National and International Efforts to Generate RWE

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Outline

- FDA Vision and Strategic Priorities
- National Evaluation System for health Technology (NEST)
- International Efforts
- Two Examples from Vascular Space
- IMDRF's Critical Role and IMDRF Proposed Pilot

MDEpiNet Launch

International Consortia (e.g. ICOR, ICCR)

THE VISION FOR NATIONAL SYSTEM LAUNCHED
FDA 4- day Public Meeting
Day 1. Launch of FDA strategy
Day 2. MDEpiNet Annual
Days 3-4. Registries

Reports:
- Planning Board
- MDEpiNet Registry Task Force
- IMDRF

MDIC
MEDICAL DEVICE INNOVATION CONSORTIUM
MDIC NEST Coordinating Center

2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017

Develop and test drive novel methods and scientific infrastructure for device evidence generation synthesis and appraisal nationally and internationally

MDEpiNet Methodology Center at Harvard

MDEpNet Science and Infrastructure Center at Cornell

MDEpiNet Partnership Coordinating Center at Duke

IMDRF

International Medical Device Regulators Forum

Title: Principles of International Systems of Registries Linked to Other Data Sources and Tools

Authoring Group: IMDRF Patient Registries Working Group

Date: 30 September 2016

IMDRF

Title: Methodological Principles in the Use of International Medical Device Registry Data

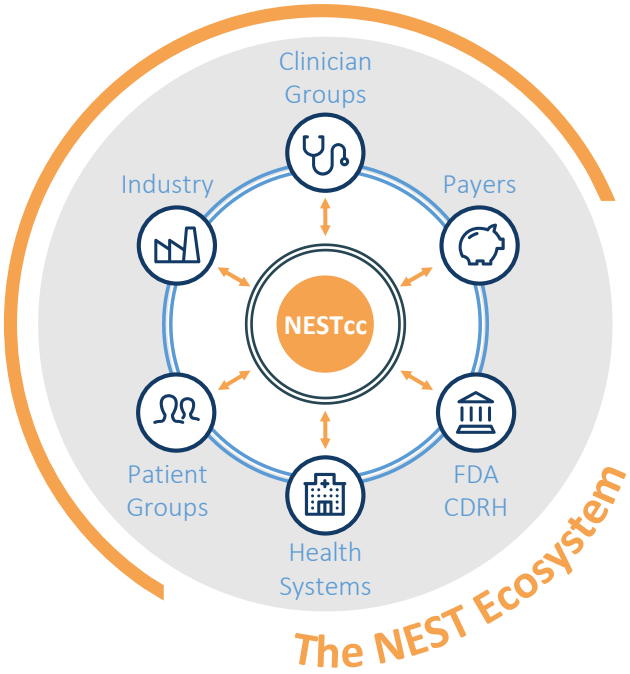
Authoring Group: IMDRF Patient Registries Working Group

Date: 16 March 2017

National Evaluation System for health Technology (NEST) :

NESTcc should serve as a catalyst to support the timely and reliable development of high-quality RWE.

- Establish **partnerships** with a range of organizations, companies, and collaborations that provide data and analytics solutions
- Set **data quality for data data partners and methods standards** for observational and randomized studies
- Offer **value** through products and services to key stakeholders in the ecosystem



ESTABLISHING DATA PARTNERSHIPS

NESTcc is seeking data partners to collaborate with to advance evaluation and use of high-quality RWD from various sources.

Potential Data Partners:

- Health systems providers
- Health payers
- Society registries
- MDEpiNet CRNs
- Sources of patient- or device- generated data

What's next?

- Data Capabilities review
- Identification of 5-10 simple test-cases to resolve
- **Formation of NESTcc Data Quality and Methods Work Groups (Fall 2017)**

Health System Partners with Formal MoU:

- Duke University Health System
- Healthcore
- Kaiser (in progress)
- Mayo Clinic
- Mercy Health
- PEDSnet
- Vanderbilt University Medical Center
- University of Florida Health System
- Weill-Cornell Medical Center
- Yale New Haven Health System

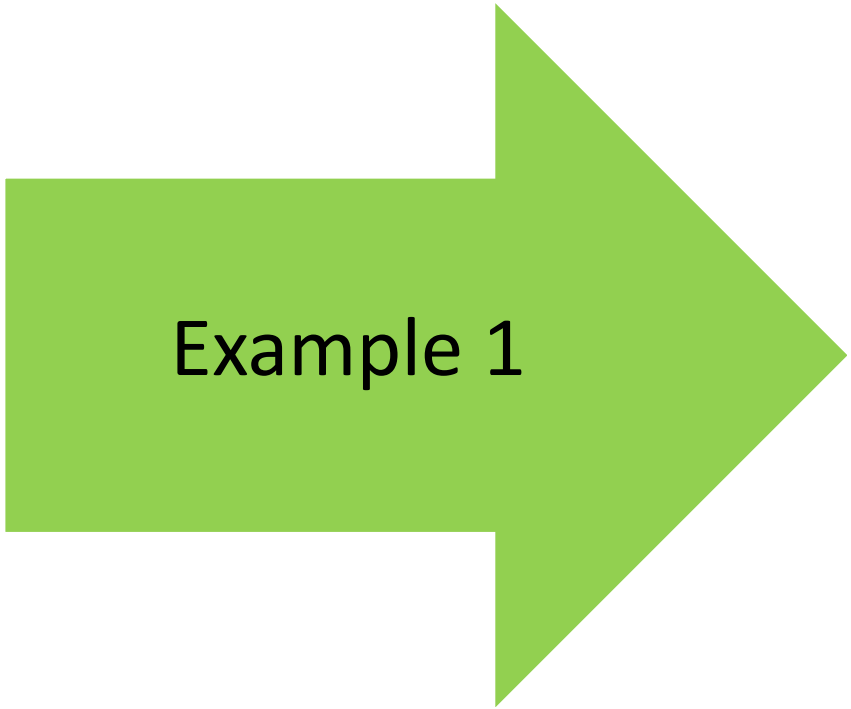
Evolving CRN Portfolio

National

- Ortho CRN
- Vascular CRN – VISION
- Cardiac CRN
- Neurology CRN – DAISI
- Gastrointestinal CRN – Obesity
- SPARED CRN – Prostate ablation
- Robotic Surgery CRN
- TMD/TMJ
- VANGUARD
- Women's Health Technologies – Uterine Fibroids, Pelvic Floor Disorders, Sterilization Devices,
- Breast Implants (NBIR pilot under way)
- Abdominal Hernia CRN

International

- International Consortium Orthopedics Registries (ICOR)
- International Consortium Vascular Registries (ICVR)
- International Consortium of Cardiac Registries (ICCR)
- International Collaboration of Breast Registries Activities (I-COBRA)


Example 1

Example: RAPID/VISION - A Scalable Framework to Efficiently Conduct Real-world Enabled Vascular Clinical Trials

- FDA funded two MDEpiNet projects VISION (led by Cornel) and RAPID (led by Duke) were launched to complement each other
- VISION - to develop National Vascular Implants Surveillance and Outcomes Network by linking VQI registry to claims and other data sources for longitudinal assessment
- RAPID - to developed a core data element (CDE) set informed by multiple registries, EHR systems, and stakeholders.
- Leveraging both efforts the SPEED pilot is now being designed to demonstrate how clinical trials sufficient to support regulatory decision-making can be efficiently implemented into existing healthcare systems for expanding the indications
- The SPEED trial that will involve 12600 patients from the VQI registry with (estimated 4200 prospective and 8400 retrospective patients data and 2940 patients with 1 year follow-up data available for developing Objective Performance Criteria – OPCs
- The projects leverage the GUDID Database to enable comparative effectiveness research of peripheral vascular technologies.
- It will involve data refinement and analyses to develop contemporary OPCs using RWE, data sharing with industry stakeholders for potential labeling modification (e.g., longer lesions, heavy calcified lesions, diabetic patients).
- The new paradigm is that industry will have access to the conglomerate of data plus their own data. Thus, if pre-specified statistical plan is met for a given subgroup analysis population as per examples above, a labeling modification could be requested/granted.

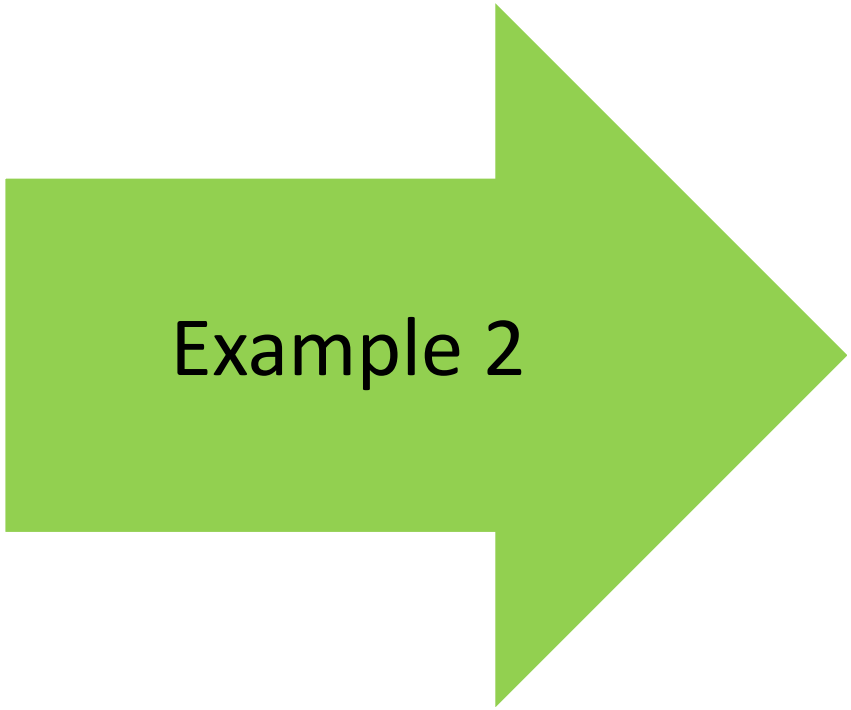
MDEpiNet

Existing MDEpiNet Chapter

Future MDEpiNet Chapter

Academic Centers

Data Sources


Example 2

Example: 17 ICVR Participating Registries


Australian Vascular Audit
Barry Beiles, MB, BCh


Danish Vascular Registry
Nikolaj Eldrup, MD, PhD


Dutch Vascular Registry
Gert Jan deBorst, MD


Helsinki Vascular Registry
Maarit Venermo, MD, PhD


German Vascular Registry
Sebastian Debus, MD


Hungarian Vascular Registry
Gabor Menyhei, MD, PhD


Icelandic Vascular Registry
Elin Laxdal, MD


Italian Vascular Registry
Carlos Setacci, MD


Japanese Vascular Registry
Massaki Kato, MD


Malta Vascular Registry
Kevin Cassar, MD


New Zealand Vascular Audit
Ian Thomson, MB, ChB


Norwegian Vascular Registry
Martin Altreuther, MD


Swedish Vascular Registry
Kevin Mani, MD, PhD


Swiss Vascular Registry
Georg Heller, MD


United Kingdom Vascular Registry
Jon Boyle, MD


United States, SVS VQI
Adam Beck, MD

IVCR Structure

Governance: leadership board with one representative from each national registry; co-chairs selected by Vascunet and VQI

Analytic Center: MDEpiNet Science and Infrastructure Center at Weil Cornell University, New York City

Co-Chairs: Maarit Venermo MD, PhD and Jack Cronenwett MD
Director, Analytic Center: Art Sedrakyan MD, PhD

Methods: Semi-annual meetings, with work groups for specific projects; submission of data by each national registry for analysis at the Cornell Analytic Center

ICVR Initial Projects

Variation in patient selection and treatment of AAA and carotid disease

ORIGINAL RESEARCH ARTICLE

Variations in Abdominal Aortic Aneurysm Care

A Report From the International Consortium of Vascular Registries

Editorial, see p 1959

BACKGROUND: This project by the ICVR (International Consortium of Vascular Registries), a collaboration of 11 vascular surgical quality registries, was designed to evaluate international variation in the contemporary management of abdominal aortic aneurysm (AAA) with relation to recommended treatment guidelines from the Society for Vascular Surgery and the European Society for Vascular Surgery.

METHODS: Registry data for open and endovascular AAA repair (EVAR) during 2010 to 2013 were collected from 11 countries. Variations in patient selection and treatment were compared across countries and across centers within countries.

RESULTS: Among 51 153 patients, 86% were treated for intact AAA (iAAA) and 14% for ruptured AAA. Women constituted 18% of the entire cohort (range, 12% in Switzerland–21% in the United States; $P<0.01$). Intact AAAs were repaired at diameters smaller than recommended by guidelines in 31% of men (<5.5 cm; range, 6% in Iceland–41% in Germany; $P<0.01$) and 12% of women with iAAA (<5 cm; range, 0% in Iceland–16% in the United States; $P<0.01$). Overall, use of EVAR for iAAA varied from 28% in Hungary to 79% in the United States ($P<0.01$) and for ruptured AAA from 5% in Denmark to 52% in the United States ($P<0.01$). In addition to the between-country variations, significant variations were present between centers in each country in terms of EVAR use and rate of small AAA repair. Countries that more frequently treated small AAAs tended to use EVAR more frequently (trend: correlation coefficient, 0.51; $P=0.14$). Octogenarians made up 23% of all patients, ranging from 12% in Hungary to 29% in Australia ($P<0.01$). In countries with a fee-for-service reimbursement system (Australia, Germany, Switzerland, and the United States), the proportions of small AAA (33%) and octogenarians undergoing iAAA repair (25%) were higher compared with countries with a population-based reimbursement model (small AAA repair, 16%; octogenarians, 18%; $P<0.01$). In general, center-level variation within countries in the management of AAA was as important as variation between countries.

CONCLUSIONS: Despite homogeneous guidelines from professional societies, significant variation exists in the management of AAA, most notably for iAAA diameter at repair, use of EVAR, and the treatment of elderly patients. ICVR provides an opportunity to study treatment variation across countries and to encourage optimal practice by sharing these results.

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On behalf of the International Consortium of Vascular Registries

Sources of Funding, see page 1958

Key Words: aortic aneurysm, abdominal ■ aortic rupture ■ practice patterns, physicians' ■ quality improvement ■ registries

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Editor's Choice — Carotid Stenosis Treatment: Variation in International Practice Patterns

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WHAT THIS PAPER ADDS

The treatment of carotid stenosis is one of the best studied disease processes in vascular surgery, and several societies have published guidelines and recommendations about the indications for CEA and CAS. However, considerable variation exists between countries and centres. In this study, variation in the treatment patterns in over 400 centres in the United States, Europe, Australia, and New Zealand are analysed. The main focus is on indications and the proportion of stenting. Furthermore, an analysis on the influence of the reimbursement system on indications was performed.

Objectives: The aim was to determine current practice for the treatment of carotid stenosis among 12 countries participating in the International Consortium of Vascular Registries (ICVR).
Methods: Data from the United States Vascular Quality Initiative (VQI) and the Vascunet registry collaboration (including 10 registries in Europe and Australasia) were used. Variation in treatment modality of asymptomatic versus symptomatic patients was analysed between countries and among centres within each country.
Results: Among 58,607 procedures, octogenarians represented 18% of all patients, ranging from 8% (Hungary) to 22% (New Zealand and Australia). Women represented 36%, ranging from 29% (Switzerland) to 40% (USA). The proportion of carotid artery stenting (CAS) among asymptomatic patients ranged from 0% (Finland) to 26% (Sweden) and among symptomatic patients from 0% (Denmark) to 19% (USA). Variation among centres within countries for CAS was highest in the United States and Australia (from 0% to 80%). The overall proportion of asymptomatic patients was 48%, but varied from 0% (Denmark) to 73% (Italy). There was also substantial centre level variation within each country in the proportion of asymptomatic patients, most pronounced in Australia (0–72%), Hungary (5–55%), and the United States (0–100%). Countries with fee for service reimbursement had higher rates of treatment in asymptomatic patients than countries with population based reimbursement (OR 5.8, 95% CI 4.4–7.7).
Conclusions: Despite evidence about treatment options for carotid artery disease, the proportion of asymptomatic patients, treatment modality, and the proportion of women and octogenarians vary considerably among and within countries. There was a significant association of treating more asymptomatic patients in countries with fee for service reimbursement. The findings reflect the inconsistency of the existing guidelines and a need for cooperation among guideline committees all over the world.

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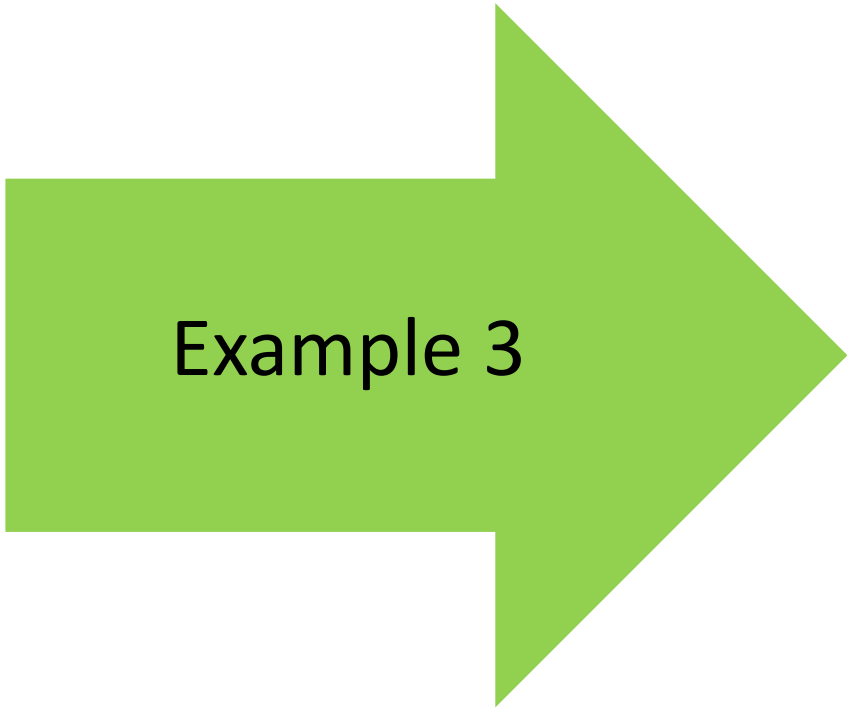

Example 3

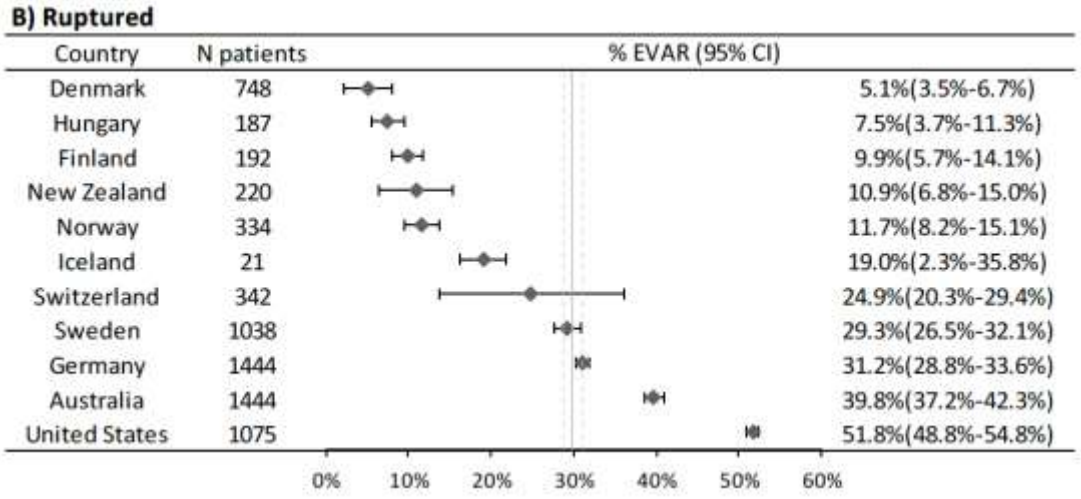
IMDRF Building on International Registries

- 2011 MDEpiNet/ICOR registry launched in orthopedics
- 2012-2014 – international efforts replicated in cardiac and vascular space - ICCR and ICVR
- 2014 – MDEpiNet proposed to IMDRF to create IMDRF Registry WG – and produce essential principles documents
- 2015 and 2017 – Three IMDRF registry principles documents produced (the concept of international CRN (iCRNs) endorsed by IMDRF along with the proposed methodology pilots)
- The MDEpiNet/ICVR is now working with manufacturers, regulators and professional associations to champion the first international pilot to for expanding the indications for rAAA devices while applying the principles of IMDRF registry documents
- The goal is to finalize the protocol by December 2017

IMDRF ICVR PROPOSED PILOT PROJECT

Ruptured AAA Treatment by EVAR (RATE) Project

- Evaluate EVAR devices used to treat ruptured AAA
  - Current devices were approved based only on elective repair
  - FDA device label is general, but warning advises that safety and effectiveness have not been evaluated for ruptured AAA
  - Observational and RCT have shown that EVAR yields lower mortality, reduced LOS and higher quality of life vs open repair
- Wide international variation is use of EVAR for rAAA



- 51,153 procedures
- 11 countries
- EVAR used in 30%
- **Range: 5 - 52%**

International Consortium of Vascular Registries (ICVR)

Ruptured AAA Treatment by EVAR (RATE) Project

- Pragmatic primary endpoint of in-hospital mortality
  - Control group of open AAA repair 2010-2016: n=5,348 patients
    - Australia, Denmark, Finland, Hungary, Italy, New Zealand, Sweden, USA
  - EVAR patients available from 2016 = 560 (from same countries)
  - Additional EVAR patients in 2017, 2018 can be added to create sufficient cohort for each manufacturer
    - Bolton, Cook, Endologix, Gore, Medtronic devices
    - Initial estimate 61- 142 patients per device type based on assumption of 40% in-hospital mortality for open vs 25-30% mortality for EVAR
    - Additional countries: France, Japan, Malta, Netherlands, UK likely able to participate to further increase power of analysis
- Multi-stakeholder working group develop detailed protocol
  - One representative from each regulatory authority, manufacturer, and registry wishing to participate
  - Analysis by ICVR Analytic Center at Cornell (Art Sedrakyan MD, PhD)
  - Co-Chairs: Adam Beck MD (SVS VQI), Kevin Mani MD, PhD (Vascunet)

International Consortium of Vascular Registries (ICVR)

Ruptured AAA Treatment by EVAR (RATE) Project

- Proposed timeline
  - Commitments from regulators, industry, registries in January, 2018
  - Complete detailed protocol in February, 2018
  - Complete missing data entry by participating registries by April, 2018
  - Complete data analysis at Cornell by July 1, 2018

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