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MDEpiNet RAPID
Phase III Working Group Meeting

Prospective Registry-based Trials Using VQI Sites: A RAPID Opportunity

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RAPID Phase I

- Develop core data elements and definitions
- Create unique device identifiers (GUDID)
- Incorporated into VQI PVI registry

VQI - RAPID

- Defined clinical variables and definitions
- Specific device identification and outcomes

Using VQI and UDI for Device performance

- Accurate tracking of devices
- Assess indications, location, anatomical characteristics, etc
- Inpatient and long term follow up
- Comparison to OPG's or historical controls

VQI Registry

- Pre market approval
- Expansion of indications
- Post approval surveillance
- Long term monitoring of safety and efficacy - TPLC

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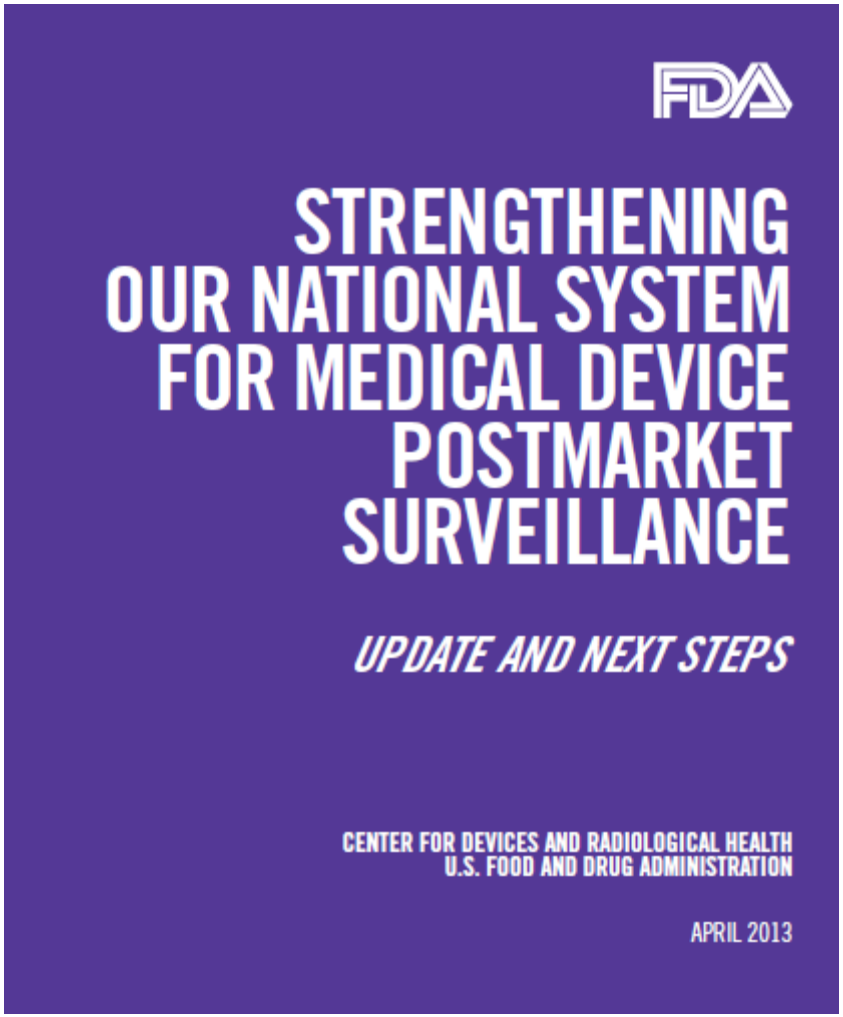
Use of VQI for Post Approval Surveillance



- "FDA believes that device **registries** should serve as the foundation of our National Medical Device Postmarket Surveillance System."

- Real world assessment
  - Not just selected patients in centers of excellence

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VQI Device Evaluation Projects

- Post-approval surveillance
  - Type B aortic dissection devices, multiple manufacturers
  - Stents for popliteal artery disease
- Expansion of existing device indications
  - In-stent restenosis in addition to de novo SFA lesions
  - Extending length of lesions approved for stent treatment
- Objective performance goals to compare new devices
  - Using data for comparable treatment with other devices
  - Large amount of data with follow-up for propensity analysis

Registry and Observational Studies

Advantages

- Ideal for description of standards
- Generalizable cohorts
- Large n (statistical power)
- Low cost

Disadvantages

- Variable data quality
- Not for comparative outcomes
- Confounding factors (despite matching, etc)

Prospective Randomized Controlled Clinical Trial

- Highest level of scientific clinical evidence
- Controls for confounding variables by establishing two groups of patients who have balanced baseline characteristics

Randomized Clinical Trials

- Narrow inclusion criteria
- Multiple exclusion criteria
- Limits generalizability

Randomized Clinical Trials

Advantages

- Well-designed studies with adequate power
- Removes confounding factors

Disadvantages

- Highly selected patients
- Specialized centers (and providers)
- Lengthy
- Complex regulatory issues
- Expensive

Randomized Clinical Trials

- Selected Centers, Providers, and Patients
- Does RCT Reflect Real World Evidence?

RCT Issues

- Increasingly expensive
- Increasing regulatory issues
- Increasingly time consuming
- Increasingly complex and prohibitive
- Difficult recruitment

Bottom Line – Delay to market ($$$)

Registry Based Trials

- *Rethinking Randomized Clinical Trials* …Ann Intern Med 2009
- *Clinical Trials and the Real World: Selection Bias* …. Cardiovasc Drugs Ther 2001
- *Practical Improvements for Medical Device Evaluation* … JAMA 2017

Registry-based RCT

- Allows rapid enrollment
- Control of non-enrolled patients
- Possible long term follow up

VQI-based RCT

- Registry can be used to ID patients
- Perform randomization
- Leverage pre-existing registry infrastructure – data elements, collection, follow up, etc

The Future of Trials

- *A Disruptive TASTE of the Future?*...Forbes 2013
- *The Randomized Registry Trial – the Next Disruptive Technology* ... NEJM 2013
- *Registry-based Randomized Clinical Trials – a New Clinical Trial Paradigm* … Nature/Cardiology 2015
- *Registry-based Randomized Controlled Trials – What are the Advantages, Challenges, and Areas for Future Research?* … Journal of Clinical Epidemiology 2016

Registry-based RCT's

Advantages

- Randomization removes confounding factors
- Large n
- Simple design
- Low cost
- More (RWE) generalizability

Disadvantages

- Variable data quality
- Variables not well defined
- Need for customized endpoints, safety reporting, core lab, etc

Registry Based Trials

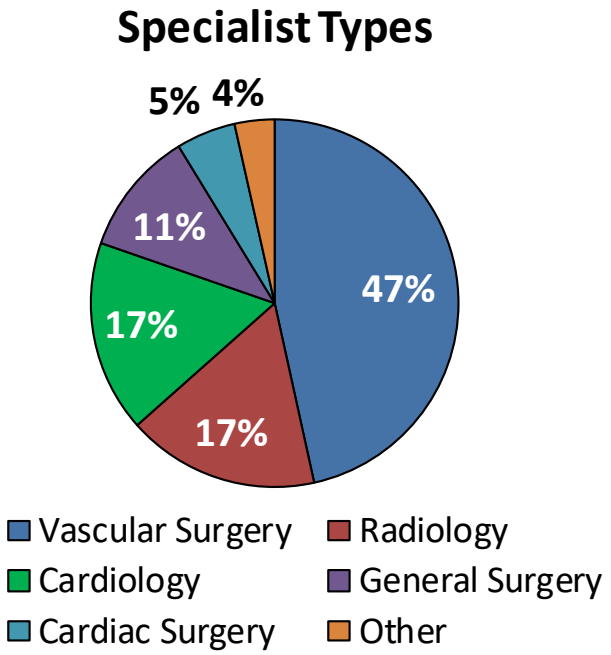
- TASTE – thrombus aspiration for acute MI (SWEDEHEART)
- SORT OUT – stent evaluation – Danish research network
- SAFE-PCI – radial vs femoral access for PCI – NCDR
- DETO$_2$X-AMI – supplemental O2 for MI (SWEDEHEART)

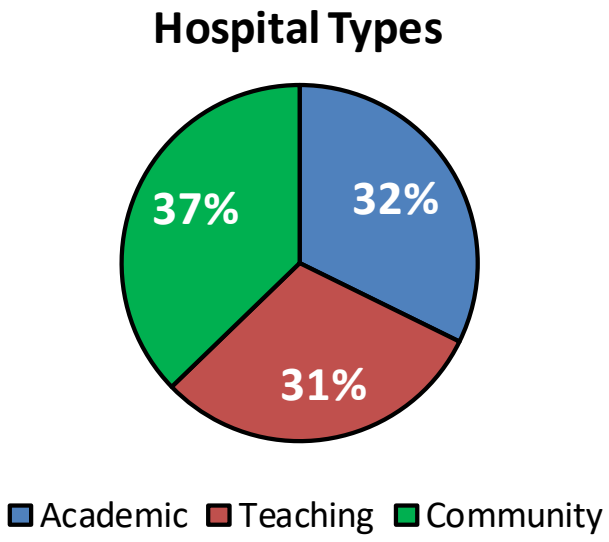
Registry-Based RCT

- Address comparative effectiveness research questions in real-world settings

VQI – Registry-based RCT

Leverages an existing network of 3000 specialists in 500 potential centers - RWE

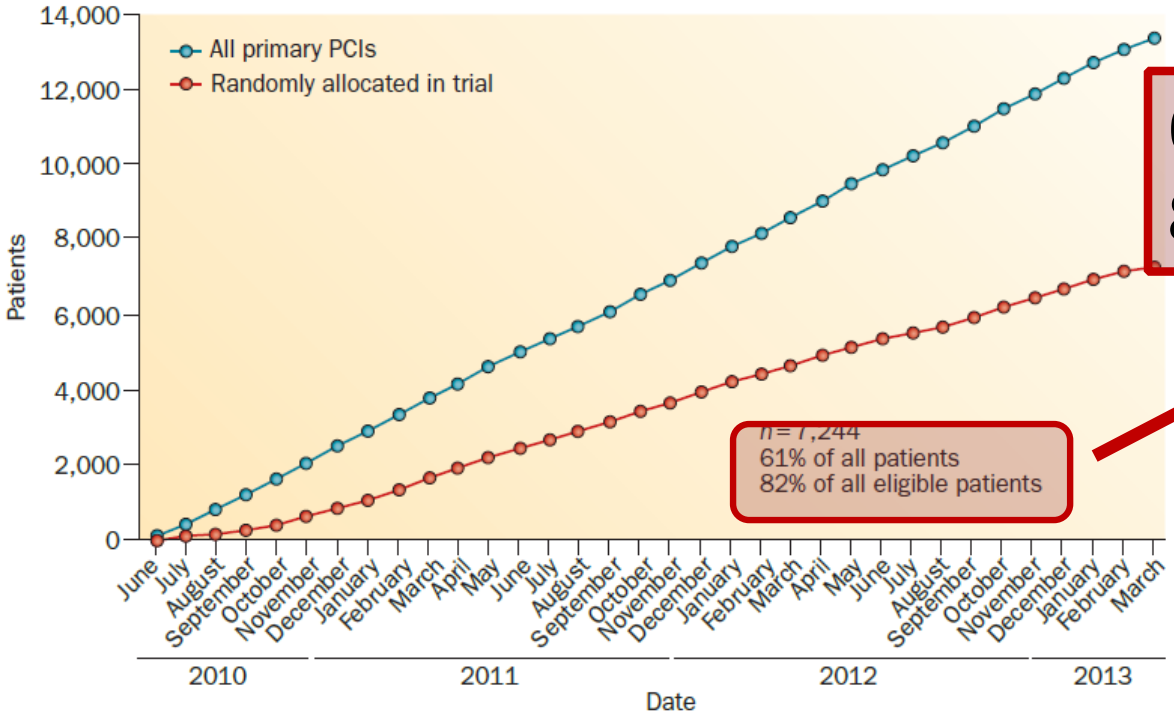




VQI – Registry-based RCT

- VQI forms can add customized variables and follow-up time points
- Sites can join VQI for project

Registry-Based RCT - Rapid Enrollment



61% of all patients
82% of eligible

Figure 1 | Inclusion rate in the TASTE trial.[18] All primary PCI procedures in Sweden between June 2010 and March 2013 are displayed in blue, and patients enrolled in the TASTE trial in red, during

Registry Based Trials

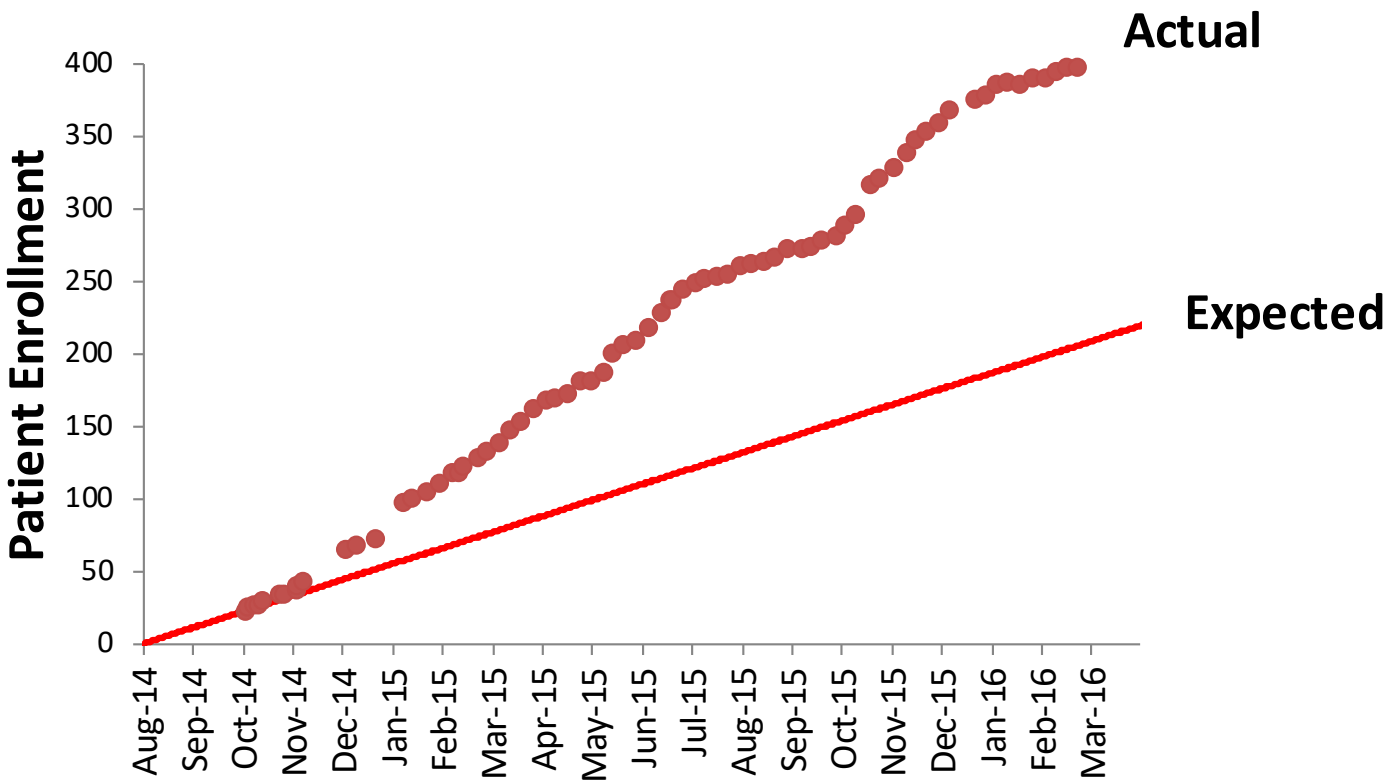
- Cost of TASTE – thrombus aspiration for acute MI (SWEDEHEART)
- $400,000 vs tens of millions
- ROI – estimated at 10-20X

Registry-Based RCT Cost Reduction

- Existing registry infrastructure
- Identify patients
- Collect baseline and study data
- Detect outcomes of interest

VQI –TEVAR Recruitment Exceeded Expectations

Existing Network of VQI Centers Allows Rapid Enrollment



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Registry-Based RCT

- Efficient
- Enhanced generalizability of findings – RWE
- Rapid Consecutive Enrollment
- Completeness of follow up

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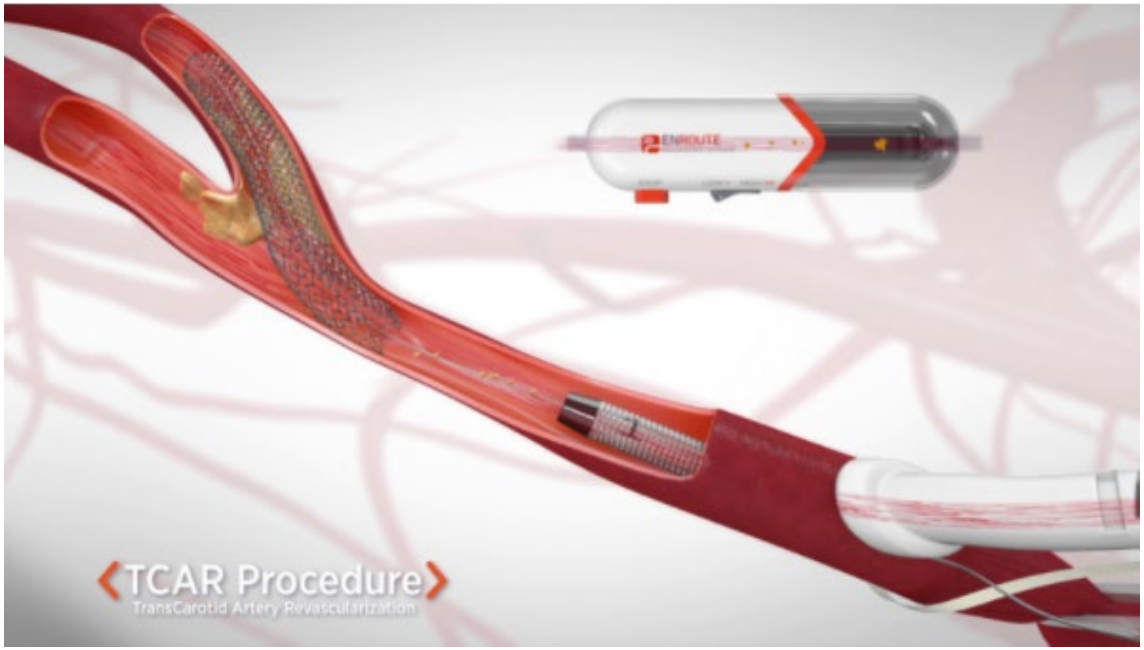
TransCarotid Artery Revascularization (TCAR)



TCAR – “minimally invasive” approach, advantages of stent while minimizing risks

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VQI TCAR Surveillance Project (TSP)

TSP - Collecting real-world outcomes of TCAR compared to CEA in VQI

FDA - scientifically valid

CMS - approves reimbursement for TCAR for centers in TSP for high risk patients based on National Coverage Determination (VQI participation)

TSP

- Evaluate safety and efficacy of TCAR vs CEA
  - Stroke and death at 30 days
  - Stroke and death at one year

- Reimbursement for TCAR for centers participating in TSP

VQI – Registry-based RCT

- Leverage existing registry infrastructure – Electronic data capture
- Customizable - additional data variables and timepoints
- Avoid duplicate data entry (CRF)
- Enhanced site recruitment
- Long term follow up
- Better, faster, cheaper

Prospective Registry-based Trials using VQI sites