

Data for Pharmacosurveillance: Needs, Availability, Challenges

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I. What is the Problem?

- Pharmacosurveillance (systematic monitoring of benefits and harms of medications in routine care) is desirable but difficult
 - Difficult to know what data to target for routine vs special situation monitoring
 - No organization of data collection or analysis for routine post-marketing surveillance purposes
 - Federal responsibility
 - Harm is not fully interpretable without benefit
 - Context is key
 - Cost-effectiveness is the main issue in many jurisdictions
 - Provinces, territories, federal drug programs
 - Multiple health database silos exist
 - Is it ethical to analyze for pharmacosurveillance?
 - Is it possible to reach valid conclusions suitable for policy implementation?

II. Examples

- Should cisapride still be available for certain groups of patients?
- For which groups of patients is clopidogrel cost-effective and worth the additional bleeding risk?
- Should patients taking any COX-2 NSAID be warned about vascular adverse effects?
- Should gefitinib's (Iressa) Notice of Compliance with Conditions (NOC/C) entail an automatic, standard data collection in Canada?
 - Including resource utilization?
- How should we be monitoring infliximab (or any other biologic)?
- How would differential formulary restriction impact on the utilization, benefits, costs of PPIs?

III. Objectives

- To formally identify the information set required to support optimal pharmacosurveillance regulatory decisions (gold standard information set)
 - Federal post-marketing surveillance
 - Provincial cost-effectiveness surveillance
- Where do these "gold standard" data reside currently?
- Explore key methodologic issues:
 - Are there valid methods to adjust for channeling bias?
 - Methods of data mining
- What impact will evolving privacy legislation have on pharmacosurveillance activities now and in near-future?

IV. Methods

- A. Information Requirements
 - Modified Nominal Group Technique
 - 12 representatives of stakeholder groups in drug decision making from all regions of the country
 - Primary care, pharmacy, clinical pharmacology, consumers, epidemiology, database management, methodology, formulary management, regulators, pharma industry, health economics, patient safety
- B. Information Availability
 - Comparing large administrative datasets (LADs), electronic medical records (EMRs), patient registry (PR)
 - Based on gold standard information set, are the data fields there and are there data in the fields?
- C. Methodologic Issues
 - HRT in elderly BC cohort, can the RCT results (HERS, WHI) be reproduced using channeling bias adjustment methods
 - Reviewed datamining methods and use in pharmacosurveillance
- D. Privacy Concerns
 - Reviewed existing federal and provincial privacy legislation, CIHR recommendations re:
 - Secondary use of databases for research
 - Secondary use of databases for regulatory purposes
 - Linkage of data across jurisdictions

V. Results

- A. Information Requirements (Gold Standard)
 - 100% YES for gender, birth year, weight, current diagnoses, hospital admission and discharge dates and discharge diagnoses, drug generic name, route, duration, reason prescribed, concurrent therapy, ADR suspected with severity, allergies
 - 100% NO for voice biometric, fingerprint, next of kin, consent for organ donation, advance directives, prior criminal convictions
 - 50% YES for beneficiary status, total plan size, BP, skin exam, MSK exam, drug exposure during pregnancy, time lost from employment, child care or caregiver costs
 - 138 items with $\geq 66\%$ endorsement
- B. Information Availability
 - EMR has more data fields but LADs has better data completeness
 - Difficult exercise to complete as data dispersed, difficult confidentiality issues, EMR database very complex
 - No single data source is adequate
- C. Methodologic Issues
 - Observational data therefore prone to fatal biases
 - Linear regression (LR), propensity score matching (PSM), instrumental variables (IV) did not completely adjust for channeling bias
 - Regression, PSM need identifiable and measureable confounders; IV supposed to account for unknown confounders
 - Adjusted for age, concomitant meds, socioeconomic, heart disease
 - IV used physician characteristics
 - Data-mining methods still experimental
- D. Health Information Privacy
 - University-based research of anonymized data permitted
 - Assumes adequate security, confidentiality, disclosure governance rules in place
 - Benefits of linkage have to be clearly in the public interest and not harmful to individuals involved
 - Does government sector use of *anonymized* data for pharmacosurveillance require legislation?
 - What is truly anonymized?
 - Can various anonymized databases be linked without consent?

VI. Main Conclusions

- Data requirements for pharmacosurveillance are intense.
- Electronic medical records with e-prescribing linkages hold the most promise as data resource for pharmacosurveillance.
- Currently, linkages across EMRs and LADs would be required for pharmacosurveillance
- Methodologic limitations of databases can lead to wrong conclusions and policies and adjustment methods at the moment are inadequate.
- Health information privacy legislation and guidelines continue to confuse researchers and policy makers.
- Use of databases for secondary research and policy purposes creates technical and information privacy challenges.

VII. Policy Recommendations

- A form of routine pharmacosurveillance is needed for federal post-marketing surveillance and provincial cost-effectiveness assurance.
- Further work on data resource availability, characterization, linkage across provincial jurisdictions, data standards, bias reduction methods and conforming with health information privacy legislation without missing data, is required
- access to unpublished trials and the use of large, simple randomized trials to explore policy options

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