Active PM surveillance and considerations for an active comparator NOAC Reversal Agents

Paul Stang, PhD

Feb 3: NOAC Reversal Agent Think Tank Follow-up
A slide from a presentation titled "Concepts that I will cover" includes the following points:

- Active Surveillance
- Identification/selection of comparators
- Benefit-Risk balance
What is ‘Active Surveillance’

• Systematic process for capturing and analyzing health care data sources to better understand the effects of medical products (in combination with data from RCTs, Pharmacovig, etc)
• Minimal lag in data availability
• Characterize ‘actual use’
• Provide insight into benefit-risk
What is the exact question we are trying to address?

- Usage (appropriate) of NOAC reversal agents?
- Events associated with NOAC reversal agents?
- Compared to what?
- Both are tied to selection of patients for NOAC vs. alternative and the rates of events for each leading to use of reversal agent.
What drives decisions: Implementing Active Surveillance

• Capture of Exposure
  – Can we ‘see’ use of NOAC reversal agent
    • Inpt, Outpt, Nursing homes

• Frequency of events (use of reversal agent)
  – Indication for reversal agents (MB) <3%

• Outcomes
  – Can we follow patient and ‘see’ outcomes of interest

• How representative must the sample be?

• Comparison/Control group
Possible study designs for Active Surveillance

PROSPECTIVE and Concurrent
- Cluster randomization/stepped wedge
- Registry
- Case-control monitoring

RETROSPECTIVE
- Database
- Registry
What you may/may not ‘see’ or not see clearly enough

- Seeing claim requires specific reimbursement, particularly outpatient
  - Procedure code but must be billed separately
  - Potential comparators (prothrombin complex concentrate (PCC) or fresh frozen plasma (FFP) in combination with vitamin K) may not be visible
- How much was administered?
- Who administered/ordered it and what was the setting for administration?
- Was the NOAC stopped? When?
- Site of bleed, how severe or was there actually a bleed?
- Rationale for reversal agent
  - initiated prophylactically (e.g., start of emergency surgery because you are on a NOAC) or once you started to bleed?
  - Will you be given the right reversal agent? May not know what NOAC you are on when they see you.
Site (place) of Use Will Influence Capture of Information

• Outpatient
• Inpatient on floor
• In the OR
• In the ER
Comparators for NOAC Reversal Agents?

• Warfarin: Discontinuation, Fresh frozen plasma, PCC, etc

• Among comparable patients (warfarin vs. NOAC or NOAC1 vs. NOAC2), how frequently are reversals undertaken and what is the outcome?
  – Comparable patients (propensity)

• Or is the question, among anti-coagulated patients who receive ‘reversal treatment’, is there a substantive difference in use and outcome?
Different ways to get to comparators

• Self-controlled designs
• Clinical rationale
• Empiric selection from database using propensity score to assure clinical equipoise
• Specify alternatives based on clinical insight
• Historical: what has happened without agents, ‘standard of care’
One approach Using Hospital Data

• Is there a situation that would meet criteria for using a NOAC reversal agent in an office setting without immediate ER/hospital referral?

• Assume that NOAC reversal agents will be administered in hospital setting
  – Will not know which NOAC patient was taking but can do source record abstraction (xx%)

• Can then ‘count’ instances of use outside of hospital in broader database that will also capture broader outcome

• Historical controls

• Comparison of rates

• Nested case-control study with record abstraction