision making have not taken advantage of potential of electronic data systems that are captured as part of routine clinical care
- Methodologies that incorporate real world experience into regulatory decision making are being developed. Prototypes can be harnessed to build a better system for device evaluation

Opportunities

- Faster, less expensive regulatory decision-making based on best available data from clinical settings
- Make data from entire product lifecycle available for regulatory review
- Upgrade data to “regulatory grade”
- Greater premarket- postmarket shift

Can we make device clearance and approval better, faster, and cheaper?

- Yes! Studies embedded in the national registries and linked to other data sources have already been done that demonstrate the approach
- MDEpiNet has been leading the effort
- Many manufacturers are already supporting the coordinated registry network approach

Another way to look at “better, faster, cheaper”: LEVI’S

- **L**
  - Leveraged
- **E**
  - Embedded
- **V**
  - Valuable
- **I**
  - Inexpensive
  - Innovative
- **S**
  - Sound Science

Adapted from Michael Lauer, 2015

MDEpiNet Efforts/RWE Work Streams

Infrastructure

- Registry Development
- National/International Consortia Development
- Electronic Device Data Capture (UDI)
- Task Force -Coordinated Registry Networks
- PASSION Initiative

Methods

- Active Surveillance
- Distributed Data Analysis
- Evidence Synthesis
- Claims Validation
- Linkage with other Data Sources
- Big Data Analytics

Patient Engagement

- Augmenting Registries with PROs and Explant Analysis for Precision Medicine
- Assessing Minimally Important Difference (MID) for orthopedics implants
- Patient and Family Engagement Committee
- Patient-led Device/Disease Specific Round Table

Early Postmarket Successes

National registries are being leveraged for:

- 15 Post-Approval studies
- 1 Continued Access study
- 1 labeling extension study
- 7 Postmarket Surveillance Studies (522)

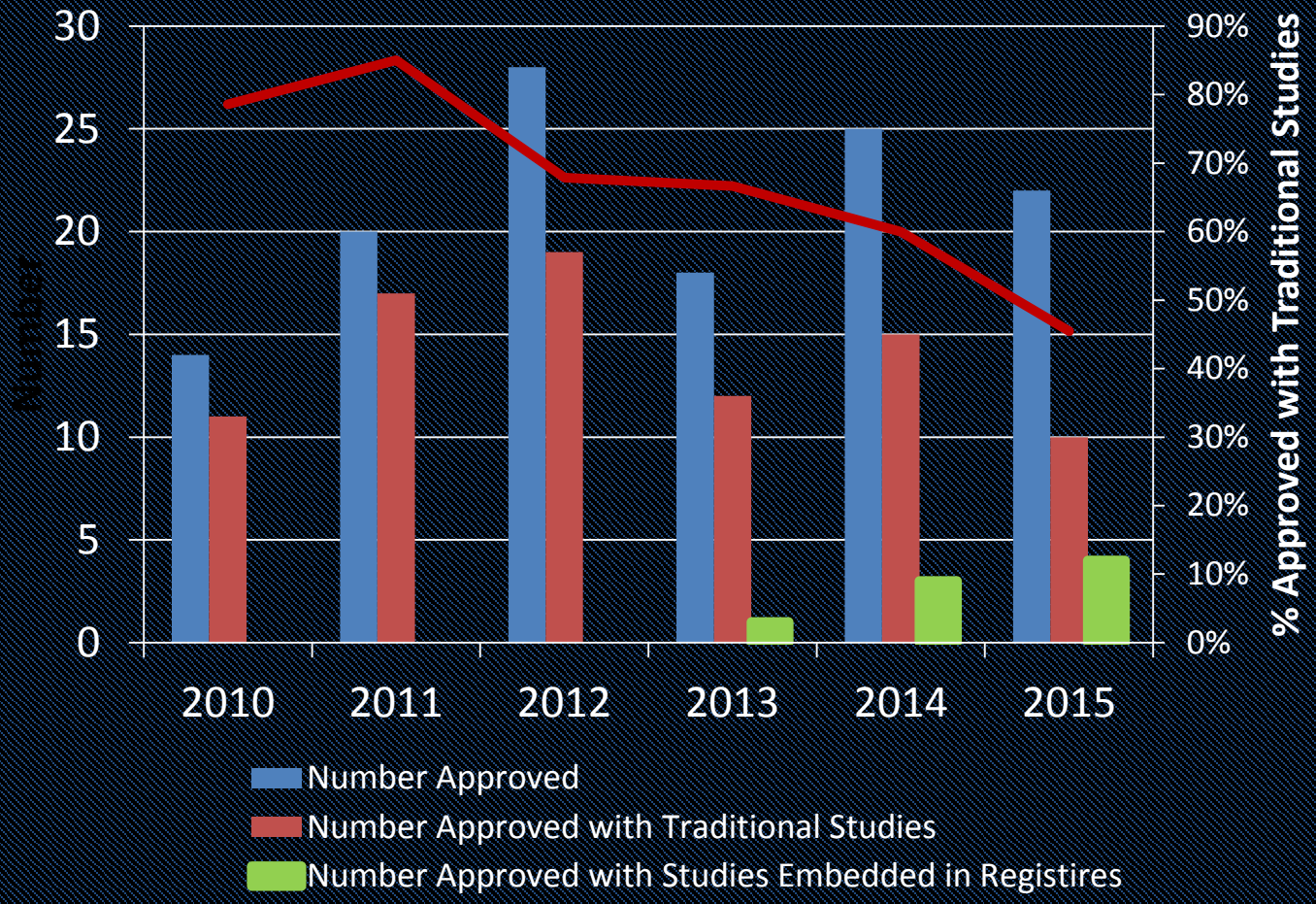
International Registries [e.g., International Consortium of Orthopaedic Registries (ICOR)] are being leveraged for:

- 3 post-approval studies

Active review/analysis of data (starting early 2016)

- American College of Cardiology (ACC) will share data with FDA quarterly for review
- Separate studies are no longer required, providing additional value

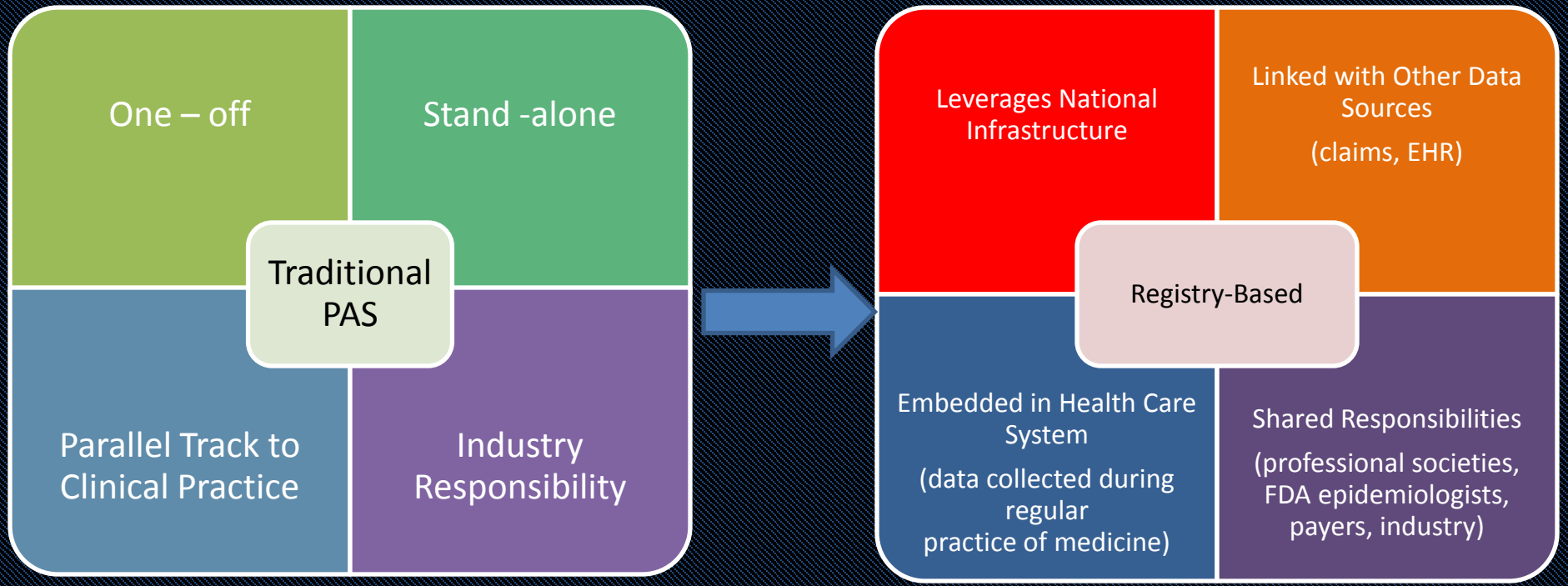
Shifts in Cardiovascular Device Post-Approval Studies Since 2010



Number of expensive studies is decreasing; replaced by cheaper studies.

Data as of November 30, 2015.

Post Approval Decision Making: Infrastructure for Comprehensive Registry-Based Surveillance



International Consortium of Orthopedic Registries (ICOR)

Partnership:
29 Registries, (8 contributing data)
Over 4,500,000 implants

UDI Promotion:
Global Clinically-Meaningful Attributes Database for Hips and Knees

Methods:
Common Data Model to combine and de-identify data

- Comparative effectiveness / safety studies used in pre/post balance reviews (27 published)
- Use in FDA mandated PAS
- Catalyzed the development of ICOR-USA and Ortho CRN
- Informed the International Medical Device Regulators Forum (IMDRF) Registry Working Group
- Serves as a model for new International Consortia of Vascular, Transcatheter Valve, and Breast Implant registries

AND MOVING TO PREMARKET:
Predictable And Sustainable Implementation Of National (PASSION) Registries

- FDA grant to MDEpiNet to prototype premarket studies embedded in registries
- Develop operational and business model for sustainable infrastructure for national registries
- Prototype premarket studies embedded in registries in cardiovascular space (peripheral, coronary, electrophysiology, valve)
- PASSION is a model for how to successfully leverage RWE for premarket review.

PASSION Predictable And Sustainable Implementation Of National (PASSION) Registries

- Develop operational and business model for sustainable infrastructure for national registries
  - accommodate different stakeholders with different expectations who value different deliverables from any one medical device registry

- Performing 4 pilot projects in cardiovascular space (peripheral, coronary, electrophysiology, valve)
  - Standardize core data elements for global case report form
  - Develop data extraction interoperability
  - Apply a coordinated registries network to a prospective clinical trial supporting a regulatory decision

A Pilot in the Peripheral Vascular Space is Underway: PASSION/RAPID

- 14 manufacturers, over 70 stakeholders via MDEpiNet PPP
- Standardize core data elements for efficient premarket and postmarket assessment of peripheral arterial interventional devices
- Develop tools for registries to automatically extract clinical and device data from hospital EHRs
- Apply a coordinated registries network to a prospective clinical trial supporting a regulatory decision (first patient to be enrolled in 2016)
- Lessons from these prototypes studies will improve other device area studies.
- We can do more together with investment

Example of Methodology Work : Data Extraction and Longitudinal Trend Analysis System (DELTA)

- Software developed – FDA collaboration with NLB and Harvard
- Provides **near real-time active safety surveillance** of clinical EHR and clinical registry data
- Supports a variety of statistical methods and allows for unadjusted and risk-adjusted safety monitoring for prospective and retrospective analyses
- Installed in NCDR/PCI and TVT Registries
- Became an open source

Impact: Traditional one-off mandated studies are being replaced by registry based surveillance!

Post-Approval (Condition of Approval) Setting

- 11 cardiovascular PAS are using NCDR registries and VQI
- 3 orthopedic PAS are leveraging ICOR registries
- 4 breast implant PAS are leveraging the
  - National Breast Implant Registry (NBIR), and
  - Patient Registry and Outcomes for Breast Implants and Anaplastic Large Cell Lymphoma Etiology and Epidemiology (PROFILE)

522 (For Cause) Postmarket Surveillance Setting

- 7 studies using National Pelvic Floor Disorder Registry (PFDR)

Impact: Registry Data Reduces Premarket Review Time!

P100041 Filed

MDUFMA II Goal

P100041/S039 Filed

MDUFA III Goal

Oct 2010 | **Nov 2011** | Dec 2011 | 2012 | Aug 2013 | **Sept 2013** | **Feb 2014**

P100041
TVT Registry used for Postmarket Surveillance.
Approved 45 days ahead of MDUFA goal

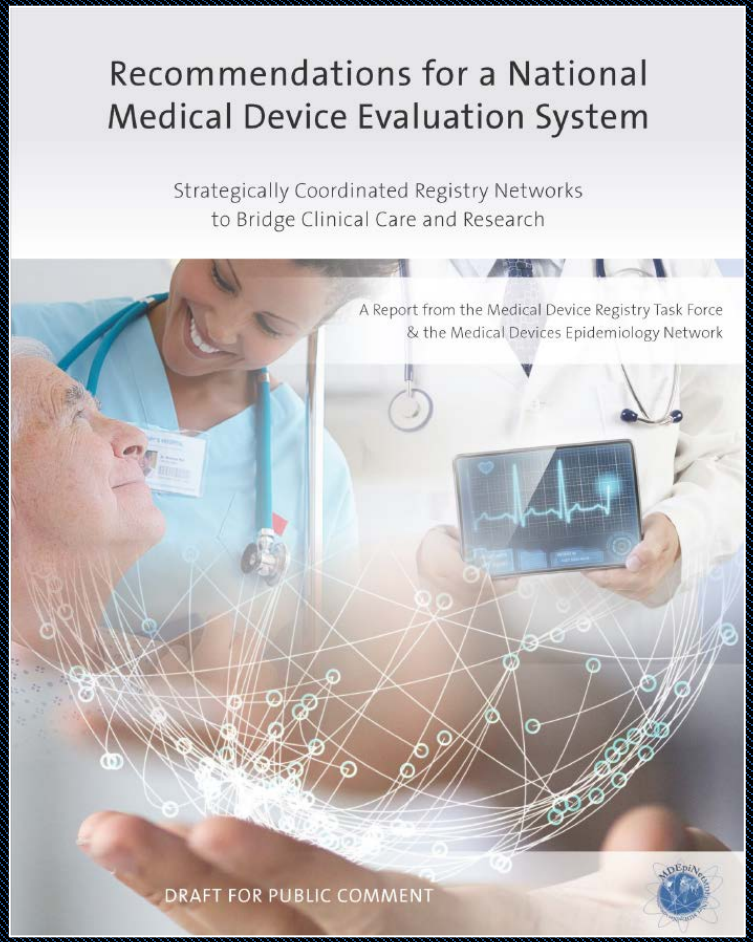
P100041/S039
TVT Registry data used for premarket approval.
Approved 154 days ahead of MDUFA goal

A glimpse into the future

- More efficient and better quality virtual registries to support this paradigm shift
  - Standardization of electronic data capture, development of common data elements and accepted definitions to ensure high quality, timely data (Coordinated Registry Networks)
  - Develop routine access to data through data sharing agreements
- Ability to use innovative methodological approaches for studies
  - Registry-derived comparison groups, EHR-driven comparison groups, big data analytics
  - Nesting new clinical trials in registries (e.g., Safe STEMI for Seniors)
  - Link registries (national and international) with longitudinal data (claims, EHR, PCORNET)
- Robust regulatory apparatus that utilizes RWE to streamline device evaluation and support innovation

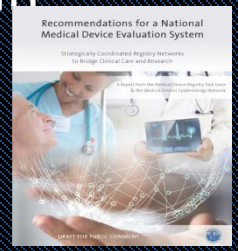
Opportunity to Replicate Successes

- Success demonstrated in the cardiac space can be replicated to benefit other clinical areas
- Medical Device Registry Task Force: multi-stakeholder national group of experts
- Proposed priority device areas in need of coordinated registry networks (registries linked to other data sources)



Alignments and beyond

- In 2015 MDEpiNet investigators received two FDA grants to (a) develop the first two CRNs (orthopedic and vascular) by linking the ICOR-USA registries with claims, Sentinel and PCORNet and to incorporate PROs and mobile apps into the CRN; and to (b) advance the UDI adoption/learning community
- MDEpiNet houses the National Medical Device Registry Task Force and its pilots – there is an opportunity to align nationally in many clinical areas!
- MDEpiNet supports IMDRF Registry Work Group to produce international registry principles documents – there is an opportunity to converge internationally !



Thanks!

Danica.marinac-dabic@fda.hhs.gov

@mdepinet

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