

MDEPINET METHODOLOGY CENTER

Sharon-Lise Normand (for Methodology Center)

Harvard University: Laura Hatfield, Vanessa Azzone, Daniel Kramer, Robert Yeh, Laura Mauri

Lahey Medical Center & Tufts Medical School: Fred Resnic

Vanderbilt University: Michael Matheny

Specific Aims

Substantive

- Bridging pre-market & post-market evidence
 - CRT devices & RCT data
 - Adverse medical device events in children & billing data
- Develop probabilistic risk assessment framework
 - Implantable cardiac defibrillators (lead reliability) & multi-center data
- Develop approach to post-market surveillance of medical devices
 - CRT devices & billing data
 - Learning curves (vascular closure devices, etc using registry data)
 - VA prosthetic risks (VA database)
 - DELTA & Lahey Clinical Data Repository

Products

- Combine RCT data to infer heterogeneous device effects
- Combine RCT data with differential follow-up
- Handle missing data in meta-analysis of individual participant data with correlated mixed outcomes
- Incorporate regulator loss functions for safety signal escalation
- Convert Lahey clinical data repository into an Observational Medical Outcomes Partnership (OMOP) structured database
- Robust machine learning techniques for device evaluations with > 2 devices
- Methodology to separate learning curves from effectiveness in device evaluations

Outreach: Webinar

- **Need:** identify & discuss areas where methodological gaps exist
- **Stakeholders:** methodologists
- Open to anyone
- Majority of audience has a quantitative background

MDEpiNet Methodology Forum

Date	Presenter & Topic
March 2015	Matthew Brennan, Duke University, Contemporary Methodology Challenges in Medical Device Surveillance . Laura Hatfield, Harvard University, Safety Signals: Mixture of Models and Loss Functions
June 2015	Vicki Petrides, Abbott Diagnostics. Evaluating Effectiveness of In Vitro Diagnostics . Constantine Gatsonis, Brown University, Post-marketing Studies of Modalities for Screening and Diagnosis: the Evaluation of Effectiveness
Sept 2015	Sherri Rose & Laura Hatfield, Harvard Medical School. Multiple Treatment Comparisons
Oct 15, 2015	Lisa Torosyan & Vahan Simonyan, FDA. The High Performance Virtual Environment (HIVE) Platform
Dec 2015	TBD



Outreach: Presentations

- **Need:**
disseminate methodological approaches to address device evaluations
- **Stakeholders:**
academic researchers, industry (Webinar)

Invited Presentations (FY2015)

Date	Forum & Topic
Oct 2014	36th Annual Meeting of the Society for Medical Decision Making. Handling missing data in meta-analysis of individual participant data with correlated mixed outcomes
Feb 2015 Webinar	Eastern North American Region of the International Biometrics Society, Statistical Issues in Comparative Effectiveness Research .
Feb 2015	CSRC Mini Think Tank, FDA. CV Safety Assessments: Signal Detection with Heterogeneous Data Sources
April 2015	L. Adrienne Cupples Seminar, Boston University, Approaches to Comparative Effectiveness Estimation in Prospective Observational Data
April 2015	G70: A Celebration of Alan Gelfand, Durham, NC. Realistic Loss Functions in Safety Signal Escalation
April 2015	8 th FDA/MGLI Workshop On the Use of Registries for Post-Market Medical Device Assessments
July 2015	Department of Biomedical Data Science, Dartmouth College. Incorporating Regulator Loss Functions for Safety Signal Escalation

Outreach: Publications

- **Need:**
transparency in methodology used for medical device evaluations
- **Stakeholders:**
academic researchers, policy makers

**ORISE fellow;
currently: NHLBI
statistician

MDEpiNet Authors	2015 Journal and Topic
Resnic, F Normand, S-L Matheny, M	Circulation: Cardiovascular Quality and Outcomes, Jan;8(1)38-46. The Data Extraction and Longitudinal Trend Analysis Network Study of Distributed Automated Postmarket Cardiovascular Device Safety Surveillance.
Kraemer, D Hatfield, L	J Am Heart Assoc. 4: e001672. Transvenous Implantable Cardioverter-Defibrillator Lead Reliability: Implications for Postmarket Surveillance.
Kunz, L** Normand, S-L Sedrakyan, A	Statistics in Medicine, 34(21):2913–2925, Meta-analysis of rate ratios with differential follow-up by treatment arm: Inferring comparative effectiveness of medical devices.
Kramer, D Hatfield, L Normand, S-L	Heart (in Press) Comparative effectiveness of cardiac implantable electrical devices
Kunz, L Normand, S-L	Methods in Comparative Effectiveness Research (in Press). An Overview of Statistical Approaches for Comparative Effectiveness Research. Eds: Gatsonis C. and Morton S. CRC Press
Krucoff, M Sedrakyan, A Normand, S-L	JAMA, August 24. Bridging Unmet Medical Device Ecosystem Needs with Strategically Coordinated Registries Networks.

Strategically Coordinated Registry Networks (CRNs)

- CRNs will involve **heterogeneity** in data collection, patient populations, clinical centers, & operators
- Information **aggregated** to the component registry level may be sufficient for some device evaluations but insufficient for others
- CRN construction should focus on:
 - Minimizing **quality heterogeneity** (data element definitions, measurement error, etc.)
 - Supporting **poolability** to maximize information from enriched
 - Patient, device, & operator populations
- Use **variation** across component registries within the CRN to quantify benefits/risks :
 - Patient subgroups
 - Medical devices
- **Signal detection** via CRN requires consistent, standardized data with sufficiently specified devices & outcomes
- Use CRN data for **premarket designs (Friday Oct. 2 session)**
 - **Label extensions**: pool data across heterogeneous patient populations exposed to a particular device to learn about benefits/risks in a **new population**
 - **Clearance** for competitive iterations of similar devices: pool data across multiple devices within a particular patient group to infer benefits/risks for a **new but similar device**