

ACTIVE Surveillance to improve the VALUE of Pharmacovigilance as a Public Health tool

Group I:
Identification of
Anticipated Signals



Issues (1)

- Anticipated events allow us
 - to avoid multiple comparisons because of focused hypothesis
 - Easier to find comparator groups
 - buy-in is easier from data sources;
 - still need to prioritize questions for allocating resources

Issues (2)

- Can't pool data – need distributed data model – but need to define what that is – need local expertise in each database to coordinate analyses – common mapping structure
- But still one voice for need for true integrated database
- 5-6 organizations/60-70 million lives in the room
- Concerns about “parallel play” – meta analysis – scientific limitations to pooling data
- Selective about data sources – “qualify” data sources – access to medical records, survey physicians, survey patients, do prospective designs (perhaps randomize), defined populations with eligibility data available,
- Understand fundamentals of research, a research group is needed that would also be “qualified” – model exists for this -

Issues (3)

- Sharing of patient-level data is concern – what is shared across data sources?
- Cannot do fishing expeditions – local data authorities will not approve
- Firewall is key for distributed data model – research group is in middle – bid to do project – standardize approach where possible – place to start for short-term goals

Issues (4)

- Common code across sites developed by central site? Makes sure that specifications are implemented uniformly by all sites
- Database development plan (DDP) for each project – automated using SAS 9.0 to standardize process – reduces variability by defining outcomes up front
- Set top 20 outcomes and start building library across data sources – refine and learn strengths and limitations within each site
- Who is central point? FDA needs to influence – needs to be research group (e.g., Duke, RTI, Ingenix, etc) – don't need to be sitting on data necessarily
- For each new drug, identify which of the pre-specified outcomes are relevant for that drug

Issues (5)

- Governance structure
 - How administer
 - How set priorities
 - Technical experts/content experts
 - Faces the public – nonprofit?

How prioritize?

- Each “node” can do whatever they want independently of surveillance-can bow out whenever they want
- Bow out of program – not on specific issues (e.g., buy in that this year you will commit to surveillance on “x” NMEs) – lists of issues generated at the beginning/approval -
- Need tax dollars to support this as a national resource
- Qualification/certification process is attractive to organizations -

Issues (6)

- Share issues with each drug outside of companies/FDA
- European construct of risk management – lays out all detail of where anticipated events can arise – can identify by therapeutic area
- FDA DMEs
- Need to define “anticipated” vs “unanticipated”
 - Is anticipated drug-driven or data-driven?
 - Start with something small – grow it
- For new drugs look for new signals – for old drugs can look for signal strengthening.
- Anticipated = what you set out to track ahead of time
- Unanticipated = datamining
- Context will still influence what is “anticipated”
- Death is very difficult to look at in these databases without link to NDI

Issues (7)

- Per McClellan's talk – would be nice to say that we will never be blindsided by MI again
- Each site in the network will have own capabilities
- Part of the work is validating the signal
- Can imbed registries within these networks
- Surveys – Part D and VA – Medicare registry – sentinel subgroup (10%) that you administer a survey to within each site – 5-10 year plan
- New drugs need to look weekly or monthly – each week or month is important – need to build an infrastructure to have each group do updates regularly using sequential frequent looks – different question if looking at new issues in older drugs

Issues (8)

- Not just NMEs – look at Avandia/Vioxx – not new – also priority list of events like MI
- Difference between one shot study (safety research) and repeated updated surveillance effort in real time (sentinel) – costs will differ
- Some sites can get daily/weekly feeds – are all set up that way? Need mechanisms to get data in the system quickly
- Old drugs get yearly sweep – newer drugs get more often and in real time

Targeted goals for 2 years

- Start setting up network
 - Set up operational business model, then governance structure to prioritize and allocate resources
 - Assemble workgroup to define criteria to “qualify” organizations to participate in a network
 - Majority view is to develop a distributed data model – periodically re-assess feasibility of integrated model
 - Identify willing participants – bring to the table and determine barriers, incentives for conducting “proof-of-principle” study
 - Identify funding for pilot – DECIDE network RFTO? (7/16 proposal deadline with completion in 15 mo)
 - Identify ways to deal with privacy/liability/safe harbor issues for participating organizations
 - Educate/communicate with public

Target goals for 2 years

- Methods development
 - Establish principles for selecting drugs and signals for surveillance (vulnerable popns, high use, increased public health impact)
 - Define data elements for case definitions
 - WHO: CERTs
- Validation of algorithms for anticipated outcomes
 - WHO: CERTs/NIH/ISPE/AHRQ
 - CMS engagement to release resources for chart retrieval