
The messenger under attack: an occupational hazard for health researchers?

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Introduction

- Outbreak at the Univ of Washington
 - Lumbar spine fusion
 - Multiple chemical sensitivity
 - Antihypertensive agents
- Themes, recent trends and public policy implications

Case I: methods and results

- Literature review and guidelines development
- Cohort study of older adults undergoing low back surgery with or without lumbar spine fusion
- Spinal fusion associated with higher risks of complications (RR=1.9), blood transfusion (RR=5.8), nursing home placement (RR=2.2), and six-week mortality (RR=2.0)

Case I: response

- Lobbying organization called “Center for Patient Advocacy” founded by orthopedic surgeon on the NASS board
- Pedicle-screw manufacturer brought an injunction to prevent the AHCPR from disseminating low-back pain guidelines
- 1996 House bill with \$0 for AHCPR
- Intimidation led the AHCPR to end guideline development work

Case II: methods and results

- Case-control study of multiple chemical sensitivity
- Immunologic testing did not differentiate cases and controls
- Complaints of decreased memory and concentration were not confirmed by neuropsychiatric testing
- Based on symptoms reported prior to the onset of chemical sensitivity, 25% of cases and no controls satisfied criteria for somatization disorder

Case II: response

- Multiple scientific-misconduct complaints submitted to federal Office of Research Integrity by MCS advocacy group
- Requests to Medical Disciplinary Boards to revoke investigators' medical licenses
- Local trial lawyer sponsored workshop promoting use of ORI procedures to dispute unwelcome research findings

Case III: rationale and results

- Millions of hypertensives were taking medications evaluated only in small short-term trials of BP-lowering
- Post-marketing surveillance study of antihypertensive agents that had been inadequately evaluated in large trials
- Compared to other active agents, short-acting calcium channel blockers were associated with a 60% increase in the risk of heart attack

Case III: response

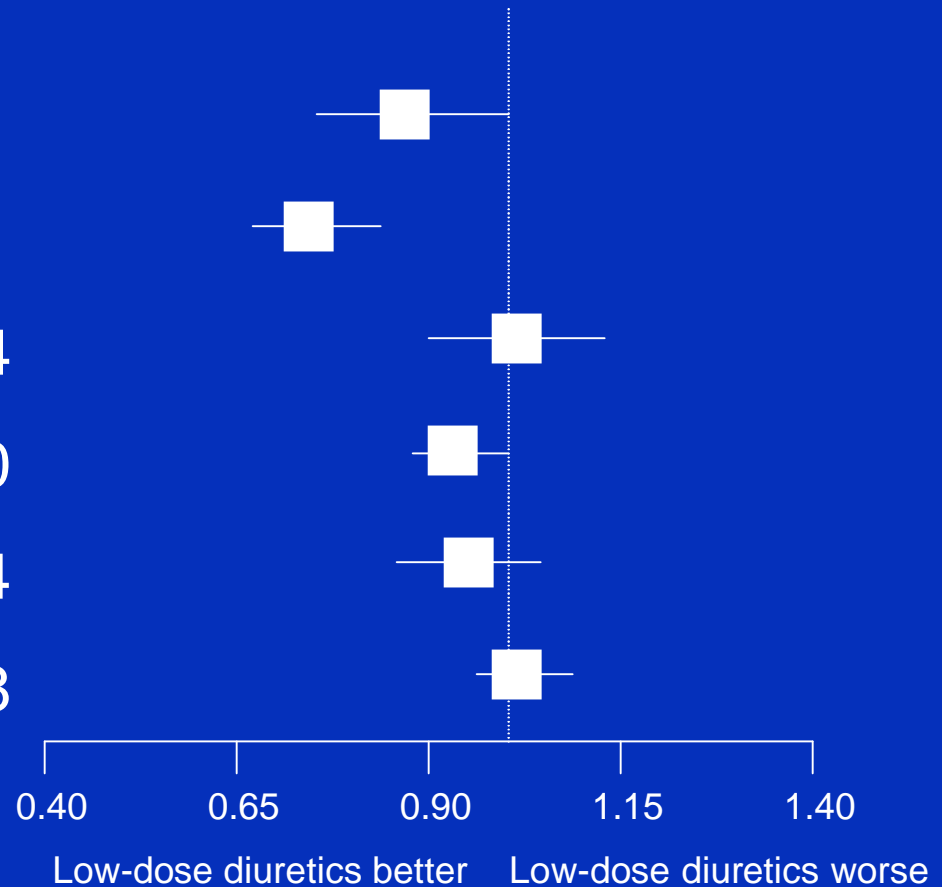
- Aggressive counter-marketing efforts
 - Overnight mailings and faxes
 - Letters and commentaries by experts
 - Funded lectures, symposia, and special supplements to journals
- FOI request for “all records relating to study design and methodology, study protocol(s), individual data for all study results and data, data sets, statistical calculations....”

Case III: consequences

- Personal
 - Sense of intimidation and vulnerability
 - Meetings with deans, chairs, lawyers
 - Public attention drawn to a minor study
 - Became subjects of studies ourselves
- Professional
 - Role of surrogate endpoints
 - Importance of large trials in guidelines
 - Advocate of low-dose diuretic therapy
 - Meta-analyses of large long-term trials

Diuretics vs calcium antagonists

Outcome	RR	95% CI
CHD	0.89	0.76-1.01
Heart failure	0.74	0.67-0.81
Stroke	1.02	0.91-1.14
CVD events	0.94	0.89-1.00
CVD mort	0.95	0.87-1.04
Total mort	1.03	0.98-1.08



Common themes

- Attacks by various groups, including physicians, on findings that ran counter to financial interests or beliefs
- Approach bypassed scientific debate
- Non-scientific efforts designed to discredit work, intimidate investigators, and deplete resources

Costs to society

- Harassment of scientists and funding agencies is a substantial disincentive to pursuing research questions
- Harassment permits interest groups to define the acceptable questions and shape the range of possible answers
- Eliminating public peer-review funding will slow research and force investigators to seek funding that may not be free of conflicts

Recent trends

- Industry's tendency to treat scientific matters as if they were marketing issues
- Studied inattention to safety issues
- Concealment or failure to publish all clinical trial results whether or not they may be favorable to the company's product

Concluding observations

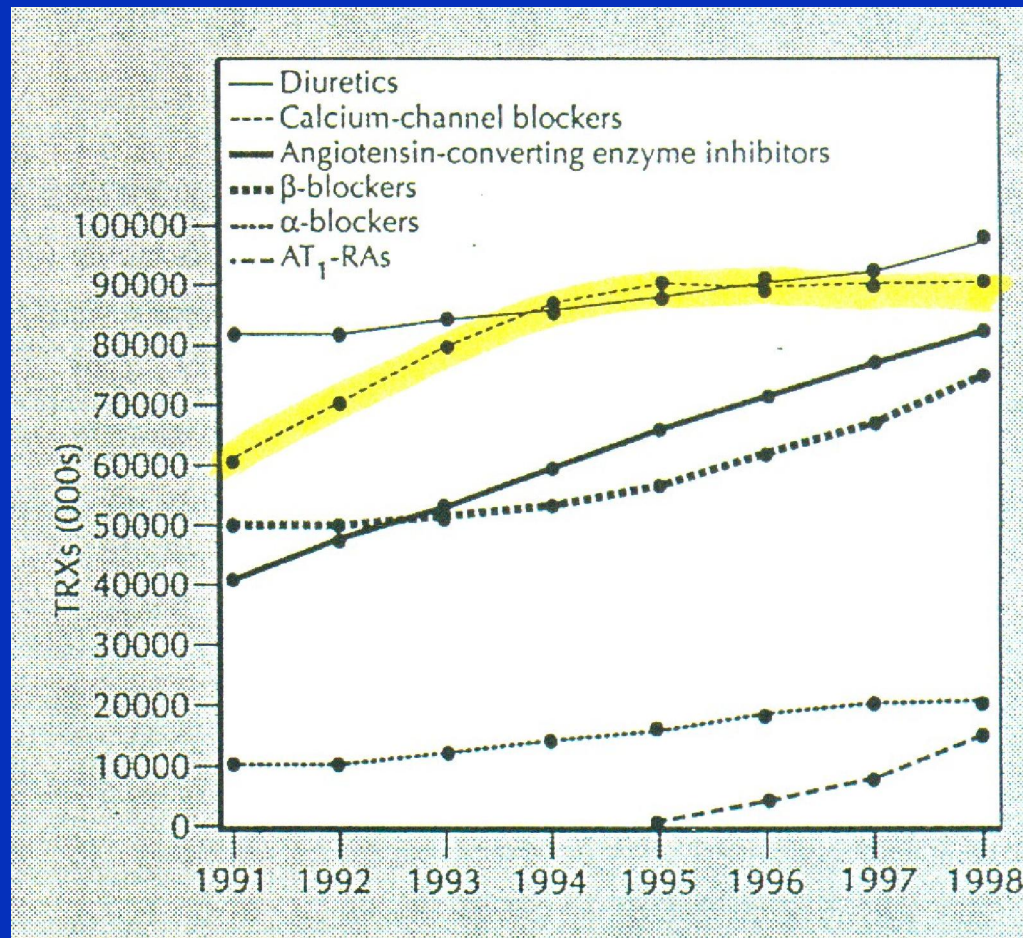
- Producing new knowledge in an unbiased and disinterested fashion is a primary role of research universities
- Research in the trillion dollar health care industry frequently has financial consequences
- Ask good questions anyway

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- Extra slides follow

Articles in Medline: 1990-2000

Type	CCB	ACEI
All articles	27314	14854
Primary focus	15249	9185
RCTs	3838	3024
Reviews	3008	3002

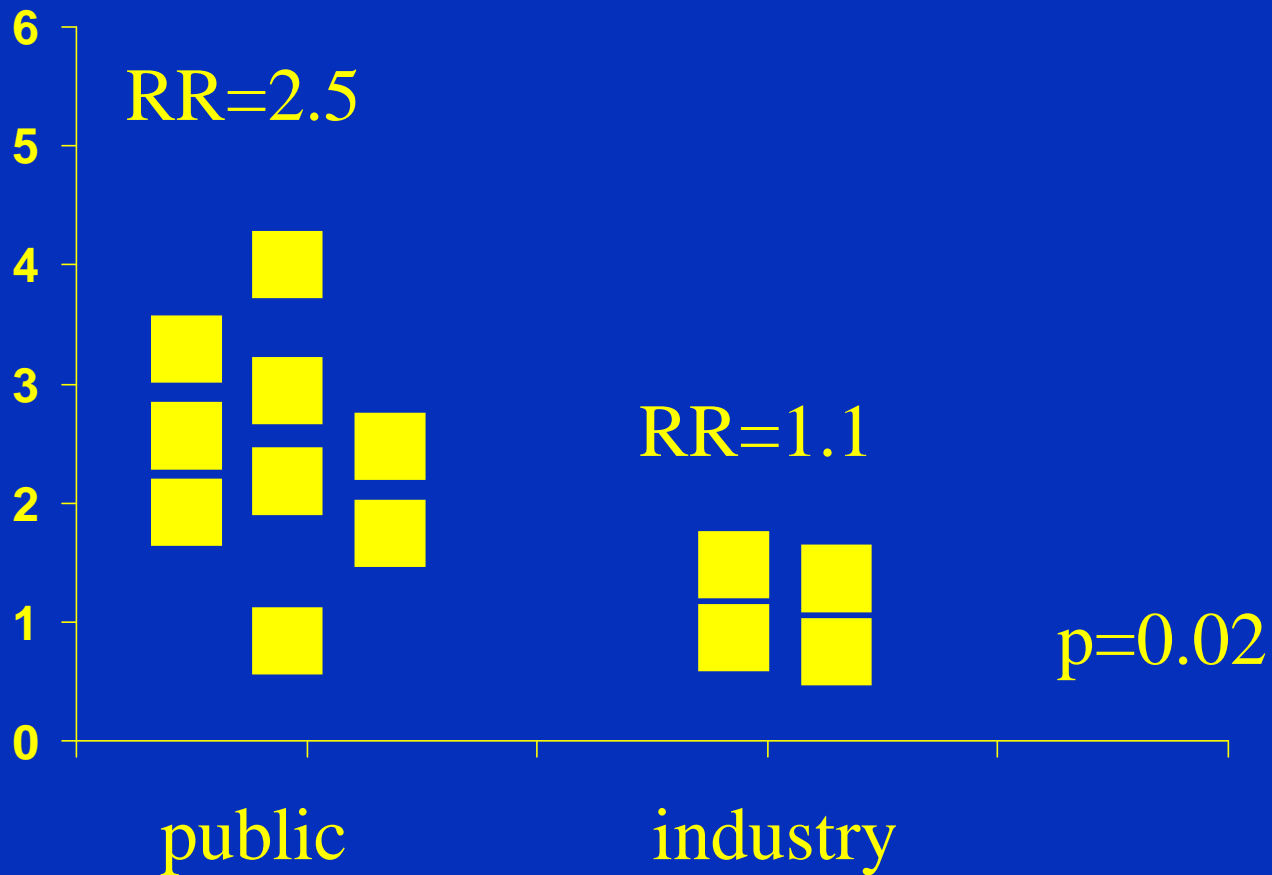
Retail prescriptions dispensed



Sica DA. Curr Hypertens Rep 1999; 1: 296-304.

CHRU

Studies and sponsors



Wyeth suppresses research

- Wyeth study that showed increased risk of DVT associated with several 3rd generation oral contraceptives remained unpublished
- Wyeth threatened legal action against Dutch radio Argos's effort to disseminate the findings

Science-as-marketing bias

- Production of scientific articles
 - Support for local investigators, who write articles, give lectures, and teach medical students
- Consumption of scientific articles
 - Over-value treatments because they appear so frequently in RCTs though they may have little scientific value

Case III: freedom of information request

One manufacturer “requested all records relating to study design and methodology, study protocol(s), individual data for all study results and data, data sets, statistical calculations, methodologies and analysis; correspondence, meeting minutes, notes and other documentation of Dr Psaty and any other University researchers...”

Scientific discourse

- Investigators were typically trained in the gentle art of scientific discourse
- Opponents generated a combative discourse operating under different rules and resembling the aggressive marketing hyperbole and relentless character attacks of political campaigns and high-profile courtroom battles

Industry's influence on data

- All papers with data on 3rd generation oral contraceptives and risk of venous thrombosis
- Plot results against funding source
 - industry
 - public funds

Concluding observations

Universities, journals, and professional organizations should not only assist investigators who evaluate the safety of efficacy of health interventions but also prevent special interests from determining the funding priorities, the research questions, and the permissible or acceptable findings.

Calcium-channel blockers

- Compared with diuretics in subjects free of clinical CVD
–OR = 1.62 (95% CI = 1.11-2.34)
- Compared with β -blockers in subjects with or without clinical CVD
–OR = 1.57 (95% CI = 1.21-2.04)

Analogy to SLAPP suits

- Strategic Litigation Against Public Participation--suits brought by financial interests against citizens
- Force them from a political or public to judicial forum, cast them as defendants, mask the original issue, undermine energy and resources