Postmarketing Surveillance of Drugs

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Postmarketing Surveillance

- FDA adverse event reporting system (AERS)
  - Case-report or case-series system
  - Data collected primarily via MedWatch forms
  - Used for “signaling” unexpected adverse events first seen after marketing
  - Cost-effective system
  - Hypothesis-generating

Limitations of AERS

- Requires that AE be recognized as such
- Depends upon voluntary reports
- Significant underreporting – estimates of 1% of serious events reported directly to FDA
- No denominator, incomplete numerator
- External events, e.g. news reports, affect reporting, as does length of time on market

Hypotheses Generated

- Increased reporting may be caused by
  - Awareness caused by literature cases
  - Initiation of web-based MedWatch reporting opening to public
  - Media coverage

Kennedy DL et al in Strom BL Ed, Pharmacoepidemiology 2000; John Wiley and Sons, West Sussex, UK
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Paroxetine: Raw counts of U.S. AERS reports of pediatric suicidal events, by type of reporter and year

Generation of Hypotheses of Drug-induced Harm

- "Signals" generated by case reports, either via regulatory agency or published literature
- Case reports reviewed, analyzed for patterns
- FDA may request epidemiologic study using automated health plan databases

Current System for FDA to Manage Risks of Marketed Drugs

- Labeling – negotiate with manufacturer to include warnings, precautions
- Request manufacturer do additional studies after product is marketed
- Various risk-management schemes including
  - Informing providers and patients
  - Restricting use through patient selection
  - Restricting distribution

Dilemma of Case-based Surveillance System

- Some signals are very dramatic and action is urged based upon only the signal
- If action is taken without definitive study, useful products may be removed from the market
- If action is delayed to allow for definitive study, more people may be harmed and repercussions ensue
- Often the most adequate data available initially

New FDA Risk-Communication Initiative: Drug Watch

- Proposes to communicate emerging safety information to the public before full study can be undertaken
- Intent is to give public options for choice of continuing to use medication or wait for more definitive information
- Guidance drafted, no web site currently available
- Example: Ortho Evra contraceptive patch warnings

Proposed Changes to Increase Drug Safety

- Allow "conditional" approval of new product
  - Required studies of 30 000 – 300 000
  - No direct-to-consumer marketing
- Empower FDA to enforce regulations
- Support non-governmental organizations to study drug safety issues
## Summary

- The only consistent system of postmarketing surveillance in the U.S. is the FDA's AERS.
- This system relies upon case reports from voluntary reporters, and reports from manufacturers.
- It has severe limitations, but is useful for signaling potential problems after marketing.
- On the basis of hypotheses of harm generated from the AERS, FDA often requests formal epidemiologic studies to confirm the signal.
- FDA's enforcement power limited; changes needed to improve safety of drugs.