



Ethical Dilemmas in Research Evaluations of New Health Information Technologies

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Overview

- . AHRQ CERT Program
- . UIC TOP-MED CERT
- . Rationale for Linking Lab and Pharmacy
- . UIC's Lab-Pharmacy Linkage Projects
- . Ethical Dilemmas in Evaluating Health Information Technologies

CERT

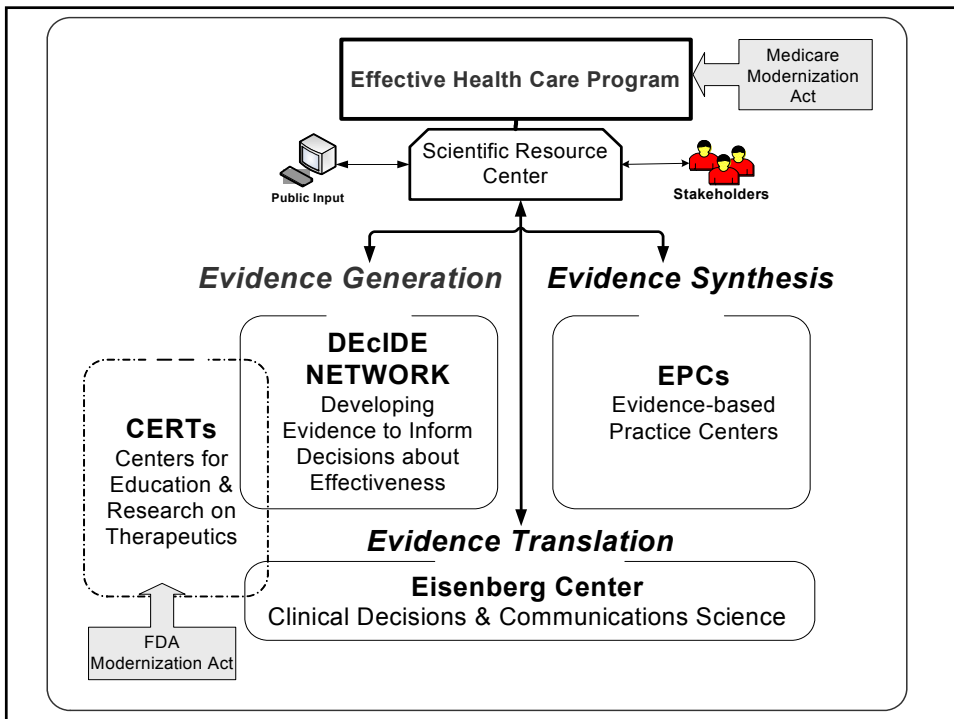
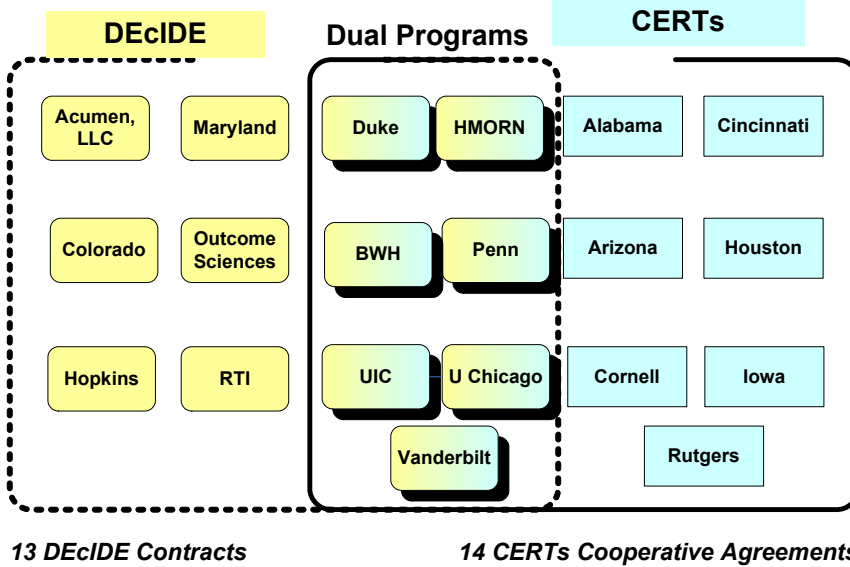
Center for Education and Research in Therapeutics

- Purpose: To conduct research and provide education that will advance the optimal use of drugs, medical devices, and biological products.
- Comprised of 14 academic centers, each with a different “theme.”
- Grant, renewed annually (2007-2011).
- Jointly administered by AHRQ and FDA.

Focus of AHRQ

- Assess the *effectiveness, comparative effectiveness, and cost-effectiveness* of health care services.
- Identify ways to improve *patient safety* and *quality* of health care systems.
- Advance the appropriate use of *health information technology*.
- Understand *system issues*: role of organizational design, management, workflow, management, and incentives on efficiency and effectiveness.
- Develop *data* on the health care system for monitoring and decision-making.

AHRQ Pharmaceutical Outcomes Programs



UIC TOP-MED CERT

- Tools for Optimizing Prescribing, Monitoring and Education (TOP-MED)
- Purpose: improve prescribing, monitoring and education
- Multiple Institutions: UIC, Stroger (Cook County) Hospital, Northwestern University (and hospital), VA PBM (Hines, IL), Advocate Health Care, U. of Washington, Cerner, Broadlane Inc.

Overarching Perspective

Improved pharmacotherapy likely to derive more from improvements in systems of medication use than from developing and marketing of new chemicals

UIC CERT Main Projects

- Reinvigorate formulary committees
- Enhance drug utilization review (and connect to formulary)
- Linking lab and pharmacy ←
- Create N-of-1 clinical trial service to customize care scientifically
- Empower formulary committee with better pharmacoeconomic support

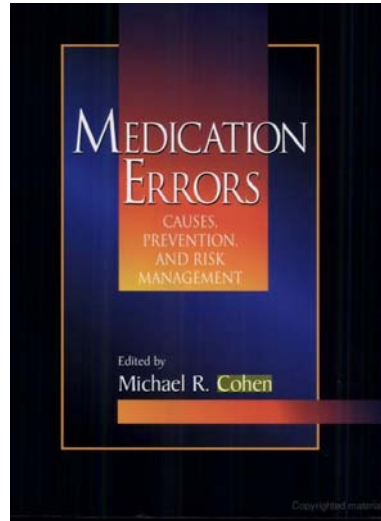
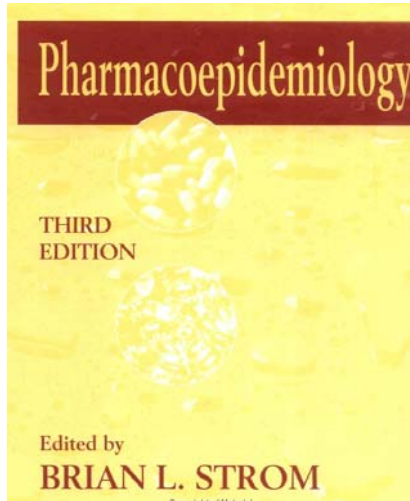
Lab-Pharmacy Disconnect

- Intimately related yet rarely communicate
- Shocking divorce: putting chemicals into body and monitoring and parameters related to these administered chemicals.

Disconnected:

- Departments/Locations
- Personnel: well demarcated boundaries
- Cultures, Journals/Literature
- Information Systems

Lab-Link Missing in Action



Core Function	Ways Lab-Pharmacy Linkages Can Help
Drug Selection	1. Lab Contraindicates Drug
	2. Lab Suggests Indication for Drug
Dosing	3. Lab Affecting drug Dose
	4. Drug Requiring Lab for Titration
Monitoring	5. Abnormal Lab Signaling Toxicity
	6. Drug Warranting Lab Monitoring for Toxicity
Lab Interpretation	7. Drug Influencing or Interfering w/ Lab
	8. Drug Impacting on Response to Lab
Improvement	9. Drug Toxicity/Effects Surveillance
	10. Quality Oversight

Linking Lab and Pharmacy

- Identify 25 lab-pharmacy pairs
- Program daily/monthly reports into Cerner
- Develop staffing plans to act on reports
- Analyze yield, trends, etc.
- Start at UIC and Stroger then disseminate to other partners and community hospitals
- Explore expansion to outpatient settings

Selecting Inpatient Lab-Drug Pairs

- Modified Delphi Process
- Started with >600 lab-drug pairs from literature
- Had panel of 12-13 national experts narrow the list first to 89 pairs then to 39 then to 25

Top 5 Inpatient Lab-Drug Pairs

Med	Trigger	Link Class	Link Name
heparin	↓Platelet	monitoring	checking for, or signaling Toxicity
potassium	↑K+	Drug Selection	Contraindication
ACE	↑K+	monitoring	checking for, or signaling Toxicity
heparin	+HIT	monitoring	checking for, or signaling Toxicity
potassium	↑K+	monitoring	checking for, or signaling Toxicity

Outpatient Lab-Pharmacy Linkage

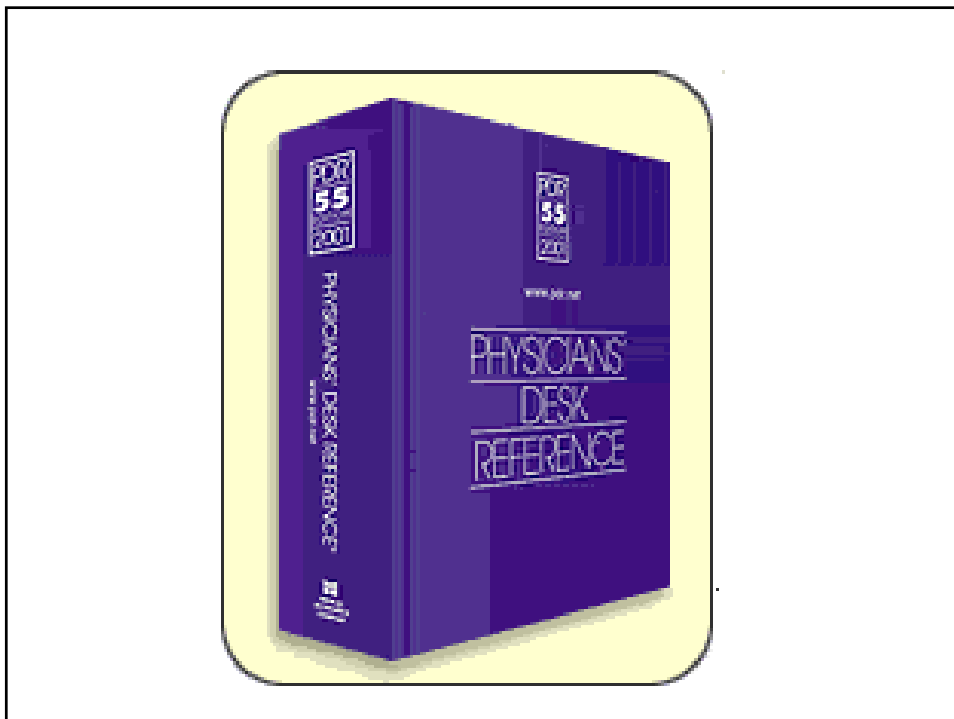
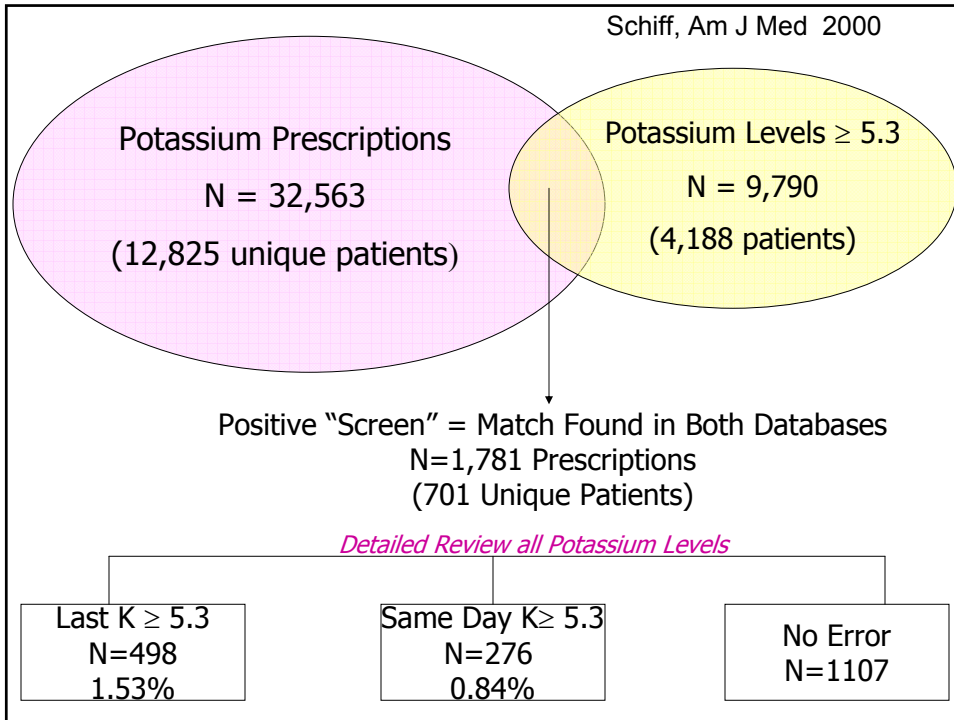
- An even bigger problem than inpatient
 - Many more outpatients than inpatients
 - Outpatients are not under observation
- No one in our Center had large database of outpatient lab-pharmacy information
- Partnered with Humana
- 10 lab-drug pairs

Outpatient Lab-Drug Pairs

LAB-DRUG PAIR	Type of relationship	Example Initial Cutoff Criteria
TSH-levothyroxine	Lab→Med	No Rx with TSH > 5-10 mIU/L
Cr-metformin	Lab→Med	Rx with Creatinine (Cr) >1.5 mg/dl, eGFR<60 ml/min
Cr-digoxin	Lab→Med Med→Lab	Rx with Dose >0.125mg/day, Cr>1.5mg/dl, eGFR<60 ml/min No check of Cr for >5 months
K ⁺ -oral KCl	Lab→Med Med→Lab	Rx with K ⁺ >5.3 mmol/L No check of K ⁺ for >5 months
K ⁺ -spironalactone	Lab→Med Med→Lab	Rx with K ⁺ >5.3 mmol/L No check of K ⁺ for >5 months
K ⁺ -ACE-inhibitor	Lab→Med Med→Lab	Rx with K ⁺ >5.3 mmol/L No check of K ⁺ for >5 months
ALT/AST- HMG-CoA reductase	Lab→Med Med→Lab	Rx with (AST or ALT) >2X normal No check of (AST or ALT) for >5 months
ALT/AST-methotrexate	Lab→Med Med→Lab	Rx with (AST or ALT) >2X normal No check of (AST or ALT) for >5 months
TSH-amiodarone monitoring	Med→Lab	No check of TSH, T4 or free-T4 for >6 months

ERROR (N=40)	#	%
Delay (>10 hrs) toxic level draw to MD action	20	50%
Excessively high (>1.5) doses CHF , liver dis	17	43%
Miss obvious GI,CNS,cardiac sx/signs toxicity	16	40%
Recurrent toxicity: unaware; failure adjust dose	11	28%
Dosing errors for non CHF pts	9	23%
ED rx despite pretreatment level already toxic	6	15%
Inadvertent overlap of i.v. and p.o. rx	6	15%
Interacting drugs (w/ failure to adjust dose)	5	13%
Discharged on same dose came in toxic	5	13%
Discharged w/ no noted MD awareness of toxicity	4	10%

Theophylline Toxicity, Schiff, Ann Internal Med 1991



	Lab-Drug Category	Top 40 Drugs		New Drugs (N=37)	
		Total	# Drugs	Total	# Drugs
		Warnings	w/Warning	Warnings	w/Warning
Contraindication for Drug	Contraindication for Drug	11	9	20	14
	Indication for Drug	7	7	3	3
Dose Adjustment	Dose Adjustment	40	31	28	23
	Indicating Toxicity	169	39	161	32
Baseline Monitoring	Baseline Monitoring	16	11	12	8
	Follow-up Monitoring	20	11	16	10
Interfered w/ by Drug	Interfered w/ by Drug	5	3	2	2
TOTAL		268	40	242	37

Drug-Lab Interactions in PDR FDA Legally Mandated Labeling

40 most commonly prescribed drugs 268
critical test & drug pairs

37 newest drugs on market
242 critical test & drug pairs

Average 6.6 drug-lab warning / drug

Ethical Dilemmas

- In the evaluation of new health information technologies, when is it appropriate to do a randomized trial (i.e., when is it ethical to withhold an intervention from patients)?
- How certain must we be in a technology's effectiveness before we feel it is unethical to withhold the treatment?

Examples

- If you have a computer system that calculates the proper medication dose based on weight and renal function, is it ethical to withhold this dosing information from half the patients in an RCT?
- Would you want a relative to be in the “usual care” arm of this trial?

Apparently, it is ethical.

ORIGINAL CONTRIBUTION

Guided Medication Dosing for Inpatients With Renal Insufficiency

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Context Usual drug-prescribing practices may not consider the effects of renal insufficiency on the disposition of certain drugs. Decision aids may help optimize prescribing behavior and reduce medical error.

Objective To determine if a system application for adjusting drug dose and frequency in patients with renal insufficiency, when merged with a computerized order entry system, improves drug prescribing and patient outcomes.

Design, Setting, and Patients Four consecutive 2-month intervals consisting of control (usual computerized order entry) alternating with intervention (computerized order entry plus decision support system), conducted in September 1997–April 1998 with outcomes assessed among a consecutive sample of 17 828 adults admitted to an urban tertiary care teaching hospital.

Clinical decision support to reduce the rate of VTE

In 2005, Kucher et al. demonstrate that chemoprophylaxis reduces the rate of VTEs.

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Electronic Alerts to Prevent Venous Thromboembolism among Hospitalized Patients

Nils Kucher, M.D., Sophia Koo, M.D., Rene Quiroz, M.D., M.P.H., Joshua M. Cooper, M.D., Marilyn D. Paterno, B.S., Boris Soukonnikov, M.S., and Samuel Z. Goldhaber, M.D.

Example: Clinical decision support to reduce the rate of VTE

- After the publication of Kucher, Galanter and colleagues decide to replicate the intervention, with modifications, at UIC.
- The UIC intervention is successful
- Manuscript is submitted for publication at American Journal of Medicine and rejected
- Primary reason for rejection was that it was not a randomized trial.

Ethical Reasoning Behind UIC's Decision Not to do an RCT

- Kucher et al. had proven that the intervention was successful
- We thought it would be unethical to deprive some patients of an intervention that was proven to reduce the rate of a serious adverse event
- Therefore, we did an observational study
- What would the IRB at your hospital have said?

Effect of CPOE on Medication Errors

Bates et al. show that CPOE prevents errors.

Original Contributions

Effect of Computerized Physician Order Entry and a Team Intervention on Prevention of Serious Medication Errors

David W. Bates, MD, Lucian L. Leape, MD, David J. Cullen, MD, Nan Laird, MD, Laura A. Petersen, MD, Jonathan M. Teich, MD, PhD, Elizabeth Burdick, MS, Mairead Hickey, MD, Sharon Kleeffeld, MD, Brian Shea, MD, Martha Vander Vliet, RN, Diane L. Seger, RPh

Context.—Adverse drug events (ADEs) are a significant and costly cause of injury during hospitalization.

Objectives.—To evaluate the efficacy of 2 interventions for preventing nonintercepted serious medication errors, defined as those that either resulted in or had potential to result in an ADE and were not intercepted before reaching the patient.

Design.—Before-after comparison between phase 1 (baseline) and phase 2 (after intervention was implemented) and, within phase 2, a randomized comparison between physician computer order entry (POE) and the combination of POE plus a team intervention.

Setting.—Large tertiary care hospital.

Participants.—For the comparison of phase 1 and 2, all patients admitted to a stratified random sample of 6 medical and surgical units in a tertiary care hospital over a 6-month period, and for the randomized comparison during phase 2, all patients admitted to the same units and 2 randomly selected additional units over a subsequent 9-month period.

patients and represented the single most common cause of injury. In addition to their human costs, ADEs are costly to health care systems. Nationally, ADEs occurring after hospitalization have been projected to cost hospitals \$2 billion per year, not including malpractice costs or the costs of injuries to patients.³³ Hospitalizations initiated by ADEs appear to be at least as expensive.

See also pp 1317, 1339, and 1360.

These data suggest that health care organizations should be working hard to

Effect of CPOE on Medication Errors

Koppel et al. show CPOE *causes* lots of errors.

Role of Computerized Physician Order Entry Systems in Facilitating Medication Errors

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Context Hospital computerized physician order entry (CPOE) systems are widely regarded as the technical solution to medication ordering errors, the largest identified source of preventable hospital medical error. Published studies report that CPOE reduces medication errors up to 81%. Few researchers, however, have focused on the existence or types of medication errors facilitated by CPOE.

Objective To identify and quantify the role of CPOE in facilitating prescription error risks.

Design, Setting, and Participants We performed a qualitative and quantitative study of house staff interaction with a CPOE system at a tertiary-care teaching hos-

Key Issues/More Dilemmas

- Be alert to the inevitable unexpected (negative) consequences of HIT
- Systems that are “proven” to work in one place may not work elsewhere under different implementation circumstances
- Fully informed consent is key, but many of these studies, done hospital wide, receive waivers of consent.

Key Issues/More Dilemmas

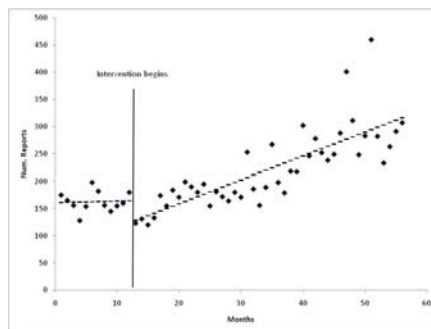
- Academic researchers have an incentive to do RCTs, regardless of the ethics
 - RCTs more likely to get funded
 - RCTs get published in better journals
- Quality improvement studies (in some ways more realistic) tend not to do RCTs
 - They lack the funds
 - They are uncertain about the ethics of withholding treatment

If We Choose an RCT, How Do We Optimize Safety?

- RCT's provide the most valid test of an intervention's efficacy, but how do we do them ethically?
- Do the smallest trial possible
- Have rigorous, external safety review with low threshold for stopping if previous benefit is confirmed (or if new harm is observed)
- What else?

What Are the Alternatives to RCTs?

- The interrupted time series is generally regarded as the most valid quasi-experimental design.



Summary/Implications

- Electronically linking pharmacy and lab data reveals temporal relationships and patterns that can be exploited to improve safety
- Evaluating health IT interventions presents difficult ethical dilemmas
 - At what threshold of certainty of benefit does it become unethical to use a “usual care” control group?
 - What are the ethical issues involved in waiving consent for whole-hospital studies of HIT?
- Choosing the most ethical option may have career consequences for academic researchers, creating an uncomfortable conflict of interest