Enhancing Public Health Through Timely Detection: Assessing the Value of Real-World Evidence with a Cardiovascular Defibrillator Leads Case Study

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BACKGROUND

- Mandates like the 21st Century Cures Act have propelled real-world evidence (RWE) into a prominent role within healthcare, driving efficiency improvements, quality enhancements, and informing regulatory decisions.[1]
- Over 90 regulatory decisions from the Center for Devices and Radiological Health (CDRH) have leveraged RWE, with 75% sourced from registry-based evidence.[2]
- Despite these advancements, challenges persist in RWE implementation. These include concerns regarding cost, time, and efficiency relative to traditional evidence-generation methods, as well as issues surrounding bias control and evidence quality.
- Persistent questions exist about the comparative cost and time demands of RWE generation versus conventional methods like post-approval studies and adverse event reporting, as well as the varying efficiencies of different RWE sources.[3,4]
- The unexpected failure of a cardiac defibrillator lead serves as a compelling case study demonstrating the value of real-world evidence (RWE) from a public health perspective.

OBJECTIVE

The objective is to compare the actual time taken to identify a safety signal (real case scenario) against the hypothetical duration if data from the National Cardiovascular Disease Implantable Cardioverter Defibrillator Registry (NCDR ICD) had been employed (counterfactual scenario), leading to the voluntary recall of the device.

METHODS

Time Frame: 36 months (September 2004 to October 2007)

Data Source: The National Cardiovascular Disease Registry (NCDR) Implantable Cardioverter Defibrillator (ICD) Registry is a component of the National Institute of Dental and Craniofacial Research (NIDCR) and encompasses a comprehensive database of cardiac device implants from over 900 reporting centers.

Real Case Scenario:

- The study identified the failure of cardiac defibrillator leads by analyzing data collected from three clinical centers. This failure was observed 36 months after the initial approval of the device, spanning from September 2004 to October 2007.

Counterfactual Scenario:

- This scenario projected the time it would take to detect the same safety signal if data from the NCDR Implantable Cardioverter Defibrillator (ICD) Registry had been utilized. It was determined that a significant signal could have been generated through prospective surveillance of the NCDR ICD Registry within 180 days of the device's approval.
- The time saved in identifying this significant safety signal using the CRN approach was calculated by subtracting the projected time from the actual time it took for the signal to occur, accounting for the necessary abstraction, validation, and submission of data to the CRN. This resulted in a time savings of 795 days, approximately 2 years and 2 months earlier than the real case scenario.

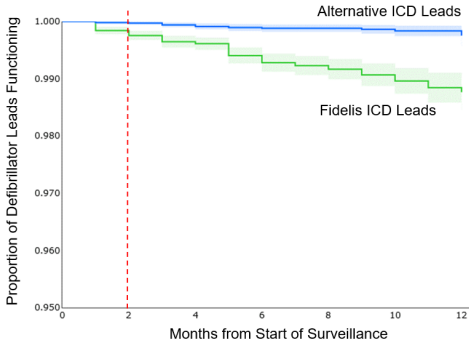

Figure 1. DELTA propensity-matched survival curve based on 12-month surveillance of the 'Likely' simulated scenario ICD Registry dataset **

**Blue indicates alternative (control) ICD lead survival, while green indicates Fidelis lead survival. The light-colored bands represent the 95% confidence interval for lead survival. An initial statistically significant signal emerges after Quarter 2 (indicated by the red dashed line), with a log-rank statistic of 13.45 (p=0.0002). As more data becomes available, the signal strengthens, and by the 12-month mark, the log-rank statistic reaches 64.27 (p<0.00001), with a Hazard ratio confidence interval of 4.65-5.43 for Fidelis lead failure relative to all other ICD leads.

Simulation of Scenarios:

- Three scenarios, labeled as "conservative," "likely," and "optimistic," were simulated to model the outcomes of prospective active surveillance of the ICD Registry. These scenarios varied in terms of the proportions of timely reported ICD lead implants, and different failure rates for the Fidelis lead were considered.
- The DELTA active surveillance system was employed to monitor the accruing simulated ICD Registry data, including follow-up events reported by calendar quarter. The volume of cases submitted to the registry and the distribution of patient-related covariates were based on publications describing the ICD Registry during its early years of use.

RESULTS

- The 'likely' scenario identified a significantly increased failure rate for Fidelis leads compared to other high-energy ICD leads, within the first six months of monitoring.
- DELTA would have alerted the FDA and the manufacturer to the substantially higher failure rate within **11 months after the product's launch**.
- It is estimated that nearly **200,000 patients** would have avoided exposure to the defective device if active surveillance of the ICD Registry had been utilized.
- In the conservative scenario, DELTA would have alerted the FDA and the manufacturer approximately 14 months after the product's launch, which is three months later than the 'likely' scenario.
- This alert would have occurred approximately **23 months** prior to the FDA's awareness of the Fidelis lead failure issue.

DISCUSSION

- This case study highlights the tangible value of RWE in public health, particularly in terms of post-market surveillance.
- The shorter detection time, had the full NCDR data source been utilized, aligns with documented cases, showcasing the significance of RWE in averting potential harm and supporting timely regulatory action.
- These findings underscore the importance of RWE in supporting regulatory decision-making compared to traditional evidence.
- Future research comparing different types of data sources and their applicability in various medical products is needed.

REFERENCES

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