Biostatistics as Narrative

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Slides available (next week):

1. Send me e-mail:
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2. Edited version on my website
   vanbelle.org

Overview

1. Introduction
2. My story
3. Mandated science/biostatistics
4. Narratives
5. Our profession
6. Audience input—your stories

2. My Story

1. University of Toronto
2. D.B.W. Reid and Harding leRiche
3. Math department mentors
4. What DeLury taught me
5. Florida State University
6. University of Washington

REVISED

CONNAUGHT MEDICAL RESEARCH LABORATORIES
UNIVERSITY OF TORONTO

SPADINA DIVISION
SPADINA CRESCENT
TORONTO 4, CANADA

Date 10th March, 1958.

Memorandum of agreement with G. Van Belle

Dating from 24th February, 1958, and in respect of your appointment in the Connaught Medical Research Laboratories as Statistician :

1. Your salary is at the rate of $70. per week , payable bi-weekly .

2. You are entitled to two weeks' leave of absence (with pay) yearly.

3. In the event of your deciding to leave the service of the Laboratories, you will give notice in writing of not less than two weeks . You will be entitled to receive similar notice in case your employment is terminated by the Laboratories.


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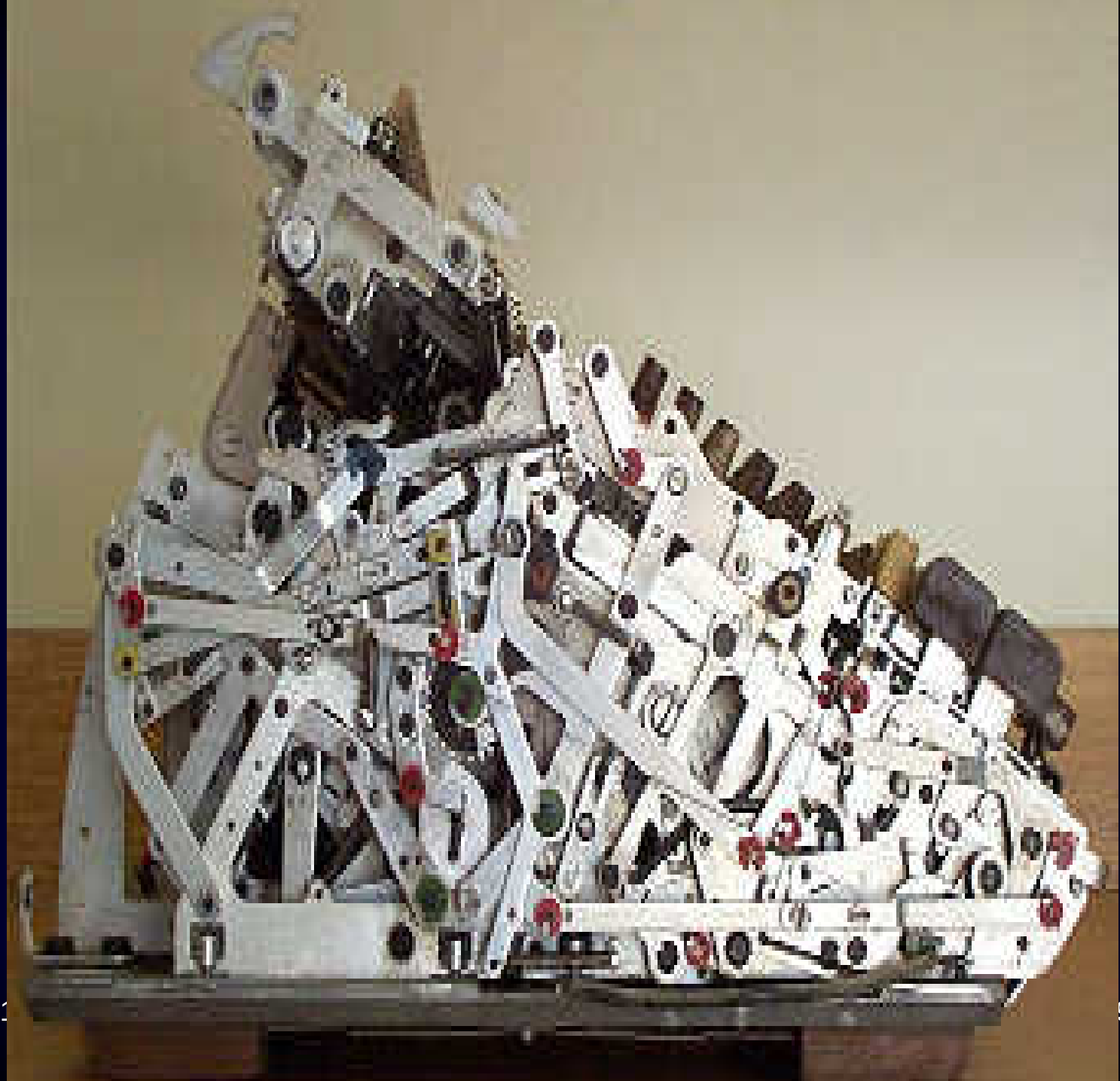


CONNAUGHT MEDICAL RESEARCH LABORATORIES
UNIVERSITY OF TORONTO

SPADINA DIVISION
SPADINA CRESCENT
TORONTO 4, CANADA

Date 19th June, 1962.

Memorandum of agreement with G. Van Belle

Dating from 1st July, 1962, and in respect of your appointment in the Connaught Medical Research Laboratories as Statistician :

1. Your salary is at the rate of $105.00 per week , payable bi-weekly .

2. You are entitled to two weeks' leave of absence (with pay) yearly.

3. In the event of your deciding to leave the service of the Laboratories, you will give notice in writing of not less than two weeks . You will be entitled to receive similar notice in case your employment is terminated by the Laboratories

What DeLury taught me…

Experiment: "An attempt to establish cause and effect. Cause and effect can be established in no other way."

Statistics: "Statistics is a subtle state of mind. Algebra and Geometry are old and absolutely predictable. Statistics is absolutely not predictable and goes back to Gauss < 200 years ago."

What DeLury taught me…

Frequency distribution: "Quality of permanence not inherent in the items."

Error: "The notion of error ensues strictly from the frequency distribution and arises from incomplete information."

What DeLury taught me…

Analysis: "Extracting information about predetermined causes. Nothing extra even if straight line. Answers to the questions first posed. Ideas and the proof that they are correct do not come from the same set of observations."

What DeLury taught me…

Randomization: "By randomization anything variable can be made into error."

"Randomization puts systematic effects into the error term."

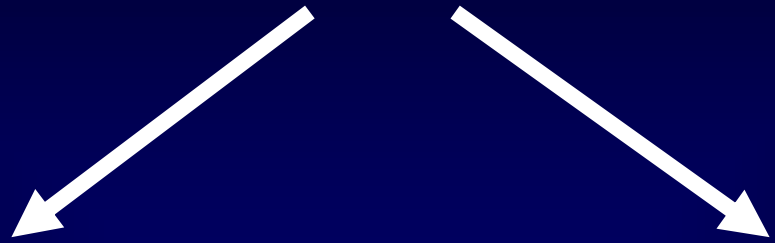
"Randomize over as small a range as possible."

What DeLury taught me…

R.A. Fisher's Design of Experiments:

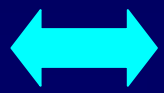
"Read it once a year for ten years. After that you may understand it."

Fundamental Questions



Where did you get the data?

(Data signature)



What do you think the data are telling you?

(Mechanism)

Data signature

A.N. Whitehead

"Observation is selection."

Seattle Times

THURSDAY
MAY 26, 2005
Metro Edition

INDEPENDENT AND LOCALLY OWNED SINCE 1896 | seattletimes.com

unscreen on: ch some rays

Numbers speak for themselves, GOP says

GOVERNOR'S

The Seattle Times

TUESDAY
JUNE 7, 2005
Metro Edition

Kitsap
ewhere

INDEPENDENT AND LOCALLY OWNED SINCE 1896 | seattletimes.c

It's over: Rossi loses in court, ends fight

Judge has barbs from the bench for King County
> A13

What's the political impact? Depends on who's talking
> A13

Republican claims picked o one by one in ruling
> A12

GOVERNOR'S ELECTION

Rossi won't appeal ruling Gregoire says she's "personally relieved"

BY DAVID POSTMAN
Seattle Times chief political reporter

WENATCHEE – Judge John Bridges yes upheld the election of Gov. Christine Gregoir roughly rejecting Republican claims of wron and leading Dino Rossi to forgo what the thought was an inevitable appeal to the st preme Court.

GOP candidate Rossi said the "political m of the high court would have made it almost sible to get Bridges' decision overturned. At

Statistical analysis of illegal votes

Republicans wanted Bridges to divide felon votes between the candidates by the same proportion as the overall vote in precincts where the felons voted. The hope was to knock votes from Gregoire's total by finding more felons who voted in precincts carried by the Democrat.

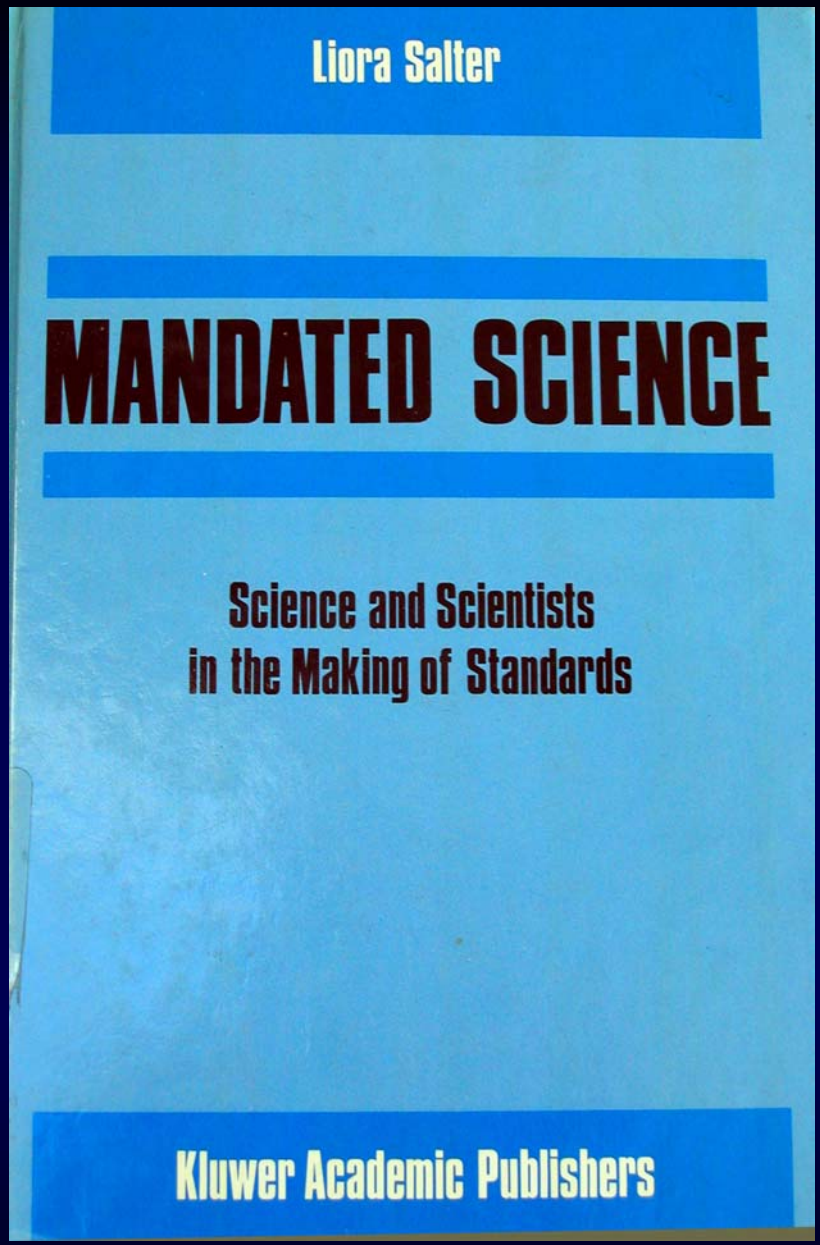
Bridges rejected that method, called proportional deduction.

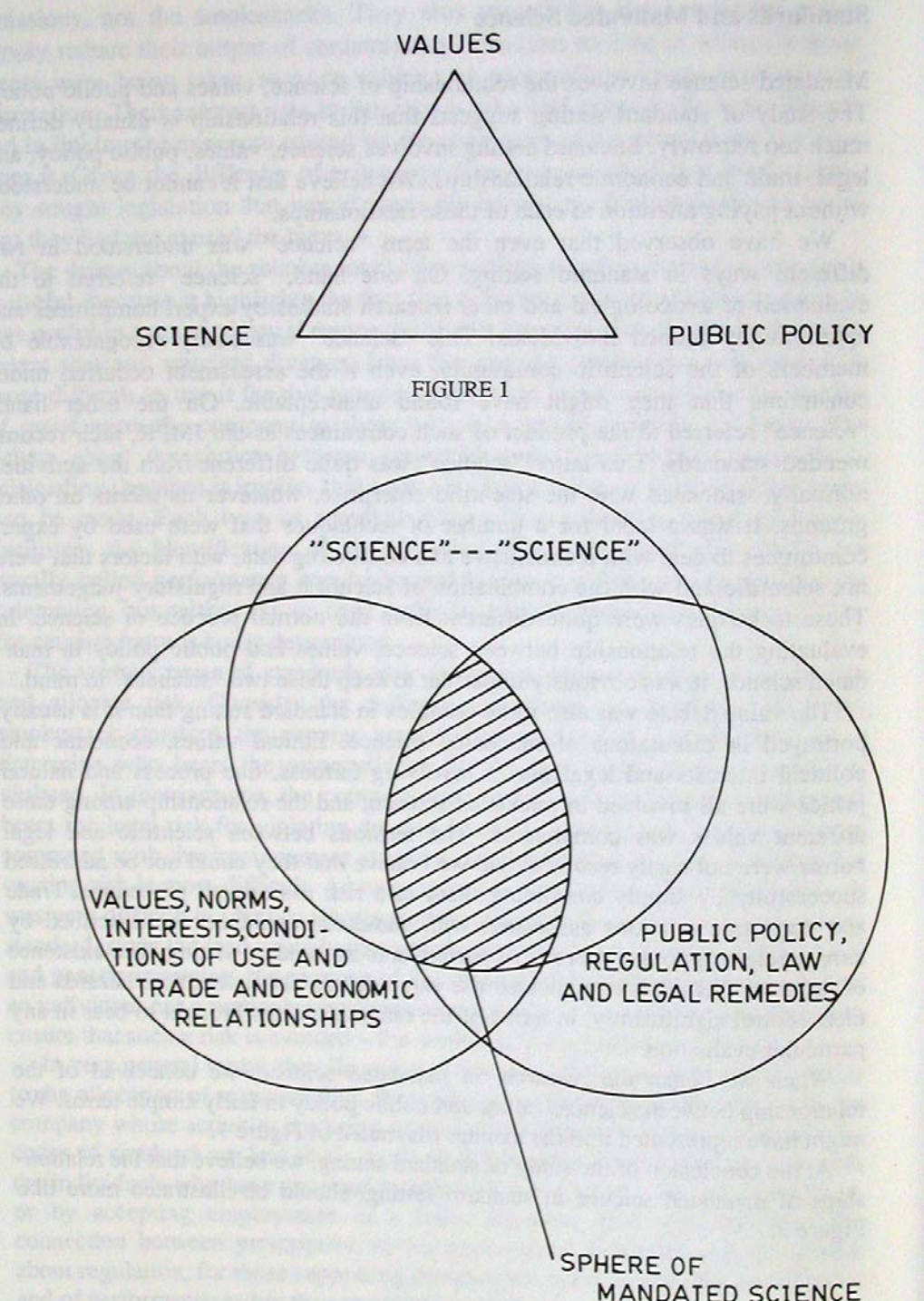
"Petitioners' data was overly weighted to include illegal votes from King County, particularly in precincts in which Ms. Gregoire prevailed. This is not consistent with generally accepted scientific standards."

3. Mandated Science/Biostatistics

"Science that is sponsored and used for the purpose of setting public policy."

Liora Salter


Liora Salter
MANDATED SCIENCE
Science and Scientists
in the Making of Standards
Kluwer Academic Publishers



Mandated Science

Liora Salter

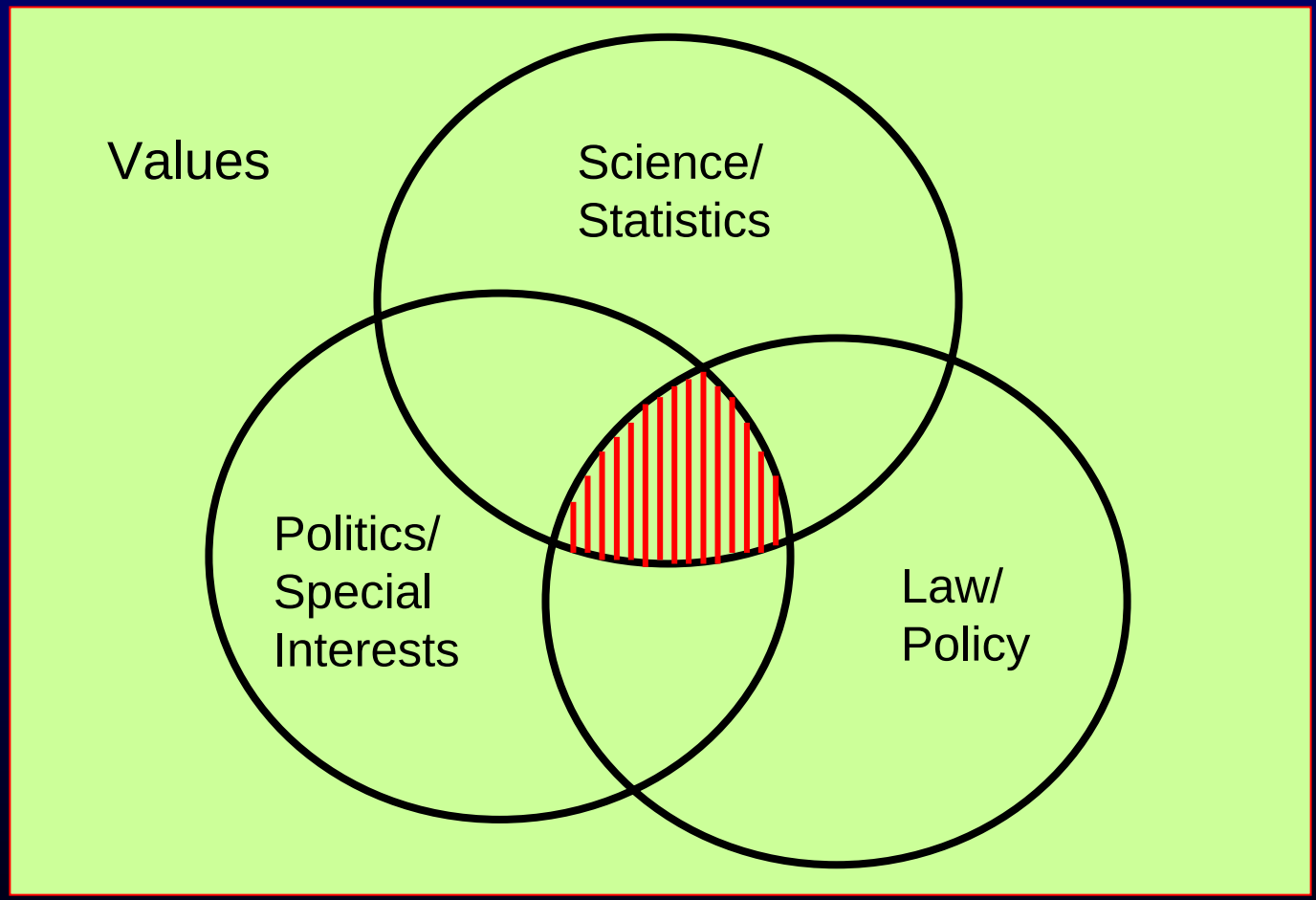
Mandated Science

Mandated science is the intersection of:

1. Science (biostatistics)
2. Politics/Policy/Special Interests
3. Law

embedded in values

Mandated Science



Characteristics

Characteristics of mandated science:

1. National support (earmark)
2. National compact
3. Sole support for many scientists
4. Adversarial, scrutinized, litigated, pressured

Process

1. Takes place in public view
   public hearings…
2. Inherently adversarial
   legal concerns…
3. Own style of discussion
   stakeholders, sponsors, special interests
4. Emphasis on “bottom line”

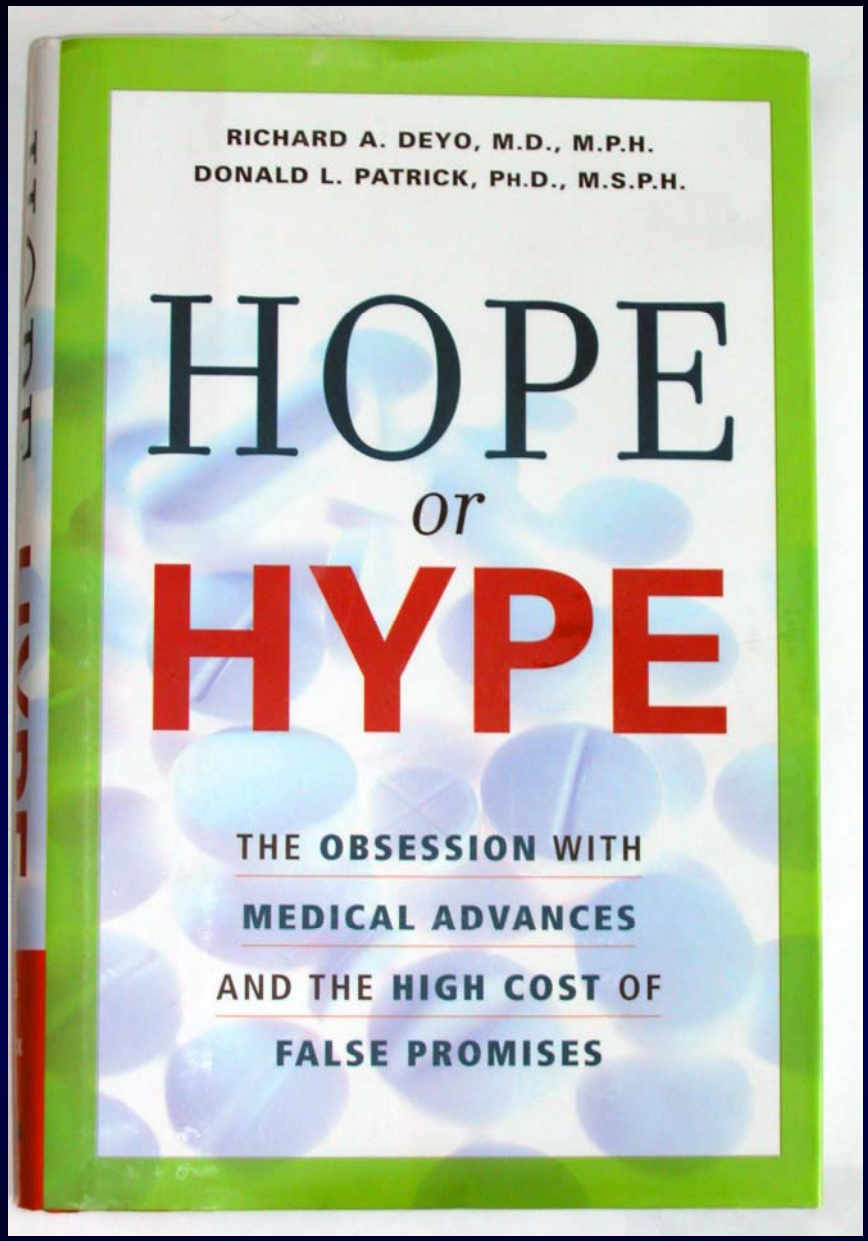
Special interest strategies

1. Raise doubts (confounding, observational data,…)
2. Ask wrong question
3. FOIA requests
4. Re-analysis of data
5. Harass, pressure

If they can get you asking the wrong questions, they don't have to worry about the answers.

--Thomas Python

Quoted in *Hope or Hype, 2005.*


RICHARD A. DEYO, M.D., M.P.H.
DONALD L. PATRICK, PH.D., M.S.P.H.
HOPE
or
HYPE
THE OBSESSION WITH
MEDICAL ADVANCES
AND THE HIGH COST OF
FALSE PROMISES

A desire to take medicine is, perhaps, the great feature which distinguishes man from animals.

--Sir William Osler, 1891

Quoted in *Hope or Hype, 2005.*

But…

1. This reflects my bias (values)
2. Cannot doubt sincerity of SIG views
3. Part of world view
4. Skepticism and cynicism occupational disease in biostatistics

4. Narratives

1. Health Effects Institute
2. Alzheimer's Disease Research Centers
3. Zymogenetics
4. Cholinesterase monitoring
5. Chairing Department of Environmental and Occupational Health Sciences

Format

A. Background
B. Special features
C. Biostatistics

Health Effects Institute

A. Background

US-EPA 1972

Clean air regulations

Lack of knowledge

Where to locate research?

Non-Government Organization (NGO)

Partnership: EPA and car producers 50/50

HEI chartered in 1980 (earmark, initially)

Health Effects Institute

B. Features

"Fierce independence" A. Cox

Research Committee

- sets agenda
- supervises research (contracts)
- modifies research

Health Effects Institute

B. Features (continued)
    - Review Committee
        - Independent review
        - Intense scrutiny
    - Reasons for this structure
        - Second look
        - Acknowledgment of PI biases

Health Effects Institute

C. Biostatistics

- Key role in research and review
- Research committee: 2 biostat
- Review committee: 2 biostat (Nancy Reid)
- Scientific Oversight Groups (van Belle, Dave Andrews…)

Alzheimer Disease Research Centers

A. Background

Formed in 1983 in US

Funded by US NIH NIA

Purpose: find cure for AD

Currently about 30 centers

Cooperative agreements

Each center has budget of ~1.5m/year

Alzheimer Disease Research Centers

B. Features

- Centers independent
- Clinical or basic science orientation
- External scientific advisory committees
- Haphazard subject collection
- Initial efforts: standardization of diagnosis, pathology, …
- Minimal data set
- Clinical or basic science orientation

Alzheimer Disease Research Centers

C. Biostatistics

- Variation by center
- Few biostatisticians initially
- Supportive role
- Little modeling
- Changing—latent variable analysis

Zymogenetics

A. Background

Zymogenetics: biotech firm in Seattle

Niche: therapeutic proteins

For example: non-animal based clotting agent to be used in surgery

Zymogenetics

B. Features

"…provide statistical educational sessions for Zymogenetics executive management…"

Four sessions of one hour each

General area: biostatistical aspects of clinical trials

Zymogenetics

Please stand and discuss with your neighbor what topics you would cover in those four sessions

Zymogenetics

C. Biostatistics

1. Refinement of everyday experience
2. Clinical trial in drug approval (E9)
3. My experience as FDA Advisory Committee member
4. Surrogates and non-inferiority trials

Zymogenetics

1. Biostatistics as the refinement of everyday experience:
    a. Variation
    b. Observation
    c. Correlation
    d. Classification

Zymogenetics

a. Variation
   - Systematic
   - Random
   - Controlling variation (blocking)
   - Inducing variation (randomization)
   - Describing variation

Cholinesterase monitoring

A. Background

1993—WA State Dept of Labor and Industries (L%I) adopts rule to monitor cholinesterase (AChE) in pesticide handlers. Not mandatory.

1997—Evergreen Legal Services sues to make rule mandatory.

2002—WA State Supreme Court orders L&I to initiate rule. Stakeholder Advisory Committee formed.

2003—Current rule adopted; effective 2004. Scientific Advisory Committee formed.

Stakeholder Advisory Members

Potato Growers

WA Growers Clearing House

United Farm Workers

WA State Department of Health

Columbia Legal Services

WA State Department of Agriculture

Department of Medicine (UW)

Department of Environmental Toxicology (WSU)

Scientific Advisory Members

Associate Medical Director, L&I
Public Health Officer, CA Health Services
*Department of Environmental Toxicology (WSU)
Chair, Dept of Env and Occ Health Sciences (UW), Chair
*Department of Medicine (UW)
Employee Health Services, U Cal at Davis
Umatilla Chemical Agent Disposal Facility
WA State Department of Health
Environmental Toxicology, U Cal at Davis
Biostatistics and DEOHS (UW)
L&I Liaison

Cholinesterase monitoring

B. Special features (charge to SAC)

1. Review first two years of monitoring
2. Oversee collection and analysis of data
3. Make first report in November 2004
4. Make second report in November 2005
5. Final report September 2006

Cholinesterase monitoring

B. Special features (rule)

1. Three action levels relative to baseline
2. 20% reduction in AChE: Follow up action
3. 30% reduction in AChE: review program
4. 40% reduction in AChE: remove from workforce

Cholinesterase monitoring

C. Biostatistics

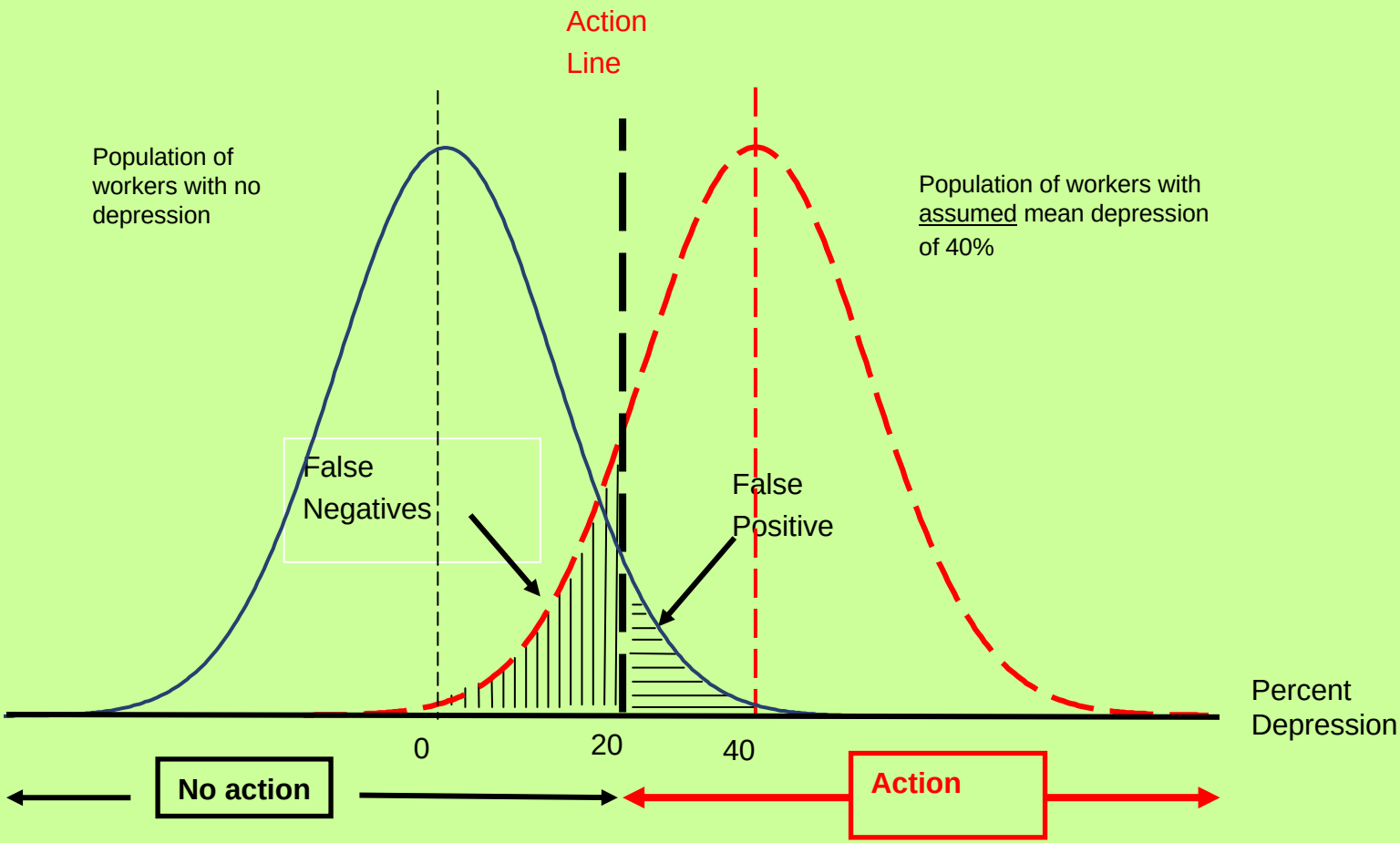
1. Data cleaning, analysis
2. Assess within worker variability
3. Assess false positive and false negative rates

Cholinesterase monitoring

Stakeholder emphasis:

“Labor”: reduce false negative rate

“Growers”: reduce false positive rate


Action
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Population of
workers with no
depression
Population of workers with
assumed mean depression
of 40%
False
Negatives
False
Positive
Percent
Depression
0
20
40
No action
Action

5. Our profession

1. My narrative demonstrates that biostatistics:
   a. is exciting
   b. has social relevance
   c. is very much in the public arena
   d. (although not shown, pays pretty well and great chance for travel)

5. Our profession

2. What are some success stories?
   a. Crucial role in research applications
   b. Increasing number of biostatisticians
   c. New opportunities for research and applications

5. Our Profession

3. How can we improve image?
   a. Within science
      Learn subject matter
      Talk subject matter—not statistics
      Realize servant role

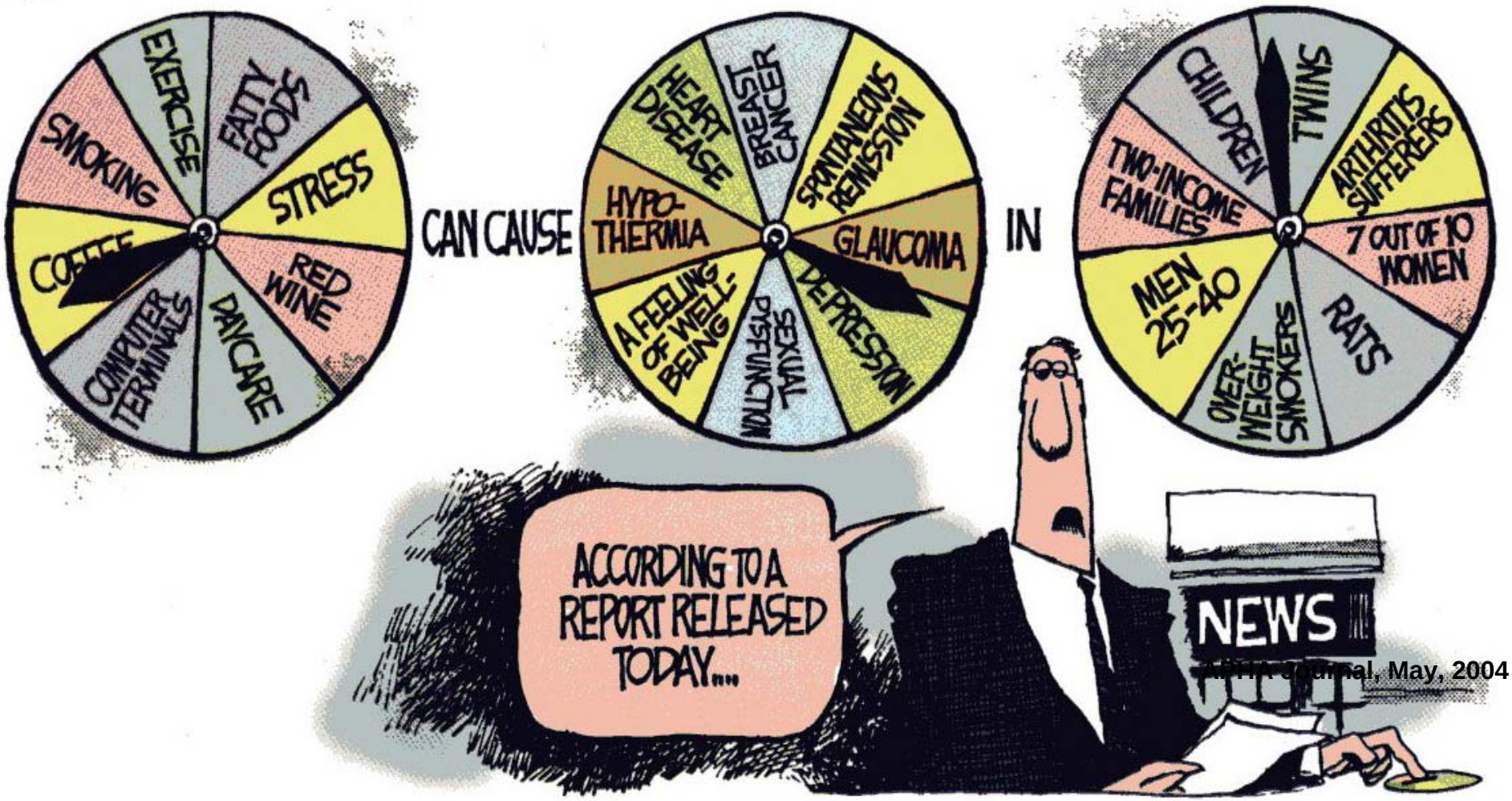
5. Our Profession

3. How can we improve image?
   b. In community
      Participate as biostatistician (elections, surveys,…)
      Be knowledgeable
      Special educational projects

Today's Random Medical News

from the New England Journal of Panic-Inducing Gobbledygook

JIM BORGMAN



APHA Journal, May, 2004

5. Our Profession

3. How can we improve image?
   b. As human beings?
      All of the above
      Constructive doubt
      Sense of humor—shift in target of inference

Conclusion

I know I’ve been preaching to the choir—I hope you can sing a little better.

Risk Assessment Paradigm-1

A. RISK ASSESSMENT

1. Hazard identification
2. Dose response assessment
3. Exposure assessment
4. Risk characterization

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B. RISK MANAGEMENT

Risk Assessment Paradigm-2

RISK ASSESSMENT

1. Hazard identification of haphazard
2. Dose response often based on animal studies; problems of extrapolation of animal to human
3. Exposure assessment difficult, expensive, time consuming
4. Risk characterization integrative, beginning to be steered more and more by values

Risk Assessment Paradigm-3

RISK MANAGEMENT

1. Scientists often leave the mandated science arena here.
2. Gets “dirty” that is, values become more prominent
3. Argument is that science defines options (or non-options) and that it’s the policy folks who need to implement.
4. Examples of risk management:
   - International Whaling Commission
   - Kyoto “accords”
   - ….
   - ….