Reporting Statistics and Clinical Research: What the Research Shows and Some Future Directions

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References


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Overview

• What is evidence-based medicine (EBM) and related terms?
• Why are we not evidence-based?
• Limitations of evidence
• Personalized medicine, big data, and the role of biomedical and health informatics
What is Evidence-Based Medicine (EBM)?

- A set of tools and disciplined approach to informing clinical decision-making (Straus, 2010)
  - Applies the best evidence available for causation (Hennekens, 2011)
  - In the case of treatments or “interventions,” this is usually the randomized controlled trial (RCT)
- Still allows clinical experience (art) to be integrated with best clinical science
- Makes biomedical literature more clinically applicable and relevant

Why are we not evidence-based?

- Kida (2006) lists six ways we arrive at false beliefs
  - We prefer stories to statistics
  - We seek to confirm, not to question, our ideas
  - We rarely appreciate the role of chance and coincidence in shaping events
  - We sometimes misperceive the world around us
  - We tend to oversimplify our thinking
  - Our memories are often inaccurate
- Medical “myths” persist (Vreeman, 2008), e.g.,
  - Sugar causes hyperactivity
  - Excess heat loss in the hatless
- Physicians have had to deal with incomplete evidence base through the ages (Jones, 2011)
Public and professionals do not necessarily understand statistics

- Patients in US and Germany have may lack numeracy skills, especially in lower socioeconomic groups (Galesic, 2010)
- Patients also tend to overgeneralize or lose details when presented with cancer information (Mazor, 2010)
- News media tends to report on aggressive treatment and survival, and less on treatment failure, adverse events, and end-of-life care (Fishman, 2010)
- Physicians also have misunderstanding of concepts, e.g., related to screening were not able to discern lead-in bias or overdiagnosis (Wegwarth, 2012)

Public is skeptical about EBM and related topics

- Hear “EBM” and related terms of policy makers and fear loss of freedom and access to care (Ross, 2009)
- Few understand terms such as “medical evidence” and “quality guidelines” (Carman, 2010)
  - Most believe more care is higher quality care and better care
- Majority of public “unconvinced” by arguments for evidence-based guidelines (Gerber, 2010)
  - Skepticism higher for those who were older and had Republican political leanings
- Health advocacy organizations may disregard evidence (Rothman, 2011)
Growing advocacy for medicine being more evidence-based

- Institute of Medicine (IOM) has called for development of a “learning health care system” so we can “know what works” (Eden, 2008)
- This may be facilitated by growing investment in health information technology (Friedman, 2010)
- Another mantra is “comparative effectiveness research” (CER), which compares test and treatments head-on in realistic settings (Sox, 2012)

Sometime skepticism is warranted: limitations of RCTs

- Sometimes there is incomplete evidence
  - Carl Sagan: Absence of evidence is not evidence of absence
  - Adverse events not always well-documented, e.g., chemotherapy trials (Fromme, 2004)
  - Publication bias – positive results more likely to be published (Dickersin, 1997), published more quickly (Stern, 1997), and published in English (Egger, 1997)
  - Selective reporting – demonstrated in psychiatric literature, where more information is provided to FDA than reported in scientific literature (Turner, 2008; Turner, 2012)
- Sometimes there is outright fraud – in past and present
  - Steady stream of NIH “Findings of Research Misconduct”
  - There are many challenges to “cleansing” literature (Sox, 2006)
Limitations of RCTs (cont.)

• Journal reviewers have a positive-outcome bias; for positive vs. no-difference reporting (Emerson, 2010)
  – More likely to recommend a positive report for publication
  – More likely to detect errors in no-difference report
  – Awarded higher scores to Methods section of positive report despite being identical to no-difference report
• Some advocate that current publication system tends to reward those who report positive results, which may distort science (Young, 2008)

What about screening tests for disease?

• “Identification of unrecognized disease”
• Aim to keep disease (or complications) from occurring (1° prevention) or stop progression (2° prevention)
• Requirements for a screening test
  – Low cost
  – Intervention effective
  – High sensitivity – do not want to miss any cases; usually follow up with test of high specificity
Americans love screening tests despite lack of evidence

• Despite their limitations, screening tests for cancer are very popular with Americans (Schwartz, 2004)
• But cost of false-positive (FP) tests is substantial; in one study of screening for prostate, lung, colorectal, and ovarian cancer (Lafata, 2004)
  – 43% of sample had at least one FP test
  – Increased medical spending in following year by over $1000
• Despite lack of evidence for benefit of annual physical exam, two-thirds of physicians still believe it is necessary (Prochazka, 2005)

Screening can also get political: the case of mammography

  – Controversial recommendation of advising against routine screening in women under 50 was caught up in healthcare reform politics and economic self-interests (Anonymous, 2010)
  – This unfortunately obscured the systematic analysis carried out by the (OHSU!) authors (Kolata, 2009; Quanstrum, 2010)
• Recent finding shows benefit in women 40-49 may be achieved with risk stratification (Nelson, 2012; van Ravestyn, 2012)
There are also conflicts of interest, especially in clinical practice guidelines

- For 192 authors of 44 guidelines endorsed by North American and European societies on common adult diseases: 87% of authors had ties to industry, 58% received financial support for research, and 38% served as employees or consultants (Choudhry, 2002)
- For 17 American College of Cardiology/American Heart Association guidelines, 56% of authors had a reported conflict of interest, most commonly being a consultant or a member of an advisory board (Mendelson, 2011)
- For 14 hyperlipidemia or diabetes guidelines, 48% of panel members reported conflict of interest while another 11% did not but were found to have one or more (Neuman, 2011)

Has ked to proposed standards for guidelines development

- Development processes we can trust (IOM, 2011)
  - Establish transparency
  - Manage conflict of interest
  - Development group should be multidisciplinary and balanced
  - Appropriate utilization and commissioning of systematic reviews
  - Rating strength of recommendations
  - External review
  - Updating
- Guidelines International Network (G-I-N, www.g-i-n.net), which aims for international standards in development (Qaseem, 2012)
Coming collision with genomics, personalized medicine, big data, etc.?

- Personalized medicine, often based on genomics, tailors treatment based on individual characteristics (Hamburg, 2010), which can be at odds with homogenizing RCTs (Ramsey, 2011)
- Big data is a new approach to science that utilizes growing number of large data collections (Hey, 2009), which may emerge from growing electronic health record adoption and large healthcare systems, i.e., development of the mega-cohort (Gaziano, 2010)
- May be at odds with EBM and CER, which aims to compare results in heterogeneous populations (Epstein, 2010)

The road to “big data” passes through “biomedical and health informatics”

- Biomedical and health informatics is the discipline that applies information, often aided by technology, to improve individual health, healthcare, public health, or biomedical research (Hersh, 2009)
  - http://www.billhersh.info/whatis
- Informatics (ideally) understands the type of information and underlying infrastructure necessary for its optimal use
  - Standards and interoperability, privacy and security, workflow and implementation, etc.
Informatics and “health IT” have been bolstered by federal investment

“To lower health care cost, cut medical errors, and improve care, we’ll computerize the nation’s health records in five years, saving billions of dollars in health care costs and countless lives.”

First Weekly Address
Saturday, January 24, 2009

Leading to a new “ARRA”

- Health Information Technology for Economic and Clinical Health (HITECH) Act of the American Recovery and Reinvestment Act (ARRA)
  - Incentives for electronic health record (EHR) adoption and “meaningful use” by physicians and hospitals (up to $27B)
  - Direct grants administered by federal agencies ($2B)
  - (Blumenthal, 2011)
Why is IT so difficult in healthcare? (Hersh, 2004)

• Cost
• Technical challenges
• Interoperability
• Privacy and confidentiality
• Workforce

Informatics goes beyond healthcare

• Bioinformatics and computational biology – genomics and personalized medicine
• Clinical and translational research – building a “learning” healthcare system
• Public health – protecting the public and promoting health
• Consumer health – for all ages, especially aging Internet-savvy baby boomers
• Imaging informatics – use of images for biomedical research, clinical care, etc.
For more information

- Bill Hersh
  - http://www.billhersh.info
- Informatics Professor blog
  - http://informaticsprofessor.blogspot.com
- OHSU Department of Medical Informatics & Clinical Epidemiology (DMICE)
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