Generating Evidence for Medical Devices
Supporting Market Approval and Monitoring Safety Post-Approval

David West, PhD, MPH
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Your Presenters

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Dr. David West assists domestic and international medical device companies develop and implement strategic and regulatory plans for developing and marketing medical devices and combination products. His areas of expertise include U.S. medical device laws and regulation, global strategies, medical device development and evaluation, regulatory strategy and policy formulation, and device/drug/biologic combination products. Dr. West has published more than 12 works in academic and/or industry publications and has done over 60 presentations in professional settings. Dr. West received his Ph.D. at University of Minnesota, M.P.H. at School of Public Health, University of Minnesota, and BS in Engineering at University of California, Santa Barbara.

Daniel Campion, MBA  
Research Director, Quintiles

Daniel Campion is responsible for developing research partnerships and special projects with government agencies, medical specialty societies, associations, and foundations. He is co-director of the Registry of Patient Registries project, funded by the Agency for Healthcare Research and Quality (AHRQ) under the DEcIDE Centers Program. Prior to joining Quintiles in 2008, Mr. Campion spent 19 years developing and directing national demonstration and technical assistance projects to expand access to care, improve quality, and control costs. Mr. Campion holds an M.B.A. from the Yale School of Management, a B.A. in biology from the College of the Holy Cross, and a certificate in Organization Development from Georgetown University.

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Dr. Nancy Dreyer leads global science teams in observational and interventional studies of safety, effectiveness, patient reported outcomes, and health economics, including patient registries and leads national and international research on quality and new methods of pharmacovigilance. With over 30 years in product safety and effectiveness, her areas of expertise include epidemiology, outcomes, comparative effectiveness and governance. She has held speaking engagements worldwide and has published more than 92 articles and abstracts. Dr. Dreyer received her PhD in Epidemiology and MPH in Public Health from the University of North Carolina, Chapel Hill and serves as a Fellow of the International Society of Pharmacoepidemiology.
Overview

- Evolving trends in US Food and Drug Administration (FDA) premarket evidence requirements for medical devices and the implications for post-approval studies and other forms of postmarket surveillance.

- Growing use of observational research and patient registries for supporting postmarket evidence needs.

- Evolving models and methods for improving and advancing postmarket safety surveillance in the US.

- Considerations for designing and implementing effective device registries and observational programs.
Today’s Webinar Audience

- Academia: 31.91%
- Biostatistician: 17.43%
- Clinical Operations: 14.47%
- Epidemiology: 18.09%
- Health Economics/Health Outcomes: 14.47%
- Medical Affairs: 5.26%
- Pharmacovigilance: 4.28%
- Regulatory Affairs: 2.30%
- Risk Management: 0.99%
- Other: 3.29%
Polling Questions

- A small number of polling questions have been added to today’s webinar to make the session more interactive
Medical Device Trends
David West, PhD, MPH
Overview

Context

Major Regulatory Trends

Impact: For Premarket and Postmarket Evidence
- 510 (k)s
- Premarket Applications (PMAs)
Classical and challenging problem in computational linear algebra is the computation of eigenvalues of a matrix. The eigenvalues of a matrix A are the roots of the characteristic polynomial det(A - \lambda I) = 0, where I is the identity matrix and \lambda is the eigenvalue. The problem is to find the eigenvalues of A. For the case of an n x n matrix, the characteristic polynomial has degree n, so there are n roots. The roots can be real or complex, and they may repeat. The problem is to find the roots of this polynomial, which is a challenging problem because the characteristic polynomial is generally not a polynomial with integer coefficients.

The problem can be solved using various methods, such as the QR algorithm for symmetric matrices, the Arnoldi or Lanczos algorithms for general matrices, and the power method for finding the dominant eigenvalue. The methods are iterative and require the computation of matrix-vector products, so the problem is also a challenge for parallel computing. The methods are also sensitive to the condition number of the matrix, which affects the accuracy of the results.

The problem has many applications, such as in the study of dynamical systems, where the eigenvalues determine the stability of the system, and in the analysis of large-scale data sets, where the eigenvalues of the data matrix reveal the underlying structure of the data. The problem is also important in numerical linear algebra, where the accuracy and efficiency of the methods are crucial for the performance of algorithms that depend on eigenvalue computations.
Overview

Context

Major Regulatory Trends

Impact: For Premarket and Postmarket Evidence
- 510 (k)s
- Premarket Applications (PMAs)
Major Regulatory Trends

For New Devices Coming to the Market

Growing public and FDA expectations for more substantial evidence of device safety and effectiveness of marketed devices; continuing scrutiny in compliance with Medical Device Reporting (MDR)

Increasing efforts by FDA and industry on risk assessment and mitigation, as reflected in regulations, guidelines and voluntary consensus standards

Growing FDA expectations for incorporating human factors engineering into risk management
  • Applying human factors and usability engineering to optimize device design and validation

Growing FDA efforts and expectations for more rigorous application of risk management principles utilizing postmarket experience, e.g., to collate postmarket data on devices from internal and external sources to track and trend the data to identify sentinels

Institute of Medicine (IOM) recommendation that FDA develop a comprehensive device postmarket surveillance program
Overview

Context

Major Regulatory Trends

Impact: For Premarket and Postmarket Evidence

• 510 (k)s
• Premarket Applications (PMAs)
Impact

For Premarket and Postmarket Evidence

• 510(k)s
  > Changing FDA requirements and expectations for demonstrating SE in 510(k)s
    - With time, as technological differences emerged, FDA increasingly sought clinical data to justify using the 510(k) pathway instead of PMA pathway
    - Increasing manufacturer interests in expanding indications & performance claims, as well as providing clinical data to healthcare payers, has led to more sophisticated studies for 510(k)s
    - Issue of necessary and sufficient evidence for SE has been and will continue to be in state of flux

  > CDRH issuance of orders for “522 Studies” (under Section 522 of Act, 21 CFR Part 822, and Agency guidance)
    - Orders for “522 Studies” were rare before 2010 (n ~ 20), but now being ordered frequently (n~275 since 2010)
      » When ordered for marketed devices, manufacturers must comply
    - Study approaches may vary, e.g., non-clinical testing, analysis of existing clinical databases, observational studies, or randomized controlled trials
    - Status updates posted on CDRH website
Polling Questions

- Has your company ever received a “522 Study” order?
  - Yes
  - No
  - Don't know
Impact

For Premarket and Postmarket Evidence

• PMAs
  > CDRH has increasingly required more rigorous pre-clinical studies prior to approving feasibility or pilot studies as well as pivotal studies under IDE
    - Under FDA Safety and Innovation Act (FDASIA) of 2012, Congress returned the Agency to the IDE regulatory standard of ‘benefits of study outweigh risks to study subjects’
  > Perhaps to counter-balance criticism of over-conservatism, CDRH issued two draft guidance documents in 2011:
    - Design Considerations for Pivotal Clinical Investigations for Medical Devices
    - Factors to Consider when Making Benefit-Risk Determinations in Medical Device Premarket Review
  > To enhance compliance of a PMA-holder’s obligation to conduct its PMA post-approval study in accordance with the PMA conditions of approval, authority to negotiate post-approval study protocols and monitor their progress was transferred from CDRH’s Office of Device Evaluation to Office of Surveillance and Biometrics
  > Status updates posted on CDRH website
Federal Initiatives Promoting the Development of Patient Registries

Daniel Campion, MBA
Overview

“Patient Registry” Definition

FDA’s Evolving Strategy for Medical Device Safety

Regulations for “Qualified Clinical Data Registries”

Agency for Healthcare Research and Quality (AHRQ) Registry Initiatives
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.

> The registry database is the file (or files) derived from the registry.

> Patient registries may be used for a variety of purposes including one or more of the following:

- Effectiveness research for drugs or devices
- Post-marketing commitments or safety monitoring
- Surveillance programs (e.g., to track vaccination status)
- Natural history of disease
- Quality improvement programs
- Certification programs (e.g., for physicians to retain membership in a professional medical organization)

Overview

“Patient Registry” Definition

FDA’s Evolving Strategy for Medical Device Safety

Regulations for “Qualified Clinical Data Registries”

Agency for Healthcare Research and Quality (AHRQ) Registry Initiatives
Vision:
A national system that conducts active surveillance in near real-time using routinely collected electronic health information containing unique device identifiers, quickly identifies poorly performing devices, accurately characterizes real-world clinical benefits and risks of marketed devices, and facilitates the development of new devices and new uses of existing devices through evidence generation, synthesis, and appraisal.

Goals:
• Provide timely, accurate, systematic, and prioritized assessments of the benefits and risks of medical devices throughout their marketed life using high quality, standardized, structured, electronic health data;
• Identify potential safety signals in near real-time from a variety of privacy-protected data sources;
• Reduce burdens and costs of medical device postmarket surveillance; and,
• Facilitate the clearance and approval of new devices, or new uses for existing devices.

Four Key Steps to Strengthen Medical Device Postmarket Surveillance in the US

1. Establish a unique device identification (UDI) system and promote its incorporation into electronic health information

- Standard, unambiguous way to document device use in EHRs, clinical information systems, and claims data sources.

- Adoption of the UDI is essential to expanding the Sentinel Initiative to cover medical devices (e.g., query large claims data sets for patterns that may indicate safety problems, as is currently being done for prescription drugs)

2. Promote the development of national and international device registries for selected products

- Rather than creating individual registries for a specific manufacturer or product, it may be “more cost-effective to pursue nationwide medical device registries focused on certain product areas of high importance,” (e.g., a subset of Class III or permanently implantable Class II devices).

- FDA will host workshops to identify priority medical device types, establish common data elements, identify registry governance models, and develop criteria that would render a registry automatically eligible to support and FDA-required post-approval study (voluntary certification).

Pelvic Floor Disorders (PFD) Outcomes Registry Partners

- Sponsor: American Urogynecologic Society
- Federal government partners:
  > FDA/CDRH
  > National Institute of Child Health and Human Development (NICHD)
- Professional association and network partners
  > American College of Obstetricians and Gynecologists (ACOG)
  > Women’s Health Registry Alliance
  > Pelvic Floor Disorders Network (PFDN) Advisory Panel
  > Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU)
  > American Urological Association (AUA)
PFD Outcomes Registry
Primary Objectives

• Evaluate the effectiveness, quality of life and safety associated with surgical options for pelvic organ prolapse (POP), including transvaginal/transabdominal native tissue repair and transvaginal mesh repair and sacrocolpopexy.

• Assess the effectiveness and quality of life associated with non-surgical management for POP, including pessaries.

• Provide a framework for clinical studies to be conducted within the registry, including industry-sponsored studies required to fulfill the FDA’s request for postmarketing surveillance for transvaginal mesh for POP, (i.e., Section 522 studies).
## PFD Outcomes Registry
### Levels of Participation

<table>
<thead>
<tr>
<th>Goal</th>
<th>LEVEL 1</th>
<th>LEVEL 2</th>
<th>LEVEL 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goal</td>
<td>Universal minimum dataset</td>
<td>Expanded dataset</td>
<td>Specific study data collection</td>
</tr>
<tr>
<td>Description</td>
<td>Effectiveness, quality of life and safety</td>
<td>Level 1 plus condition specific QOL, POPQ, surgical details, etc</td>
<td>Level 1&amp;2 plus Allows unique cohort studies (522 compliant)</td>
</tr>
<tr>
<td>Attributes</td>
<td>Minimal patient and provider burden</td>
<td>More detailed provider (i.e. POPQ) and patient data entry</td>
<td>Allows for additional study specific outcomes</td>
</tr>
<tr>
<td>Research Questions</td>
<td>Epidemiologic Descriptive</td>
<td>Provides comparison group for level 3 &amp; more detailed outcome comparison</td>
<td>Used for sponsored studies (i.e., NIH, post market surveillance, etc). Restricted access.</td>
</tr>
</tbody>
</table>
3. Modernize adverse event (AE) reporting and analysis.

- Develop automated AE reporting systems: E.g., Adverse Spontaneous Triggered Events Reporting (ASTER) facilitates use of EHRs and Incident Reporting Systems to detect AEs and generate reports.

- Increase the number of medical device reports (MDRs) received electronically

- Develop mobile applications for AE reporting

- Modernize the medical device AE database: Replace the antiquated Manufacturer and User Facility Device Experience (MAUDE) database with a new FDA Adverse Event Reporting System (FAERS).

- Rapidly identify safety signals using automated, computerized statistical methods to discover safety signals

• When the Initial Reporter enters data in the patient’s EHR, a call is made to the SIE
• Via RFD (*Retreive Form for Data Capture*), the SIE’s version of the 3500A form is launched within the EHR.
• After review of the AE, with the potential for manual entry of additional data, the completed AE is ready for submission to FDA
• A complete and approved 3500A form is transformed to HL7 ICSR and transmitted to the FDA’s eMDR (Electronic Medical Device Reporting)
• The AE data are ultimately stored in MAUDE (Manufacturer and User Facility Device Experience Database)
Four Key Steps to Strengthen Medical Device Postmarket Surveillance in the US (cont.)

4. Develop and use new methods for evidence generation, synthesis and appraisal

- FDA has conducted public workshops and established the Medical Device Epidemiology Network (MDEpiNet) to explore a range of methodological issues:
  » Quantitative decision analysis to evaluate benefits and risks
  » Combining data from diverse data sources
  » Automating and refining signal detection and management

Overview

“Patient Registry” Definition

FDA’s Evolving Strategy for Medical Device Safety

Regulations for “Qualified Clinical Data Registries”

Agency for Healthcare Research and Quality (AHRQ) Registry Initiatives
DHHS Developing Rules for “Qualified Clinical Data Registry” Participation

- American Taxpayer Relief Act of 2012, Section 601(b): *Advancement of Clinical Data Registries To Improve the Quality of Health Care*

- In lieu of submitting data annually to the Physician Quality Improvement System (PQRS), reporting of measures may be accomplished through participation in a “qualified clinical data registry”
  
  > For 2014 and subsequent years, the Secretary shall treat an eligible professional as satisfactorily submitting data on quality measures…. if the eligible professional is satisfactorily participating…in a qualified clinical data registry…for the year.
  
  > The Secretary shall consider the following criteria when establishing requirements for a “qualified clinical data registry”:
    
    - Has in place mechanisms for the transparency of data elements and specifications, risk models, and measures;
    
    - Requires the submission of data from participants with respect to multiple payers;
    
    - Provides timely performance reports to participants at the individual participant level; and
    
    - Supports quality improvement initiatives for participants.

- The Secretary may designate one or more independent organizations to make such determination.
Overview

“Patient Registry” Definition

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Regulations for “Qualified Clinical Data Registries”

Agency for Healthcare Research and Quality (AHRQ) Registry Initiatives
  > Registry of Patient Registries (RoPR)
  > AHRQ Registries “Handbook”
What is RoPR?

The Registry of Patient Registries (RoPR) is:

• A searchable central listing of patient registries
• Similar to ClinicalTrials.gov, but designed specifically to collect data relevant to patient registries
• Funded by the Agency for Healthcare Research and Quality (AHRQ) under the Effective Health Care Program
• Produced in collaboration with the National Library of Medicine
• Available at https://patientregistry.ahrq.gov
Why Should I Register My Registry in RoPR?

From a voluntary perspective, registry owners might be motivated to participate in the RoPR in order to:

- Be transparent
- Seek collaborators for their registry
- Aid in recruitment of patients and providers to their registries
- Market the availability of their data assets for use or collaboration
- Ensure the continued use of the data for the public good even when the registry otherwise ends
How the RoPR Works

1. Register the registry in ClinicalTrials.gov

2. Select “observational study” as the study type. Check the box to indicate that the study is a patient registry

3. Click to complete the registration in RoPR

4. Enter remaining data elements in RoPR and submit for posting
The 1<sup>st</sup> and 2<sup>nd</sup> editions of the AHRQ Registries User’s Guide are widely used.

As registries continue to evolve, many new methodological and practical issues have arisen.

The 3<sup>rd</sup> edition, due out later this year, will address 11 new topics, including a chapter on medical device registries.

Available at http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productId=D=531
Polling Questions

- Does your company participate in a medical device registry?
  - Yes
  - No
  - Don't know
Successful Device Registries

Nancy Dreyer, PhD, MPH
Overview

- Unique Issues for Devices
- Registry Design and Data Collection Considerations
- Potential Uses of Emerging Technology
- Observational Study Types of Interest
Unique Issues for Devices

Regulatory oversight achieved through
- Regulatory controls
- FDA classification process (I, II, III)
  - Class I – lowest risk device, minimal regulations
  - Class II – low to medium risk (e.g. hearing aids, ultrasonic equipment)
  - Class III – high risk (e.g. balloon catheters)

Lifecycles of devices vs. drugs
- Similarities: heterogeneity of patients using products after approval
- Differences
  - Shorter product lifecycle
  - Iterative nature of medical device production
  - Operator experience
Unique Issues for Devices

Device Systems and Components

Device approval by the FDA

• Approval means “no less safe” and “no less effective” than predicate devices.

• Devices can be approved as separate components or full systems, e.g.,
  > Implantable pacemaker and ICD systems involve implantable leads, pulse generators, external programmers and angioplasty
  > Stenting systems involve balloon catheters and guide wires
  > Ancillary factors may be important, e.g., Methods of mesh adhesion (staples, glue, sutures) in hernia repair

Surgeons sometimes “mix and match” components from multiple manufacturers into one system

  > Cannot assume homogeneity within system
  > Components may have different lifecycles, which affects effectiveness and long-term safety of entire system
DePuy ASR XL Acetabular Cap System (Metal-on-Metal Hip Implant)*

95 predicate devices over 50 years

Unique Issues for Devices

Patient outcomes can be affected by:

- Patient characteristics
- Device factors (e.g., biomaterials, manufacturing characteristics)
- User interface/operator characteristics
  - (e.g., surgical technique, preference, or experience)
- Ancillary technologies (e.g., choice of imaging)

Adverse effects can be localized (e.g., stent thrombosis) or systemic (toxic, allergic, autoimmune effects)

Reasons for device malfunctions can also include:

- Manufacturing problems
- Design-induced errors
- Operator characteristics (experience, settings)
- Poor maintenance
- Environmental factors (e.g., heat, humidity)
Unique Issues for Devices

Registry Design and Data Collection Considerations

Potential Uses of Emerging Technology

Observational Study Types of Interest
Total Resurfacing Hip Replacement

In the 2007 Annual Report the Registry identified the ASR, Cormet 2000 HAP and the Durom as having a higher than anticipated rate of revision. The same three prostheses have been reidentified this year. The Cormet 2000 HAP is no longer used, however the ASR and Durom continue to be used, although the number is declining. All three prostheses have more than twice the risk of revision compared to all other total resurfacing prostheses combined (Tables HT50-HT52).

Prosthesis Specific Outcomes

The three total resurfacing systems with over 1,000 observed component years are the BHR, ASR and Durom. The number of revisions per 100 observed component years for BHR is 0.8, for ASR is 2.6 and for Durom is 2.3. The three year cumulative percent revision for BHR is 2.5% and for ASR is 6.0% and for Durom is 5.8%. This year the Registry is able to report a seven year cumulative percent revision for the BHR (4.6%) (Table HT46).

DePuy Had Time to Recall Device, Chose to Not Notify Public

This blog has noted several times that DePuy knew of the likely failure rates of its ASR hip implants several years before the medical device manufacturer issued its 2010 recall of the product. In light of this knowledge, DePuy nevertheless waited years before it decided to remedy the dangerous situation caused by its defective hip implants. Instead, it chose to shift the blame for reported problems elsewhere before finally initiating the recall.

New evidence has been uncovered showing that DePuy had received credible notification of its ASR hip implant failure rates as far back as 2007. According to The Independent, the Australian joint registry, the second largest registry of its kind in the world, informed DePuy of identified problems in seven separate reports. One of the most striking findings made by the registry was the higher than usual amount of revision surgeries needed to replace previously-implanted ASR hip units. DePuy sat on this knowledge until 2009, when the company finally withdrew the ASR hip implants from the Australian marketplace, citing "commercial reasons." DePuy initially blamed the Australian joint registry findings on "imprecise surgical techniques" by doctors, but was forced to retreat from that position in response to the multiple reports of problems sent the company’s way.
Accurate device identification is critical

> Different distribution system than drugs
> Need device type, model number and any other unique characteristics
> UDIs are available for some devices, but not routinely captured in observational data sources (e.g., claims data)
> FDA UDI will eventually ensure standardized identifiers for all devices, including
  - Manufacturers lot or batch number
  - Serial number
  - Manufacture date
  - Expiration date
Registry Design and Data Collection

Device Identification

When UDI is not available

> Substitute other identifiers (e.g., catalogue, model, serial, lot numbers) – although not standardized and not always unique

> Comprehensive checklists (e.g., heart valve devices in STS Adult Cardiac Database)

> Photos of the device – inefficient, but can be useful when few devices on market and which have marked differences in design
Example: Complexity of Medical Devices

Manufacturing Characteristics Associated with Strut Fracture in Björk-Shiley 60° Convexo-Concave Heart Valves
Alexander M. Walker, Donnie P. Funch, Sandra I. Sulsky, Nancy A. Dreyer

It is concluded that welder identity and strut flexibility appear to contribute to the risk of outlet strut fracture in Björk-Shiley CC60° valves. Neither of these factors, however, is sufficient to account for much of the previously unexplained variation in risk. No other characteristic measurable in existing manufacturing records appears to predict risk of strut fracture in any useful way.

The Journal of Heart Valve Disease 1995;4:640-648
Shop Order Fracture Rate as a Risk Factor for Strut Fracture in Björk-Shiley CC60° Heart Valves
Alexander M. Walker¹², Donna P. Funch¹, Lisa Bianchi¹³, William J. Blot⁴

Background and aims of the study: Previous studies have implicated a number of characteristics that predict strut fracture in Björk-Shiley convexo-concave heart valves, including valve size and position, opening angle, and weld date. This study examines whether the specific batch (shop order) with which a valve is associated during manufacture is related to the risk of fracture.

Material and methods: Our case-control study of CC60° valves obtained detailed information on the manufacturing characteristics of 147 case and 1094 control valves used. Shop order fracture rate for each valve (percentage of other valves in the same shop order with a fracture) was obtained from the research database maintained by the valve manufacturer.

Results: Shop order was associated with fracture risk. Valves originating from shop orders with the highest two categories of fracture rate were at approximately twice the risk of fracture as other valves, after accounting for the effect of known risk factors.

Conclusions: Shop order information may provide additional data for assessing the likelihood of valve fracture in individuals being considered for prophylactic explant of heart valves.

The Journal of Heart Valve Disease 1997;6:264-267
Registry Design and Data Collection

Device Performance

• Anticipate a range of performance issues (e.g., failure rate and timing)

• Plan for verification and adjudication of performance issues

• Automated surveillance may be appropriate for issues that present uniquely
  > Requires standardized data elements and collection procedures across sites, e.g., FDA’s Data Extraction and Longitudinal Trend Analysis (DELTA) network study
    - Designed to evaluate the safety of new cardiovascular devices used during percutaneous coronary intervention (PCI)
    - Uses standardized data elements from the American College of Cardiology National Cardiovascular Data Registry
Consider channeling bias, e.g., drug-eluting stents (DES)
> Approved by FDA in 2003 for cardiac patients with uncomplicated coronary lesions
> As adoption rate increased, patient population changed – sicker patients more likely to receive DES
> Rate of stent thrombosis also found to be higher at one year post-implant in DES patients v bare-metal stent patients

Consider confounding from concomitant treatments
> Consider collecting data to flag possible drug interactions (e.g., concomitant drug dosing information at time of implantation and prospectively over time)
Registry Design and Data Collection

Outcomes & Follow-up

• Must have clinically meaningful outcomes
• Delayed risks and benefits are also important
  > E.g., how long will my new hip last?

• Challenge: patients often aren’t required to return to provider unless they experience issues with device (unlike drugs, which require prescription refills)
  > Risk preferential loss to follow-up of patients with no issues

• Consider:
  > Direct-to-patient follow-up in addition to follow-up through provider
  > Linking registries with administrative billing data or other sources
Registry Design and Data Collection

Provider Experience and Training

• Provider experience/training can influence selection of device, device performance, and patient outcomes - especially for implantable devices

• Consider collecting:
  > Provider identifier
  > Device-specific training of provider
  > Experience-oriented factors (practitioner annual volume, practitioner lifetime volume, facility volume, facility characteristics such as academic teaching status)

• Consider how these factors will affect analysis:
  > Clustering (for devices with few qualified surgeons) → increase sample size and/or use appropriate statistical analysis methods
  > Statistical adjustment for surgical volume, at provider or hospital level
Association of Physician Certification and Outcomes Among Patients Receiving an Implantable Cardioverter-Defibrillator

Conclusions  In this registry, nonelectrophysiologists implanted 29% of ICDs. Overall, implantations by a nonelectrophysiologist were associated with a higher risk of procedural complications and lower likelihood of receiving a CRT-D device when indicated compared with patients whose ICD was implanted by an electrophysiologist.

JAMA 2009;301(16):1661-1670
Unique Issues for Devices

Registry Design and Data Collection Considerations

Potential Uses of Emerging Technology

Observational Study Types of Interest
Potential Uses of Emerging Technology

• Data transmission - directly to EHRs or registries
  > ↑ timeliness of registry data, ↓ burden of data entry

• Automatic measurement and adjustment of programming (in pacemakers and other implantable devices)
  > ↑ efficient use of hospital time and resources, registries can collect all automated changes at one time point, rather than ad-hoc as changes occur

• Diagnostics for implantable devices (e.g., heart rate, heart rate variability, respiration rate, symptom markers, patient activity)
Unique Issues for Devices

Registry Design and Data Collection Considerations

Potential Uses of Emerging Technology

Observational Study Types of Interest
Observational Study Types

Product and/or condition registries to study
  > Safety
  > Effectiveness
  > Provider characteristics
  > User preferences (useful for marketing data)
  > Label changes?
Broader Indication for Intraocular Lenses

Analysis of data from FDA databases, the AAO NEON database, post mortem eyeballs and explanted IOLs from the Center for Research on Ocular Therapeutics and Biodevices, and the published literature, allowed FDA personnel to conclude that there was substantial scientific evidence to support the use of IOLs in adults younger than 60 years. Their conclusions were presented in the publication, ‘Retrospective evaluation of intraocular lenses in adults younger than 60 years’ [12]. References to this publication, with its extensive review of epidemiological data, has allowed manufacturers to request that FDA change the indication for their IOLs from ‘use in adults 60 years and older’ to ‘use in all adults’.

In summary, utilization of epidemiological data has played a major role in the evaluation of IOLs by FDA. It has allowed FDA to develop policies that helped to facilitate the 25 year improvement in the quality of cataract patients’ treatment unparalleled in medicine today [8].

Conclusions

• Safety:
  > When ordered to conduct a “522 Study” or committed to undertake a PMA post-approval study, your progress will be posted by FDA on its website

• Thinking of registries:
  > The FDA envisions multi-stakeholder patient registries as an important component of the evolving postmarket medical device surveillance system for selected products.
  > The Secretary of DHHS is developing regulations for “qualified clinical data registries” that eligible professionals can join as an alternative to submitting measures under the Physician Quality Reporting System.
  > AHRQ’s Registry of Patient Registries is a central database for listing registry programs and is integrated with ClinicalTrials.gov.

• If you conduct a registry:
  > Collect as much detail as possible about the device (UDI or other).
  > Best to have clinically meaningful outcomes.
Upcoming Events

Post-Approval Summit

www.postapproval.org

• May 7-8, 2013
• Conference Center at Harvard Medical School, Boston, MA
• Key Topics:
  > Comprehensive Approaches to Evidence Development for Safety and Effectiveness
  > Evolving Roles of the RCT and Observational Research
  > Big Data: Leveraging EHR and Health System Data for Safety and Effectiveness
  > Updates on Changing Safety and Risk Management Requirements
  > Comparative Effectiveness, Market Access and HTA
  > Approaches and Models for Addressing Multi-Stakeholder Demands
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