The Limitations of Evidence Based Medicine in a Biomedical Paradigm

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Objectives

1) Re-summarize the trends of healthcare spending and chronic disease prevalence in the US compared to other countries
2) Define EBM and discuss current trends and limitations
3) Discuss problem of financial incentives
4) Discuss problem of peer review process and journal publications
5) Discuss where we are spending our time
6) Focus on a new paradigm that starts with us
Health spending in the OECD

Total spending on healthcare as a proportion of GDP in OECD countries in 2014

Source: Organisation for Economic Co-operation and Development, Health expenditure and financing data (January 2017)
Sources: Centers for Medicare & Medicaid Services (CMS) National Health Expenditure Accounts (NHEA); CMS projections of NHE; OECD Health Division’s HealthData
Only three countries in the world have seen a reduction in life expectancy in both men and women since 2010: Syria, Iraq and the United States.
Figure 5: Projected rates of obesity

Note: Obesity defined as Body Mass Index (BMI) ≥30kg/m². OECD projections assume that BMI will continue to rise as a linear function of time.
Source: OECD analysis of national health survey data.
How did we get here?

To summarize: We spend more and have worse outcomes than any other civilized high GDP country in the world, why?

- Where we spend our money in the evidence based biomedical model of western medicine
- How financial incentives have driven us toward drugs and devices with the highest return on investment vs interventions that promote health and well-being
- How we spend our time and awareness of bias
Evidence Based Medicine Defined

● Evidence based medicine (EBM) is the conscientious, explicit, judicious and reasonable use of modern, best evidence in making decisions about the care of individual patients.

● The most important reason for the interest in evidence-based medicine is that it works. There's a lot of data that shows if health systems diligently use the best clinical evidence and expertise, and ensure treatments are consistent with patient values, they'll realize better outcomes in every way.
Evidence Based Medicine

My favorite definition: “The integration of best research evidence with clinical expertise, and patient values”
We should only fund evidence based medicine.

You mean like Vioxx, Fen Phen, Redux, SSRI's, Propulsid, Raxar, Baycol, Rezulin, Trasylol, arthroscopy for arthritic knees, routine hysterectomy and mercury in vaccines?!!
The Biomedical Paradigm

1. Reductionism: All of medicine can be reduced to physics and chemistry

2. Uni-directional causality: Disease starts at the smallest level of function and percolates upwards

3. Positivism: Those things that are not amenable to scientific investigation are not important

4. Individualism: The individual is the focus of care

5. Marketism: The value of new knowledge is determined by the market rather than the contribution to shared values
The United States spends $116 billion annually on research directed at new drugs and medical devices, which comprise 13% of total healthcare costs, but only $5.0 billion aimed at the remaining 87% of costs. Why the disparity in investment? One major difference is that new drugs and devices command favorable prices, and their value accrues directly to the firm that invests in them. In contrast, service innovations can reduce morbidity and mortality while also reducing cost, but financial returns to innovators may be negligible or even negative.
US jury's Neurontin ruling to cost Pfizer $141 mln

Thu, Mar 25 2010

* Pfizer ordered to pay $47 million in Neurontin case
* Penalty triples under RICO law
* Pfizer to appeal decision

NEW YORK, March 25 (Reuters) - Pfizer Inc (PFE.N: Quote, Profile, Research, Stock Buzz) violated federal racketeering law by improperly promoting the epilepsy drug Neurontin, a Boston jury found on Thursday, and the world's largest drugmaker was ordered to pay $47 million in damages.

Under federal RICO law (Racketeer Influenced and Corrupt Organizations act) the penalty is automatically tripled, so the finding will cost Pfizer $141 million.

In 2004, Pfizer agreed to pay $430 million to federal and state governments and pleaded guilty to criminal charges of illegally marketing Neurontin, a drug the company obtained with its 2000 acquisition of Warner Lambert Corp.
The Evidenced Based Dilemma

The NIH provides greater funding for basic and translational research than for clinical research, and the new Patient-Centered Outcomes Research Institute is inadequately funded to address the scope of needed clinical research. An increasing portion of clinical research is funded by industry, which leaves many important clinical issues unaddressed. There is an inadequate supply of skilled clinical researchers and a lack of external support for clinical research. Thus, many clinical problems will continue to be evaluated and treated with inadequate or even absent evidence-based knowledge.

doi: [10.1212/WNL.0000000000001818]
Commercialization of the Production and Dissemination of Medical Knowledge

- 85% of clinical trials are now commercially funded
- 97% of the most frequently cited articles are commercially funded
- Compared to non-industry sponsored studies, industry-sponsored trials have significantly more favorable efficacy results (RR 1.24), harm results (RR 1.87) and overall conclusions (RR 1.31)
- The majority of physicians’ CME is funded by industry
- 59% of the authors of expert guidelines have financial ties to an interested manufacturer

Relman A. Industry Sponsorship of Continuing Medical Education Reply to Letters. JAMA, 2003;290:1150
From Evidence-based Medicine to Marketing-based Medicine: Evidence from Internal Industry Documents

While much excitement has been generated surrounding evidence-based medicine, internal documents from the pharmaceutical industry suggest that the publicly available evidence base may not accurately represent the underlying data regarding its products. The industry and its associated medical communication firms state that publications in the medical literature primarily serve marketing interests. Suppression and spinning of negative data and ghostwriting have emerged as tools to help manage medical journal publications to best suit product sales, while disease mongering and market segmentation of physicians are also used to efficiently maximize profits. We propose that while evidence-based medicine is a noble ideal, marketing-based medicine is the current reality.

Completeness of information for trial outcomes in CSRs, registry reports, and journal publications.

- Access to unpublished clinical study reports (CSRs) is currently being discussed as a means to allow unbiased evaluation of clinical research.
- We analyzed 101 trials with CSRs; 86 had at least one publicly available source, 65 at least one journal publication, and 50 a registry report. The trials included 1,080 patient-relevant outcomes.
- The CSRs provided complete information on a considerably higher proportion of outcomes (86%) than the combined publicly available sources (39%).
- CSRs also provided considerably more information on harms (87%) compared with Journal Publications (26%).
- Complete info in CSRs on benefits (84%) vs Publications (19%).
- What is needed is public availability of CSRs presenting trial results to a level of detail required for full evaluation of a trial.

Data "Ownership" and Transfer

- Pfizer-sponsored studies belong to Pfizer, not to any individual
- Purpose of data is to support, directly or indirectly, marketing of our product
  - Through use in label enhancements, sNDA filings
  - Through publications for field force use
  - Through publications that can be utilized to support off-label data dissemination
- Therefore commercial marketing/medical need to be involved in all data dissemination efforts

Spielmans GI, Parry PI, From Evidence-based Medicine to Marketing-based Medicine: Evidence from Internal Industry Documents, Bioethical Inquiry, 2010; DOI 10.1007/s11673-010-9208-8

BACKGROUND:
Scientific findings must withstand critical review if they are to be accepted as valid, and editorial peer review (critique, effort to disprove) is an essential element of the scientific process. We review the evidence of the editorial peer-review process of original research studies submitted for paper or electronic publication in biomedical journals.

AUTHORS' CONCLUSIONS:
At present, little empirical evidence is available to support the use of editorial peer review as a mechanism to ensure quality of biomedical research. However, the methodological problems in studying peer review are many and complex. At present, the absence of evidence on efficacy and effectiveness cannot be interpreted as evidence of their absence. A large, well-funded programme of research on the effects of editorial peer review should be urgently launched.
For Science's Gatekeepers, a Credibility Gap

“However, even the system's most ardent supporters acknowledge that peer review does not eliminate mediocre and inferior papers and has never passed the very test for which it is used. Studies have found that journals publish findings based on sloppy statistics. If peer review were a drug, it would never be marketed, say critics, including journal editors.”

“Journals have devolved into information-laundering operations for the pharmaceutical industry, say Dr. Richard Smith, the former editor of BMJ, the British medical journal, and Dr. Richard Horton, the editor of The Lancet”
Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention or Metformin

**METHODS**
We randomly assigned 3234 nondiabetic persons with elevated fasting and post-load plasma glucose concentrations to placebo, metformin (850 mg twice daily), or a lifestyle-modification program with the goals of at least a 7 percent weight loss and at least 150 minutes of physical activity per week. The mean age of the participants was 51 years, and the mean body-mass index (the weight in kilograms divided by the square of the height in meters) was 34.0; 68 percent were women, and 45 percent were members of minority groups.

**RESULTS**
The average follow-up was 2.8 years. The incidence of diabetes was 11.0, 7.8, and 4.8 cases per 100 person-years in the placebo, metformin, and lifestyle groups, respectively. The lifestyle intervention reduced the incidence by 58 percent (95 percent confidence interval, 48 to 66 percent) and metformin by 31 percent (95 percent confidence interval, 17 to 43 percent), as compared with placebo; the lifestyle intervention was significantly more effective than metformin. To prevent one case of diabetes during a period of three years, 6.9 persons would have to participate in the lifestyle-intervention program, and 13.9 would have to receive metformin.
CONCLUSIONS
Lifestyle changes and treatment with metformin both reduced the incidence of diabetes in persons at high risk. The lifestyle intervention was more effective than metformin.


58% reduction in Lifestyle group vs 31% reduction in Metformin group
A Review of Statins

- Lipitor is the best selling drug of all time at $150 Billion through 2017
- Lipid Lowering Guidelines cite nine randomized trials in support of statins for primary prevention of CVD in persons over 65. Yet not one of these studies provide such evidence.
- People at low risk of cardiovascular disease are regularly being recommended to take statins for primary prevention and yet lifestyle factors account for 80% of CVD and 140 low risk people must receive a statin for five years to prevent one MI or CVA
- The side effect of statins - including muscle sxns, increased risk of Diabetes (esp in women), liver inflammation, cataracts, sexual dysfunction, and exertional fatigue - occur in 20% of people treated with statins

*BMJ 2013;347:f6123*
In August 2014 an expert panel convened by The BMJ called for the anonymised individual patient data from the statins trials to be made available for independent scrutiny. Our subsequent inquiries, guided by an expert advisory group (www.bmj.com/campaign/statins-open-data) have revealed the worrying extent to which these data remain hidden...

We also wrote to the principal investigators of 32 major statins trials, 27 of which were included in CTT analyses. Despite follow-up emails and phone calls, only seven have responded.
Statins for people at low risk
Independent review of the trial data is an essential next step
Emma Parish editorial registrar, Theodora Bloom executive editor, Fiona Godlee editor in chief

... the statins saga forces us to confront the deep flaws in our current system for evaluating medicines and guiding clinical decisions. In particular, how can it be right to recommend mass treatment of healthy people without independent review of the patient level data, especially the data on adverse effects? ... The statins trialists have huge potential influence, and they have a choice. They can take the lead on transparency or be pulled kicking and screaming into the light.
How are we spending our time?

From the *Annals of Internal Medicine* comes a downright depressing study: "Allocation of Physician Time in Ambulatory Practice: A Time and Motion Study in 4 Specialties."

The painful results: Physicians overall, spend about 33% of their net workday actually taking care of and interacting with patients. For every hour of direct patient care activity, 2 hours are spent on typing, data entry, and paperwork. Over the course of an entire workday, we spend only about half of our time in exam rooms, but even while in the exam rooms we're focusing on and interacting with actual patients about half of that time. Just as much exam-room time is spent typing or dictating into our computers as spent talking with and examining patients. And, after the work day is over, doctors spend an average of 1.5 hours working from home, spending most of this time on -- you guessed it -- more data entry into electronic medical records.
How are we spending our time?

The right financial incentives are not in place to promote the use of lifestyle interventions. In the traditional fee-for-service healthcare payment model, providers are paid for consultations and procedures and not outcomes. There are only a small handful of billing codes that reimburse lifestyle related services like obesity counseling or working with a diabetes educator. Providers are generally not reimbursed for or measured on their ability to get their patients to eat healthier or exercise. Lifestyle counseling plays a very small role in the traditional fee-for-service healthcare payment model. In the world of 5-20 minute appointments, it is estimated that Providers spend less than 5% of their time on lifestyle interventions.
WHO Global Strategy on Diet, Physical Activity and Health

Eating a healthy diet, increasing physical activity and avoiding tobacco use can prevent:

• 80% of premature heart disease,
• 80% of type 2 diabetes cases, and
• 40% of cancers.

Conclusions

● The US spends more on healthcare and has worse outcomes in terms of overall health and chronic disease than any other civilized country.

● The primary purpose of most new medical knowledge is to support the use of new drugs or devices, and not necessarily to promote lifestyle changes, prevention, resiliency and overall well-being.

● Healthcare providers need access to real data.

● Biomedical science is not the whole picture, incorporate the science of resiliency as well as belief, meaning and purpose for a new US paradigm of medical care.

● Industry and government are unlikely to rectify the problems, it starts with us.