Medical Reversal
Why 46% of What We Do Is Wrong

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Disclosure

Funding:

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Disclosure

- Some of this talk is controversial.
- It is not my purpose to disparage any particular practice
- Broad patterns of medical progress/innovation/evidence (& hijacked) and missteps in medicine

What is Medical Reversal?

Often in medicine new practices replace older ones.

H2 -> PPI
MOMP -> MOPP -> ABVD
Streptokinase -> TPA -> PCA BM stent/-> drug eluting
What is Medical Reversal?

Many other times, something we had been doing is found to be no better or worse than a prior or lesser standard of care (incd. doing nothing)

Routine use of Swan Ganz for monitoring ICU patients
Routine HT for post-menopausal women
Routine PCA for stable angina

What is Medical Reversal?

Is much more like this....
Definition of Medical Reversal

A large, well done study; typically RCT (with better blinding/controls/power/endpoints aka less bias) contradicts current medical practice.

Reversals of Established Medical Practices
Evidence to Abandon Ship

Rarely, some investigators find the courage to test established "truths" with large, rigorous randomized trials. When this happens, empirical evidence suggests that "medical reversals" may be quite common. In an evaluation of Strategies that were published in a major clinical journal in 2000 and then rumors an established clinical practice, 15 (65%) re-

Similar to other concepts

- No-value or low-value care
- De-adopt failed practices
- Contradicted or refuted practices
- Slow med
Talk outline

• Select examples of reversal
• Frequency estimates
• Harms
• Origins
• Solutions
• Objections
• What will EBM look like in the age of recognition of Medical Reversal
Though common practice, ASTRAL showed no benefit for stenting over optimal medical management for RAS.

Stenting and Medical Therapy for Atherosclerotic Renal-Artery Stenosis

Christopher J. Cooper, M.D., Timothy P. Merz, M.D., Donald E. Cutlip, M.D., Kenneth Jemecut, M.D., William H. Young, M.D., David M. Reed, M.D., David H. Cohen, M.D., and Alan M. MacFarlane, M.D.

Kathleen H. Torte, M.B., Joseph J. Shapiro, M.D., W. Frei, J.D., J. Hamblet, M.D., Joseph M. Kowalewski, P.D., Hugh J. D. Maginnis, Jr., P.D., and Land B. Hechts, M.D., for the CORDA Investigators

Hazard ratio with stenting: 0.94 (95% CI: 0.76–1.17)
P = 0.38 by log rank test

Niacin, Fenofibrate
Steroid injection for spinal stenosis

Talk outline

- Select examples of reversal
- **Frequency estimates**
- Harms
- Origins
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- What will EBM look like in the age of recognition of Medical Reversal
Our own estimate

A Decade of Reversal: An Analysis of 146 Contradicted Medical Practices

Vinay Prasad, MD; Andrea Vandross, MD; Caitlin Toomey, MD; Michael Cheung, MD; Jason Rho, MD; Steven Quinn, MD; Satin Jacob Chacico, MD; Durvi Borkar, MD; Victor Gall, MD; Santosh Selvaraj, MD; Nancy Ho, MD; and Adam Cht, MD

Abstract

Objective: To identify medical practices that offer no net benefit.

Methods: We reviewed all original articles published in 10 years (2001-2010) in one high-impact journal. Articles were classified on the basis of whether they addressed a medical practice, whether they showed a new or existing therapy, and whether results were positive or negative. Articles were then classified as 1 of 4 types: replacement, when a new practice surpasses standard of care, back up by the drawing board, when a new practice is no better than current practice, reaffirmation, when an existing practice is found to be better than a lesser standard, and reversal, when an existing practice is found to be no better than a lesser therapy. This study was conducted from August 1, 2011, through October 31, 2012.

Results: We reviewed 2044 original articles, 1344 of which concerned a medical practice. Of these, 981 articles (47.7%) examined a new medical practice, whereas 363 (17.7%) treated an established practice. A total of 647 studies (70.5%) had positive findings, whereas 397 (29.5%) reached a negative conclusion. A total of 756 articles addressing a medical practice constituted replacement, 165 were back up by the drawing board, 146 were medical reversals, 136 were reaffirmations, and 159 were inconclusive. Of the 363 articles testing standard of care, 146 (40.7%) reversed the practice, whereas 128 (35.6%) reaffirmed it.

Conclusion: The reversal of established medical practice is common and occurs across all classes of medical practice. This investigation sheds light on low-value practices and patterns of medical research.

How often does it happen?

2044 Articles

1344 (65.8%) Concern a medical practice
How often does it happen?

FIGURE 1. A breakdown of articles concerning a medical practice.
We detail all 146 Reversals in the Supplementary Appendix

Reversals include

- Medications/ Procedures/ Devices/ Surgeries/ Screening tests/ OTC medications/ Vitamins/ Supplements/ Treatment algorithms (P2y12 testing)/ Diagnostic instruments (Swan Ganz)/ Systems interventions/ Quality and performance measures

- In short, every corner of health care
Talk outline

- Select examples of reversal
- Frequency estimates
- **Harms**
  - Origins
  - Solutions
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What are the harms of reversal

- Harms are threefold:
  - People who undergo the practice during the years it fell in favor
  - People who undergo the practice during the lag time before it falls out of favor
    - Ten years of inertia
  - Loss of trust in medical system
What are the harms of reversal

- Harms are threefold:
  - **People who undergo the practice during the years it fell in favor**
  - **People who undergo the practice during the lag time before it falls out of favor**
    - Ten years of inertia
  - **Loss of trust in medical system**

Why is reversal problematic?

- No benefit to patients in years it was in favor
- Lag time to reversal
- Loss of trust in medical system
Why is reversal problematic?

- No benefit to patients in years it was in favor
- Lag time to reversal
- Loss of trust in medical system (mammography)

Talk outline

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- **Origins**
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Why does Reversal happen?

• We adopted something based on inadequate & biased studies (w/o definitive trials ongoing or forthcoming)
  – Pathophysiology alone
  – Pathophysiology plus anecdotal evidence
  – Epidemiological evidence (with residual confounding)
  – Historical controlled evidence
  – Randomized trials
    • Inappropriate controls (too young/ non representative)
    • Inappropriate dosing/ comparators/ concom. medications
    • Single center
    • Drug run periods
    • Inappropriate endpoints (surrogates)
    • Early termination
    • Selective reporting/ publication bias
  – Meta-analysis – based on caliber of included studies & completeness
• Y = Mortality

• X1 = Vitamin E exposure
• X2 = Age
• X3 = Sex
• X4 = Race
• Y = Mortality

• X1 = Vitamin E exposure
• X2 = Age
• X3 = Sex
• X4 = Race
• X5 = Income

• Y = Mortality

• X1 = Vitamin E exposure
• X2 = Age
• X3 = Sex
• X4 = Race
• X5 = Income
• X6 = Smoking
• Y = Mortality
• X1 = Vitamin E exposure
• X2 = Age
• X3 = Sex
• X4 = Income
• X5 = Smoking
• X6 = body mass index (BMI), hypertension, diabetes, cholesterol, alcohol consumption, education, family history of heart disease, heart disease, any cancer, physical activity) and race/ethnicity
Observational/ Epidemiology studies can say anything

Propensity score is not better

• Literature on concordance of RCT & Obs on same Q (a select set)
Before and After Studies

- Gown and glove precautions
- RRT
- Many historically controlled cancer trials

Randomized Trials

- Best way to make clinical recs/ causal claims; but not any RCT is a good RCT

Hard-Wired Bias: How Even Double-Blind, Randomized Controlled Trials Can Be Skewed From the Start
Drug run in periods

Sham controls needed for subjective endpoints

- Meniscectomy for knee OA
- Debridement for knee OA
- RV pacing for HOCM
- Vertebroplasty
- Lumbar steroid injections
- PCA for stable angina (IMA ligation, Cobb)

Sham Controls in Medical Device Trials
Rita F. Redberg, M.D.
The Media doesn’t help

Randomized trials

Observational trials

New drugs are hailed as breakthroughs

- 14% had no human data
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Solutions*

- Book: Education/ Regulation/ Reimbursement

- How much of what we fund doesn’t help our patients?

- How can we elucidate that?
Solutions*

• New costly technologies that are being introduced to health systems are ideal for testing in RCTs, especially if they are tested in dubious trials with unrepresentative populations

Solutions*

• Be careful about studying interventions before and after (overemphasizes benefits)
• Paying for drugs based on outcomes (also prone to this)
• Be careful in choosing cost-effective practices that assume benefit over practices that have shown benefit, but seem less cost-effective.
Solutions

- We have to identify costly low value practice, and dis-incentivize continued use
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What about RCTs of parachutes

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell

Abstract

Objectives To determine whether parachutes are effective in preventing major trauma related to gravitational challenges.

Design Systematic review of randomised controlled trials.

Data sources Medline, Web of Science, Embase, and the Cochrane Library databases; appropriate internet sites and citation data.

Study selection Studies showing the effects of using a parachute during free fall.

Main outcome measure Death or major trauma, defined as an injury severity score > 15.

Results We were unable to identify any randomised controlled trials of parachute intervention.

Conclusions As with many interventions intended to prevent ill health, the effectiveness of parachutes has not been subjected to rigorous evaluation by using randomised controlled trials. Advocates of evidence-based medicine have utilised the adoption of parachutes as an example of the futility of using only observational data. We think that everyone might benefit if the most radical protagonists of evidence-based medicine were organised and participated in a double-blind, randomised, placebo-controlled, crossover trial of the parachute.
What about RCTs of parachutes

- Two limits of the analogy
  - 1. A single clear etiology (BCR-ABL)
      - Trauma –
  - 2. A huge effect size

Prior “parachutes” were no such thing
Most medical practices don’t have large treatment effects

Empirical Evaluation of Very Large Treatment Effects of Medical Interventions

Some advances have been tested without RCT

When are randomised trials unnecessary? Picking signal from noise

The relation between a treatment and its effect is sometimes so dramatic that bias can be ruled out as an explanation. Paul Glasziou and colleagues suggest how to determine when observations speak for themselves.

- Some historical examples of treatments with dramatic effects
  - Insulin for diabetes
  - Blood transfusion for severe haemorrhagic shock
  - Sulphadiazine for purpuric septicaemia
  - Streptomycin for tuberculous meningitis
  - Defibrillation for ventricular fibrillation
  - Closed reduction and splinting for fracture of long bones
  - Salicylic for acute rheumatism
  - Neostigmine for myasthenia gravis
  - Tocopherol for haemochromatosis
  - Suturing for repairing large wounds
  - Drainage for pain associated with abscesses
  - Pressure or suction for arresting haemorrhage
  - Ether for anaesthesia
  - One-way valve or underwater seal drainage for pneumothorax and haemothorax
  - Phototherapy for skin tuberculosis
  - Combination chemotherapy with cisplatin, vinblastine, and bleomycin for disseminated testicular cancer
Talk outline

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EBM

• We need to move from a model where the conflicted parties design, conduct and set the clinical trials agenda to one where the choice of clinical question and design is conducted by impartial bodies
• We will see a continued erosion of practices that gained prominence in the era of eminence based medicine (and lack empiric study, including screening)
EBM

- Discourage sensationalist claims in preclinical/epidemiologic/observational work
- May have to defund duplicative, low-yield, or uncertain research
- Variations of peer review should undergo empirical testing (non-blinded/post publication)

The arc of medicine

- History has taught us that the arc of medicine bends towards higher standards of evidence
Acknowledgements

Dr. Adam Cifu
Dr. Sham Mailankody
Dr. John Ioannidis
Dr. Andrae Vandross
Dr. Jason Rho
Dr. Caitlin Toomey
Dr. Victor Gall
Dr. Senthil Selvaraj
Dr. Durga Borkar
Dr. Nancy Ho
Dr. Joel Jorgenson
Dr. Jacob Chacko
Dr. Steven Quinn
Dr. Michael Cheung
Dr. Sham Mailankody
Dr. Chul Kim
Dr. Mauricio Burotto
Mr. Matt Abola
Dr. Usama Bilal

Purpose of this talk is not to litigate any *particular* practice
But to speak broadly about patterns of medical progress and missteps.
If you liked the talk, check out the book

Questions

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