



Can Current Electronic Systems Meet Drug Safety and Effectiveness Requirements?

Addressing Canada's National Pharmaceutical Strategy

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Co-Hosts:

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What is the Problem?

- National Pharmaceutical Strategy (2004 First Ministers Meeting)
 - “Strengthen evaluation of real world drug safety and effectiveness “
 - “Enhance analysis of cost drivers and cost effectiveness”
- What is Pharmacosurveillance?
 - Systematic monitoring of benefits and harms of medication(s) in routine clinical care
 - Desirable but difficult
 - Difficult to know what data to target for a) routine vs b) special situation monitoring
 - No organization of data collection or analysis for routine PS purposes
 - Harm is not fully interpretable without benefit
 - Context is key
 - Cost-effectiveness is the main issue in many jurisdictions
 - Multiple health database silos exist
 - Is it possible to reach valid conclusions suitable for policy use?



Study 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?
- Are there valid methods to adjust for channeling bias?
- What impact will evolving privacy legislation have on pharmacosurveillance activities now and in near-future?



Consensus Methods

- Modified Nominal Group Technique
- 12 representatives of stakeholder groups in drug decision making
 - Primary care, pharmacy, clinical pharmacology, consumers, epidemiology, database management, methodology, formulary management, regulators, pharma industry, health economics, patient safety
- Represented all regions of country
- 3 - stage process



Consensus Methods

- Premise
 - 4 case scenarios, 2 regulatory situations
 - Rating information need for a) routine and b) special situation
 - Time frame to cover next 20 yr
 - Stage 1
 - Individually read sample scenarios, rated 193 items via e-mail
 - 7 categories
 - Demographics (19), socioeconomics (15), outcomes (39), medical history (35), family history (9), drug use (50), cost variables (26)
 - Rated for necessity of availability (yes/no)
 - Additional items added prn
 - Group ratings tabulated and returned to participants
 - Stage 2
 - Teleconference to discuss disagreement
 - Must discuss those with 20-80% agreement
 - 4 hour facilitated discussion
 - Stage 3
 - Re-rate entire list plus additions (N = 224 items)
 - Final list = items rated yes by > 70%



Consensus Results – Routine Surveillance

- 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

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Consensus Results ⁽²⁾

- 138 items \geq 66% endorsement
 - 0 in family history
 - 64 items on drug use
- Limitations noted
 - Privacy concerns; technical accessibility, proprietary exclusions; costs of collection, storage & analysis; proof that these data exist; proof that this improves regulatory decisions

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II. Data Availability

- Comparing Large Administrative Databases (LADs), patient registry (PR), Electronic Medical Record (EMR)
 - Ontario linked data as held by ICES
 - CANOAR database (OA registry targeting COX-2 NSAIDS)
 - COMPETE 1 EMR data (primary care)
- Using consensus ratings for data
 - Are the desired data fields there?
 - Are there any data in those fields?
 - Could not assess accuracy of data

Data Availability (Items Requested by 100% Panel)

Data Items	LADs		Pt Registry		EMR	
	Field?	Data in Field?	Field?	Data in Field?	Field?	Data in Field?
Gender	Y	100%	Y	95%	Y	100%
Birthdate/year	Y	100%	Y	99%	Y	100%
Weight	Only babies	N	N	N	Y	100%
Current Diagnoses	Some	Billing and hosp'ns	6 diagnoses only	99%	Y	100%
Hospitalization dates	Y	100%	N	N	Y	43%
Discharge diagnosis	Y	100%	N	N	Y	9%
Drug name dispensed	If ODB	100%	N	Focused on 3 drug groups	N	N
Drug route dispensed	If ODB	100%	N	"	N	N
Prescribed duration	N	N	N	N	Y	100%*
Reason prescribed	Few	LU codes	4 drug groups only	98%	Y	N/A
Concurrent therapies	If Rx billed to ODB	If on ODB	5 drug groups only	97%	Y	100%
ADR Suspected	N	N	N	N	Y	N/A
Medication allergies	N	N	N	N	Y	N/A
Nature of allergy	N	N	N	N	Y	100%



Data Availability

- Key Messages
 - Difficult exercise
 - Data dispersed, confidentiality issues, EMR extraction very complicated
 - Did not address data validity/accuracy
 - No single data source is adequate
 - EMR with e-pharmacy linkage has most potential
 - What to do about missing data?
 - What about linkage across these databases?



III. Channeling Bias Exploration

- Pharmacosurveillance deals with observational data
 - Fraught with unavoidable biases
 - Potentially totally misleading, potentially fatal conclusions
 - Methods developed to adjust for channeling bias
 - Can we compare and contrast the value of these methods?



Channeling Bias Exploration

- Methods compared
 - Linear regression
 - Propensity score matching (PSM)
 - Instrumental variables (IV)
- Topic of exploration
 - Proposed COX-2 NSAID analysis in grant but data unavailable
 - HRT perfect topic since recent RCTs form “gold standard”



Channeling Bias Exploration

- Neither regression, PSM or IV able to reproduce the RCT results
 - Regression, PSM need identifiable and measurable confounders
 - Adjusted for age, concomitant meds, socioeconomic, heart disease
 - IV supposed to account for unknown confounders
 - Used physician characteristics



Conclusions

- Data requirements for pharmacosurveillance are intensive
 - Would require database linkages
- Methodologic issues in interpretation of pharmacosurveillance data are major
 - Useful for detecting potential issues for follow-up
 - Still need RCTs to show harm or benefit
- Privacy legislation and guidelines are still in evolution