How Can We Make Automated Post-Market Surveillance Work in the ACHQC?

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Abdominal Core Health Coordinated Registry Network (CRN)

- MDEpiNet: Global Public-Private Partnership that brings together leadership, expertise, and resources to advance a national device surveillance system
  - Health care, industry, patient groups, payers, academia, gov’t

- Organized system that leverages variety of resources to address key questions

- Objectives
  - Establish CRN capable of addressing clinical questions and enabling post-market surveillance
  - Harmonize the collection of abdominal core health data

Example CRN
What is active post-market surveillance?

Goal: assess device performance in a time frame that permits appropriate action

**FDA:** Non-research efforts that are part of routine post-market vigilance programs for specific (typically high-risk) medical devices.

**Industry:** Exploratory, non-research, post-market, device performance monitoring.

**Academic:** Prospective, pre-specified, risk-adjusted, time-limited analysis of RWE.

**Active Surveillance**
- Continuously generating and evaluating data on device performance
- Retrospective, Single Study
- Accruing Data, Sequential Study
- Accruing Data, Near Real-Time Sequential Study

**Automated Surveillance**
- Real Time, Routine, Continuous Device Performance Monitoring
- Accruing Data, Near Real-Time Sequential, Programmed

**Inexorable** progression toward real-time, high quality RWE availability as EHR, Registry/CRN and Informatics technologies mature.

Figure courtesy Fred Resnic, MD, MSc Lahey Hospital & MC
DELTA surveillance system

- **Data Extraction and Longitudinal Trend Analysis**
- Prospectively monitors the AEs of medical devices through continuous surveillance of existing clinical databases using a variety of statistical monitoring strategies
- Led by Frederic Resnic, MD, MSc (Lahey), Michael Matheny, PhD (Vanderbilt), and Sharon-Lise Normand, PhD (Harvard).
- Part of the MDEpiNet programs, supported by FDA/CDRH research grants and private philanthropies
- First prospective use as part of active surveillance strategy for cardiovascular registries/devices
- Tested and validated (Vidi et al., Contemporary Clinical Trials, 2011)
- Demonstrated the capability to identify low frequency safety signals early in the device lifecycle (publications in NEJM, JAMA, Circulation)
DELTA analytical monitoring strategy

• Prospectively collected data from multiple sources submitted at regular time intervals (i.e. monthly, quarterly) and pooled with current data

• Calculating event rates: Propensity score matched cohort
  • Previously published risk factors of outcome + factors influencing device selection
  • Propensity score matching enforced between the groups within a time interval (e.g. controls selected within 6-months of date of exposed case).

• Safety alerts triggered if the cumulative event rates for exposed group exceeded the upper confidence limit of the control group by X% (e.g. 20%)
  • Adjusted for multiple comparisons (type I error inflation)

• 2+ consecutive safety alerts generate a “significant/sustained alert”
  • Trigger detailed sensitivity analyses to verify/refute safety signal
Device event rate (red = higher than expected)

Event rate in PS match control

Confidence interval

CI adjusted for multiple comparisons

Challenges of active surveillance

- Everything is prespecified
  - Alert thresholds
  - Multiple comparisons plan
  - Missing data plan
  - Sensitivity, subgroup analyses if signal detected
  - Analyses if signal not detected

- Limitations and challenges
  - Limitations inherent to observational studies
  - Appropriately selecting and defining comparison group
  - Defining alert thresholds
  - Data quality and completeness
  - Risk of false alarms and data dredging
  - Data ownership, sharing, timeliness of data collection
Ongoing projects that support active/automated surveillance

• Data linkage
  • Link ACHQC registry with administrative databases
  • Supplement long-term follow-up

• Administrative algorithm validation study
  • Validate accuracy of clinical outcome identification in administrative databases

• Critical Outcomes of Mesh Placement Questionnaire (COMP-Q)
  • PRO tool sensitive to long-term mesh related complications
Thanks!
Outlier assessment methods

Risk adjusted mortality rate = RAMR

Interpretation:
Actual patient outcomes vs. predicted patient outcomes if they were to receive an average device

RAMR > population mean -- O/E > 1: The device had worse outcomes than average

\[
RAMR = \frac{\text{Observed mortality}}{\text{Expected mortality}} \times \text{population mortality}
\]
What is active post-market surveillance?

• Continuously generating and evaluating data on device performance and clinical outcomes in routine clinical practice after product is in the market
  • Appropriate risk adjustment and signal thresholds. Minimize false alarms (type II errors) without missing real issues
• Primary goal is to assess device performance in time frame that permits appropriate action (by manufacturer, clinicians, and regulators).
  • Repeated assessments to minimize delay
• The term “Active Surveillance” includes differing strategies to different stakeholders.

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What is automated surveillance?

• Automated surveillance = active surveillance + “high tech”
  • Leverage software tools for near real-time, prospective, evaluation of accruing experience
  • Pre-programmed

Inexorable progression toward real-time, high quality RWE availability as EHR, Registry/CRN and Informatics technologies mature.
DELTA cont’d

• Event rates will be calculated at regular time intervals

• **Safety alerts** triggered if the cumulative event rates for exposed group exceeded the upper 90% confidence limit of the control group by 20%
  • Corrected for multiple looks using O’Brien–Fleming $\alpha$-spending method
  • 90% CI selected to increase the sensitivity of detecting a safety issue and to minimize false alarms
  • 20% selected to represent a clinically meaningful difference in safety

• 2+ consecutive safety alerts generate a “significant alert”
  • Trigger detailed sensitivity analyses to verify/refute safety signal