Truth and Truthiness in Surgery

Jeffrey B. Matthews, M.D.
Dallas B. Phemister Professor of Surgery
Chairman, Department of Surgery, The University of Chicago
Surgeon-in-Chief, The University of Chicago Medical Center

No Disclosures
Crescat scientia, vita excolatur  
*Let knowledge grow from more to more,*  
*and so be human life enriched*

Knowledge, in practice and theory

- GI surgeon (use knowledge)
- Scientist (create knowledge)
- Educator (impart knowledge)
- Department Chair (possess knowledge)
- American Board of Surgery (test knowledge)
- Journal editor (filter knowledge)
What is Knowledge? What is Truth?

- Epistemology
- Levels of knowledge
  - know-\emph{that} (facts)
  - know-\emph{how} (skills)
  - know-\emph{who} (network)
  - know-\emph{why} (science)

Plato: knowledge lies between truth and belief

What is Truthiness?

Stephen Colbert
American Philosopher

“Truth that comes from the gut, not books.”
Preference for concepts or facts one \emph{wishes} to be true rather than concepts or facts \emph{known} to be true.
Truth and Truthiness in Surgery

• Evidence, and what we do with it
• Bias and cognitive distortion
• Cognitive repairs for Evidence-Based Medicine
• Complexity, tacit knowledge, and uncertainty

Current Surgical Practice

An accumulated wisdom mixing fact, opinion, and magical thinking … in unknown proportions
But it works (doesn’t it?)

- We might be fooling ourselves
- What we do is more true than false
- Our choices have less impact than we think
- Decision paths are redundant and converge
- *The truthiness is deeply embedded*

You are called at 10 p.m. to evaluate postop fever the second night after colectomy.

The patient denies symptoms. Diminished breath sounds at the left base; otherwise your exam is unremarkable.

*What is the most likely diagnosis?*
Postoperative atelectasis

“Fever within 48 hours after surgery is usually caused by atelectasis. Re-expansion of the lungs causes body temperature to return to normal. [Atelectasis]...is responsible for over 90% of febrile episodes.”

Doherty and Way. Current Surgical Diagnosis and Treatment. 12th ed

Ritual

Chest X-ray confirms atelectasis
Chest PT, incentive spirometry ordered
Febrile episode resolves by morning, leading to accolades from your chief
The diagnosis and the intervention have been validated, reinforcing your beliefs.
But...

The relationship between atelectasis and fever is **unsupported** by clinical or experimental evidence.

- Atelectasis does not induce fever in animal models
- Pneumothorax does not cause fever
- Incidence of postoperative atelectasis is similar in patients with and without postoperative fever

Why do we believe that atelectasis causes postoperative fever?

- Anecdotal experiences of powerful thought leaders

Frank Lahey, in discussion of 1941 ASA paper
Postoperative fever and atelectasis

- Confusion of correlation-causation-association?
- **Truth by consensus**: a reality where, if enough people agree, it becomes the truth (a “Wikiality”)
- (I have no better explanation for the fever)
- Hidden benefit to the myth (behavioral imprint)
How do we decide what is “true”?

- Scientific Method
  - observable, measurable evidence
  - hypothesis that can be refuted
  - iterative and predictive
- Positivism, scientism
- Reductionism: Descartes

Evidence-Based Medicine is grounded in positivism and scientific reductionism

- Decisions informed by best available scientific evidence
  - Avoid opinion, anecdote, or unsystematic observation
The EBM approach

- Ask a clinical question
- Locate the evidence
- Appraise and synthesize the evidence
- Apply the evidence

- **PICO** *(Patient-Intervention-Comparison-Outcome)*
  - Real-time point of care clinical decisions
  - Develop guidelines and “best practices”

EBM is an **epistemology**

- Are **objective parameters** inherently superior?
- Can results from research studies be applied to **individuals** who don’t perfectly fit the “average”?
- Is there only one question? Only one way to ask it? What about questions with little or no evidence?
- When can/should **clinical judgment** trump evidence?
Is Evidence-Based Medicine evidence-based?

Notable successes: SCIP measures?
Notable failures: SCIP measures?

*EBM is conceptually attractive.*
*But in daily practice, it often falls short.*

38 yo female with hx of bronchiectasis developed severe acute necrotizing pancreatitis. She was transferred to UCMC 7 days later. Meds included “prophylactic” ciprofloxacin and imipenem.
Is antibiotic prophylaxis indicated for acute necrotizing pancreatitis?

P: patients acutely admitted with severe acute pancreatitis
I: prophylactic antibiotics started on admission
C: therapeutic antibiotics for proven infection only
O: infected necrosis, infectious complications, or death

Antibiotic prophylaxis for necrotizing pancreatitis

• Multiple prospective randomized controlled trials
• Many meta-analyses and systematic reviews
Meta-analysis of meta-analyses

“All patients with ANP should be given prophylaxis with an antibiotic with proven efficacy in necrotic pancreatic tissue” (Sharma, Pancreas 2001)

“Strong consideration should be given to treating patients with severe pancreatitis with broad spectrum antibiotics, selective digestive decontamination, and enteral nutrition.” (Bassi et al., J HBP Surg 2001)

“There was strong evidence that intravenous antibiotic prophylactic therapy for 10 to 14 days decreased the risk of superinfection of necrotic tissue and mortality in patients with severe acute pancreatitis with proven necrosis at CT.” (Bassi et al., Cochrane, 2003)

Antibiotic prophylaxis is evidence-based.
Or is it?

Meta-analysis of meta-analyses

X "Antibiotic prophylaxis appeared to be associated with significantly decreased mortality but not infected pancreatic necrosis." (Cochrane, 2006)

X "Prophylactic antibiotics do not prevent infected necrosis or death." (Br J Surg, 2006)

✓ "Overall, the use of antibiotics in patients with necrotizing pancreatitis appears to decrease infectious complications and mortality." (Curr Gastro Rep, 2006)

✓ "Patients with necrotizing acute pancreatitis should receive effective antibiotic prophylaxis ... to decrease the risk of infected necrosis and sepsis and need of surgery." (Medicina, 2007)

X "Prophylactic antibiotics cannot reduce infected pancreatic necrosis and mortality in patients with ANP" (Am J Gastro, 2008)

X Antibiotic prophylaxis of SAP does not reduce mortality or protect against infected necrosis, or frequency of surgical intervention. (Am J Surg 2009)

= No benefit of antibiotics in preventing infection of pancreatic necrosis or mortality ... except for when imipenem ... was considered on its own, where a significantly decrease in pancreatic infection was found. None of the studies ... were adequately powered. (Cochrane, 2010)

X "To date there is no evidence that supports the routine use of antibiotic prophylaxis in patients with SAP" (Scand J Gastro, 2011)

✓ Early use of prophylactic antibiotics for acute necrotizing pancreatitis is associated with reduced mortality and lower incidence of infected pancreatic necrosis. (J HepatPancre Sci, 2015)

X Antibiotic prophylaxis does not significantly reduce the incidence of infected pancreatic necrosis but may affect all-cause mortality in acute necrotizing pancreatitis. (J Gastrointest Surg, 2015)
Evidence is elusive

• Positive studies had much stricter entry criteria
• The effect size is small
• Apparent benefit in tightly controlled clinical trial setting is lost in “real world” for unknown reasons

or,

• It used to be true, but it isn’t anymore

Does our everyday clinical practice reflect the best available evidence?

Karen Slim, M.D., Yves Panis, M.D., Ph.D., Jacques Chipponi, M.D., Ph.D., for the Société Française de Chirurgie Digestive

The French Society of Digestive Surgery conducted a survey among its members to assess whether or not the routine practice of gastrointestinal surgery is evidence-based. The questionnaire included 13 questions focusing on several aspects of gastrointestinal surgery and for which strong evidence exists. The participants (n = 379) were asked to respond according to their usual practices. The response rate was 75%. Only 57% ± 15% of the responses were in accordance with the evidence. That rate of evidence-based responses did not differ according to the age of participants but was higher at university hospitals (P = 0.05). (J GASTROINTEST SURG 2004;8:1079–1082) © 2004 The Society for Surgery of the Alimentary Tract

Only 57% of the responses agreed with the evidence

We’re no better than the French...

<table>
<thead>
<tr>
<th>Responders</th>
<th>% “correct”</th>
</tr>
</thead>
<tbody>
<tr>
<td>French Society of Digestive Surgery</td>
<td>283</td>
</tr>
<tr>
<td>MSKCC Surgical Oncology Fellows</td>
<td>15</td>
</tr>
<tr>
<td>University of South Florida</td>
<td>57</td>
</tr>
<tr>
<td>University of Chicago</td>
<td>38</td>
</tr>
<tr>
<td>Junior residents (PGY 1-2)</td>
<td>11</td>
</tr>
<tr>
<td>Senior residents/fellows</td>
<td>17</td>
</tr>
<tr>
<td>Attendings</td>
<td>10</td>
</tr>
</tbody>
</table>

Mechanical Bowel Preparation in Colorectal Surgery

- 3 meta-analyses
- 9 RCT’s of over 1500 pts
- NO PREP better for:
  ✓ anastomotic leak
  ✓ wound infection
  ✓ septic and non-septic comps

![Effect on anastomotic leakage](image)

Despite the abundance of “evidence”, clinical practice did not change

- Nearly all colorectal surgeons use MBP
  - “among the reasons...are tradition and the fact that MBP facilitates surgeons’ work by improving bowel handling.” (Peppas, G et al J Gastrointest Surg 2008)
What kind of evidence is necessary to effect a change in practice?

• Why are surgeons slow to reject time-honored practices despite contradictory evidence?
• And why are we so quick to adopt others with little or no evidence?

Is the evidence “true”? 
"It can be proven that most claimed research findings are false."


**Essay**

**Why Most Published Research Findings Are False**

John P. A. Ioannidis

**Summary**

- There is increasing concern that most current published research findings are false. The probability that a research claim is true may depend on study power and bias, the number of other studies on the same question, and, importantly, the ratio of true to no relationships among the relationships tested in each scientific field.

- **Modeling the Framework for False Positive Findings**
  - Several methodologists have pointed out [9-11] that the high rate of nonreplication (lack of confirmation) of research discoveries is characteristic of the field and can vary a lot depending on whether the field targets highly likely relationships or searches for only one or a few true relationships among thousands and millions of hypotheses that may be posited. Let us also consider, for computational simplicity, circumscribed fields where either there is only one true relationship (among many that can be hypothesized) or...

**Pervasive False False Positives**

- Small studies, small effect size, few confirmatory studies
- *p*-values and tests of "significance" (Fisher) instead of pre-study odds and prior probability (Bayesian)
- Data manipulation (transforming negative into positive), and overfitting of data
- Large scale data-mining where the ratio of tested-to-true relationships is high

There is good evidence that you should question the evidence

• One-third of highly-cited studies showing strong treatment effects are followed by reports of much smaller effects or even contradictory findings
  - Only 44% are ever confirmed; 24% are never challenged
  - Citations of contradicted studies persist for years (echo chamber)

Ioannidis J. *JAMA* 2005; 294: 218
Tatsioni A et al. *JAMA* 2007; 298: 2517

There is good evidence that you should question the evidence

• “One in five surgical randomised controlled trials are discontinued early, one in three completed trials remain unpublished, and investigators of unpublished studies are frequently not contactable.”

Chapman SJ. *BMJ* 2014; 349: 6870
There is good evidence that you should question the evidence

2/3 of published drug discovery data was **not able to be reproduced** by Bayer’s in-house target validation research teams

Prinz F et al Nature Reviews/ Drug Discovery 2011

Is the evidence “fair and balanced”? 
Published evidence is highly biased

- **Publication bias** favors positive or "hot" results
- **Time-lag bias** delays reports of negative results
- **Citation bias** increases visibility of positive studies
- **Reporting bias** highlights positive over negative
- **Prevailing field bias** supports entrenched opinion

**Publication bias**

- Two otherwise-identical versions of a well-designed randomized trial differing only in the study endpoint
  - one “positive”, one “no-difference”
  - identical, purposefully-placed errors
- 2 journals, 238 reviewers randomly allocated
- 97% vs. 80% recommended positive vs. no-difference
  - errors found more frequently in the “no-difference” version
  - higher scores given to Methods of the “positive” version

Emerson GB et al Arch Int Med 2010; 170: 1934-39
“Truth” is subjective

Cognitive distortion occurs when “knowledge” is filtered through the imperfect lens of human perception.

Opinions are powerfully shaped – and can be manipulated – by these distortions.

Choices are made with limited degrees of rationality.
Cognitive distortion takes many forms

- **Bandwagon effect** – “groupthink”
- **Déformation professionelle** - seeing only through eyes of own profession without broader view
- **Focusing effect** - placing too much importance on one aspect of an event
- **Framing effect** - conclusions depend on how data are presented
- **Confirmation bias** - searching for information that matches preconceptions or supports vested interests

Surgical or endoscopic therapy for large-duct chronic pancreatitis?
Endoscopic versus Surgical Drainage of the Pancreatic Duct in Chronic Pancreatitis

- Randomized, prospective
- 2 yr follow-up
- 19 endoscopic stent
- 20 surgical therapy

“Although surgery has now been shown to be superior for long-term pain control in two randomized, controlled studies, many patients are anxious to avoid surgery if at all possible. Although endoscopic treatment is not without risks, patients perceive it as safer and simpler... (E)ndoscopic therapy remains a reasonable treatment option, depending on patient preferences. Patients ... can always undergo subsequent surgery.”

- Accompanying endoscopist editorial
Surgeons are especially susceptible to cognitive distortion and bias

- Dogma and the influence of mentors
  - respect for hierarchical organization
- Narrative and anecdotal rationalization
  - deriving from “culture” of M&M
- Predilection for linear causality
  - inherent to our action and decision oriented mindset
- Belief in ourselves and our results
  - vested economic interest, concern for the future

Is it possible to “fix” EBM to better account for bias and distortion?
Cognitive Repairs

• Avoid focusing effects through heuristics: “rules of thumb” (e.g., trauma ABC’s)

• Limit framing effects and groupthink via multidisciplinary teams (which might include non-MDs, patient advocates, etc.)

• Minimize confirmation bias through use of guidelines and decision support tools

Decision support tools are helpful, but…

• Proliferation of guidelines can be overwhelming and unmanageable in practice

• Many are incompletely validated or updated

• Overemphasis: despite best intentions, often applied context-free by inexperienced or overworked clinicians

• Beware false precision: the illusion of mathematical certainty that “fools” both physician and patient

• Many try to force the messy continuum of human disease into inappropriately discrete categories
The mind easily allows itself to be deluded by the deceptive appearance of precision which statistics retain even when wrong and it relies confidently upon mistakes apparently clothed in the forms of mathematical truth.

de Tocqueville, 1831

An 80 yo man has a resectable 2 cm biopsy-proven adenoCa in the pancreatic head.

Would you recommend a Whipple?
“What are my chances?”

• Reach for the nearest available risk calculator
  ✓ Perioperative mortality in the elderly?
  ✓ Disease-specific survival?
  ✓ Are there other “odds” you need?

• Knowing the odds, how do you use them?
• Do we all agree on that?
• Is your calculator better than your hunch?

(show of hands, please)

Would you recommend a Whipple for this 80 year-old man if:

Periop mortality was calculated at 2%?

20%?

5%?

88 year-old with comorbidities?

IPMN, not established pancreatic cancer?
It’s always messy, if you’re honest

- How do your results compare? Local experience?
- Specific anatomic circumstances?
- Individual health and comorbidities?
- Quantity or Quality of Life? Make it home? Baseline?
- Family situation? Value systems of patient, family?
- Resource utilization? Comparative effectiveness?

“As the population ages and the prevalence of chronic degenerative diseases increases, the patient with a single condition that maps unproblematically to a single evidence based guideline is becoming a rarity.”

Trisha Greenhalgh  *BMJ*  2014; 348: g3725
Improving EBM

• Make evidence more understandable for individuals (e.g., patient-centered endpoints, number needed to treat/harm)
  - Mutual understanding of goals of care must inform the dialogue
  - Avoid default to rigid rules/algorithms for the “average” patient

• More realistically approach complexity and acknowledge the irreducible uncertainties in recommendations to screen, decisions to treat, etc.

Geriatric Assessment Improves Prediction of Surgical Outcomes in Older Adults Undergoing Pancreatoduodenectomy: A Prospective Outcomes Study

W Dale MD PhD, J Hemmerich PhD, E Melstrom, A Kamm, MC Posner MD, JB Matthews MD, EA Choi MD, R Rothman, A Palakodeti PhD, KK Roggin MD  Annals of Surgery 2014
Geriatric Assessment and Prediction of Outcomes in Older Adults Undergoing Pancreaticoduodenectomy

- Prospective assessment of 76 older patients referred for PD
- Fried's Model of Frailty, Vulnerable Elders Survey, Short Physical Performance Battery
- Significant unrecognized vulnerability identified, after controlling for standard preoperative variables
- “Exhaustion” correlated with major complications, LOS, rehab stays, readmissions


Genome-guided Medicine for Pancreatic Cancer

- Biomarkers of response to therapy and toxicity prediction
  - “staging the aging”, using fatigue phenotype and potential biomarkers of physiological fitness
- Rapid assessment of patient and pancreatic cancer genomes to search for “druggable” targets
- Pancreatic cancer genome analysis to evaluate risk of cystic lesion progression to malignancy

Kevin White, PhD
Institute for Genomics and Systems Biology

Kevin Roggin, MD
Surgical Oncology

William Dale, MD, PhD
Geriatric Medicine
Big data and the future of personalized medicine

Will it ever be possible to get enough data for bias-free, precisely-targeted clinical decisions in individual patients?

Big data and health care

- Electronic medical records
- Publicly available databases/quality/outcomes
- Cost/variations in care/comparative effectiveness
- Phenotype/genotype correlation
- Drug discovery/targeted therapy
- Hypothesis-generation, discovery
“Information is no longer a scarce commodity; we have more of it than we know what to do with. We perceive it selectively, subjectively, and without much self-regard for the distortions that this causes.”

Nate Silver (’00), *The Signal and the Noise* (2012)

**Precision Medicine**

- New packaging of “personalized” medicine
- The potential and the promise:
  - early detection and improved prognostic prediction
  - development of new drugs and interventions
  - selection of more precisely “tailored” therapy
- Many notable achievements, proofs-of-principle
The (current) reality: *we want it to be true*

- Limits of scientific reductionism in face of complexity
- Ability to acquire data outpaces methods to manage and translate, or to account for multi-morbidity
- Validation/confirmation/reproducibility
- Exaggerated benefit for making treatment recommendations in individuals?

High-performance computing to model complexity

Evidence-Based Medicine is an important concept.

“Big Data” is exciting

But EBM and big data remain insufficient to encompass all forms of knowledge needed for good care.
Tacit Knowledge

- Tacit knowledge is gained in a local context, through traditions and experiences not universally shared
- “Facts” (explicit knowledge) cannot be dissociated from unconscious, and subjective elements
- Examples/manifestations of tacit knowledge:
  - The meaning between the words; informed intuition and judgment; Gestalt and Eureka moments

Smith DG. Academic Medicine 2008; 83: 268-73

Daily clinical practice involves hundreds of decisions that requires varying proportions of explicit and tacit knowledge

Much (most?) lies outside the reach of EBM

“the increase in the scientific nature of medicine does not make medicine a science”
- Andrew Miles
Major challenge for surgical education

• More than the facts (SCORE)
• Importance of the “hidden curriculum”
• Preservation of experiential learning
• Implications for examinations/MOC etc
• Skills acquisition and clinical judgment – is tacit knowledge quantifiable and measurable?

Confronting uncertainty

• Uncertainty as the 7th core competency
  - Learning to make decisions with incomplete information
  - Recognizing glib argument, false precision, overfitting, oversimplification
  - Buffering oneself from the overconfidence of the “decisive” surgical mindset
  - Appreciating the ethical challenges, within the context of the doctor-patient relationship
Summary

• Truth and Truthiness will inevitably coexist – it’s OK to learn to trust your gut.
• Evidence is elusive and fluid.
• Knowledge is inseparable from experience.
• EBM is an incomplete epistemology that inadequately accounts for the complexity of individual clinical decisions, and the omnipresence of uncertainty.

“Before I came here, I was confused about this subject. Having listened to your lecture, I am still confused -- but on a higher level.”

Enrico Fermi, PhD
(1901-1954)
Charles H. Swift Distinguished Service Professor of Physics
The University of Chicago
Nobel Prize in Physics (1938)
Thank You