Improving Cardiovascular Drug Therapy: The Duke Center for Education and Research on Therapeutics

UNC PHO Seminar
January 24, 2003
Judith M. Kramer, MD, MS

...a program of the Agency for Healthcare Research and Quality (AHRQ)

Centers for Education & Research on Therapeutics

AHRQ

Centers for Education and Research on Therapeutics (CERTs): a National Initiative

- History and Organization

Centers for Education & Research on Therapeutics

AHRQ

Environment

- Pharmaceutical industry – $82 billion
- Device industry – $60 billion
- Limitations of premarketing studies
  - Relatively small, limited populations
  - Surrogate endpoints
  - Very little study of combinations
  - Lack of long-term follow-up
- Many medical errors being committed
- Need for postmarketing surveillance system

CERTs Origins

- 1992: AHRQ begins to study outcomes of Rx drugs
- 1997: Food and Drug Administration Modernization Act of 1997 (FDAMA)
  - Authorizes AHRQ to create CERTs demonstration program in conjunction with FDA
- 1998: AHRQ solicits research topics

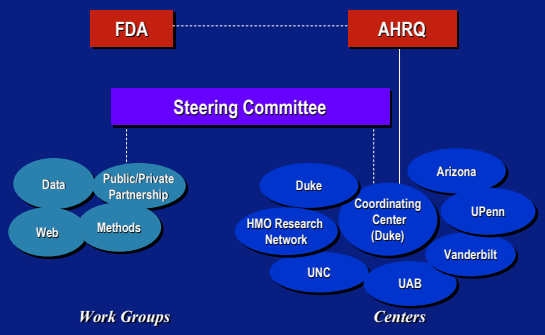
CERTs Origins (continued)

- Sept. 1999: Demonstration program begins — 4 research centers and coordinating center
- Dec. 1999: Congress authorizes permanent program
- July 2000: Center #5 added
- Sept. 2000: Centers #6 and #7 added

CERTs Centers

- Duke University
- HMO Research Network
- University of Alabama at Birmingham
- University of Arizona Health Sciences Center
- University of North Carolina at Chapel Hill
- University of Pennsylvania
- Vanderbilt University

CERTs Structure



CERTs Overview

- Demonstration project
  - Testing designs
  - Transfer to other centers
- Cooperative agreements
  - Allows for government involvement
  - Sharing resources
  - Initially 3 years; now 5 years
- Public-private partnerships
- $17 million AHRQ funding 1st 3 yrs

CERTs Vision and Mission

- **Vision:** To be a trusted national resource for people seeking to improve health through the best use of medical therapies.
- **Mission:** To conduct research and provide education that will advance the optimal use of drugs, medical devices, and biological products.

Carrying Out the CERTs Mission

- We achieve our mission through activities that:
  - *Develop knowledge* about the best use of therapies
  - *Manage risk and benefit* by improving the ability to measure risks and benefits of therapies as used in practice

Carrying Out the CERTs Mission (cont'd.)

- We achieve our mission through activities that:
  - *Improve practice* by advancing strategies to ensure that therapies are used always and only when they should be
  - *Inform policy-makers* about the clinical science and effects of current or proposed policies

The CERTs Mission at Duke

- To conduct research and provide education that will advance the optimal use of *cardiovascular* drugs, medical devices, and biological products.

Prime Targets in Cardiovascular Disease

- Coronary Heart Disease (CHD or CAD)
  - 12.6million Americans have CHD (61.8 m total CVD)
  - 55% of the deaths from total CVD is from CHD
  - CHD is the single largest killer of American men & women (Every 29 sec an American has a coronary event
- Heart Failure/Left Ventricular Dysfunction (HF/LVD)
  - 4.8 million Americans have HF
  - 550,000 new cases of HF yearly
  - 80% of men and 70% of women <65yo with HF will die within 8 years.
- From the American Heart Association's Statistical Update accessed 9/28/02: www.americanheart.org/downloadable/heart/

Discovery of Life-Saving Therapies in CV Diseases: the last 15 years

Drug	Indication	Studies
Aspirin	AMI	ISIS-2
Thrombolytic therapy	AMI	GISSI; ISIS-2; GUSTO-1;
ACE Inhibitors	CHF	SOLVD; VHEFT II CONSENSUS
Beta-blockers	CHF	Carvedilol trials; MERIT-HF; CIBISII; Copernicus
"Statins"	CAD	4S; LIPID; CARE

Magnitude of Survival Benefit

- Aspirin ↓ events in patients with CAD by up to 25%
- Beta-blockers in HF/LVD: Relative risk reduction: 10-65%
  - 17-78 lives saved per thousand patients treated
  - NYHA Class IV HF: 35% reduction with carvedilol

Critical Problem

How can physicians and patients keep pace with accumulating developments and new standards of care?

Kong 04/99

Gaps between research and practice:

- Errors of Omission

  Failure to prescribe drugs known to improve survival (e.g. beta-blockers in patients with CHF)
- Errors of Commission (High risk therapies)

  Failure to heed labeled contraindications, warnings, or drug interactions (e.g. Cisapride; dofetilide)

Duke CERT Projects: First 3 Years

Research Area	# Projects
Evidence-based therapies: CAD & HF	8
Economic implications of EBM	1
Cardiac devices: post-market surveillance	2
Dofetilide risk management program	3
QT interval and QT-prolonging drugs	3
Antiarrhythmic prescribing and dosing	2
Educational materials: module & guide	2

Potential Impact of Increased use of Evidence Based Therapies

- **Gusto IIB Substudy**: 7743 patients with non-ST-elevation acute coronary syndromes
  - use of aspirin, beta blockers, angiotensin-converting enzyme (ACE) inhibitors, and calcium-channel blockers determined at discharge
  - If medication use had been more evidence-based, one-year mortality would have been reduced by a relative 22% (18 lives saved per 1000 patients treated)

Alexander KP, Peterson ED, Mahaffey KW, et al. J Am Coll Cardiol, 1998;32:2023-30

Potential Impact (continued)

- Bahit et al:
  - analyzed medication use from clinical trials databases; registries of AMI/ACS (Worcester Heart Attack Study, Grace Registry); claims databases (CCP); and clinical databases (Duke Databank for CV Disease)
  - applied estimated risk reductions from systematic overviews & large clinical trials

Bahit MC, Granger CB, Alexander, et al. Circulation 2000; 102:II-873

Potential Impact (continued)

Conclusion of Bahit et al:

- increasing the use of aspirin, beta-blockers, statins, and ACE inhibitors to 80%–90% of ideal could save 80,000 additional lives annually

A key research platform for the Duke CERTs:

- **The Duke Databank for Cardiovascular Disease (DDCD)**
  - **A clinical database**
  - **In existence since 1969**
  - **Includes all patients undergoing a cardiac procedure at Duke**
  - **Patients with documented CAD followed annually; >26,000 alive & followed**
  - **Since 1995, patient-reported medications have been collected.**

Using the DDCD to perform retrospective, longitudinal analyses of medication use

- **Population of patients with CAD**
  - **27,088 patients with documented CAD**
  - **Follow-up available between 1995 & 2000**
- **Population of patients with HF/LVD**
  - **7,329 patients with HF/LVD (clinical diagnosis or left ventricular ejection fraction less than 40%**
  - **Follow-up available between 1995 & 2000**

DDCD AS THE PLATFORM

- **Performance indicator:**
  Use of recommended, life-saving medications
  - *Annual point prevalence*
  - *Longitudinal use (established "patterns" of use)*
- **Factors associated with use or non-use**
- **Outcomes**
  - Survival

Duke CERTs: Studies of Evidence-Based Medications

- Coronary artery disease:
  - Aspirin*
  - Beta-blockers
  - Lipid lowering therapy
- Heart failure/LVD
  - Beta-blockers*
  - ACE Inhibitors

*Studied more extensively

CAD Patients: Point Prevalence of Medication Use

CAD Patients: Patterns of Use

Combined Therapy for CAD-Year 2000*

Most Significant Predictors for ASA Use

Variable	OR (95% CI)
DDCD entry >1995 vs. <1980	7.07 (5.40–9.25)
New bypass surgery	3.23 (2.41 –4.31)
New MI	1.91 (1.40– 2.62)
Prior cardiac cath	1.76 (1.54 –2.00)
New stroke	1.76 (1.33 –2.32)
Prior bypass surgery	1.55 (1.37 –1.74)
Male sex	1.51 (1.35 –1.70)

Califf RM *Am J Cardiol* 2002

Significant Predictors for Not using ASA

Variable	OR (95% CI)
Age at entry*	0.85 (0.81 –0.90)
Hypertension	0.85 (0.76 –0.94)
Cerebrovascular disease	0.82 (0.70 –0.97)
Prior smoking	0.81 (0.72 –0.91)
Congestive heart failure	0.76 (0.66 –0.86)
Diabetes	0.73 (0.65 –0.83)
Other antiplatelet use	0.54 (0.46 –0.64)

Califf RM *Am J Cardiol* 2002

*Per 10 year increase in age

Survival Benefit from Aspirin in DDCD Patients with CAD:

- Estimate consistent with the literature:
  Relative risk of death: 0.5

Conclusions regarding Aspirin Use in Patients with CAD

- Patients at greater risk for cardiac events (diabetics, elderly, hypertensives, smokers, and patients with cerebrovascular disease) are less likely to be taking the drug

HF/LVD Patients: Point Prevalence of Medication Use

HF/LVD Patients: Patterns of Medication Use over Time

Therapy for HF/LVD: Year 2000

Specific beta-blockers used: 1999

Significant Predictors for Beta-blocker Use

Significant Predictors for Not using Beta-blockers

Survival Benefit from Beta-blockers in DDCD Patients with HF/LVD:

Conclusions regarding Use of Beta-blockers for HF/LVD

Duke CERTs Demonstration Project: Beta-blockers for HF/LVD

Rationale:

- Use of beta-blockers in patients with HF/LVD was low
- This treatment was particularly appropriate for an educational intervention
  - Data on efficacy and safety in heart failure only became available in the mid 1990's
  - Most practicing physicians were trained that beta-blockers were contraindicated in patients with HF/LVD

Rationale (continued)

- Soumerai and others in the literature have found that "academic detailing" is an effective intervention
- We proposed that Internet-based education might allow a broader geographical reach for "academic detailing" and be a more generalizable intervention

Rationale (continued)

- The literature suggested that multifaceted interventions may be more effective than single interventions
- We decided that both intervention and control groups should receive traditional written educational materials so that the study was ethically appropriate

Demonstration Project: Beta Blockers

Duke CERTs: Phase II

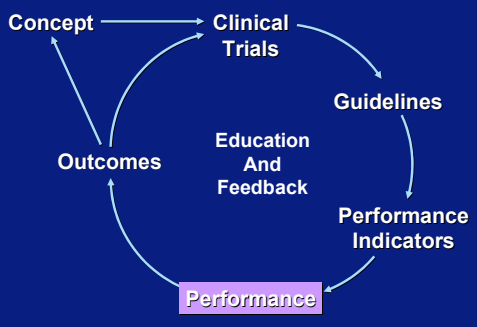
- 5-year renewal began October 1, 2002
- Future projects build on our findings from the studies in the Duke Databank of evidence-based medication use, and our demonstration project to increase appropriate use of beta-blockers in patients with HF/LVD.

Duke CERTs: Phase II

Specific Aims:

- Dissect the cycle by which data from clinical research are translated into clinical practice guidelines and performance indicators for CV disease

The Cycle of Clinical Therapeutics



Duke CERTs: Phase II

Specific aims (cont'd)

- Improve adherence to CV clinical practice guidelines
  - Implement a Systematic Approach to Secondary Prevention of Coronary Artery Disease (CAD) and Heart Failure (HF)

Duke CERTs: Phase II

- Improve adherence to CV clinical practice guidelines (cont'd)
  - Evaluate the Effect of Involving Clinical and Community Pharmacists in a Team Effort to Ensure Patients' Compliance with Evidence-based Therapies for HF and Secondary Prevention of CAD

Duke CERTs: Phase II

Specific aims (cont'd)

- Develop cost-effectiveness models to assess the policy impact of fully adopting evidence-based therapies for CV disease

Duke CERTs: Phase II

Specific Aims (cont'd)

- Collaborate with the U.S. Food and Drug Administration in their efforts to manage the risks of drugs, biologics, and devices that affect CV health

Duke CERTs: Phase II

Specific Aims (cont'd)

- Continue to assess the value of drugs, devices and biologics intended to treat CV disease through randomized controlled trials, outcomes studies, and economic evaluations

Duke CERTs: Phase II

Specific Aims (cont'd)

- Continue to train new investigators both in academia and practice to contribute to the quality cycle.