Commercial Bias in Psychiatry
Literature and Practice
Objectives

- Increased knowledge of pharmaceutical industry influence in psychopharmacology

- Question popular concepts in psychopharmacology

- Appreciate the utility of knowledge about pharmaceutical industry influence for mitigating commercial bias in education and clinical practice
Disclosure

No financial conflicts of interest.
The Billion Dollar O-Gram

David McCandless

The US Defence Budget
$440
China

Feed and educate every child on Earth for 5 years
$465
Iraq War estimated total

Walmart Revenues
$392
$11 Russia

Iraq War Predicted Cost 2003
$60
Iraq War 06

Iraq War 07
$102
$133

Big Tobacco Settlement
$206
$515
Per year to shift the entire world to solar power and renewable energies

Yearly amount given to charity by Americans
$300
OPEC earnings
$520

Beijing Olympics
$41
Global illegal drug market
$90

Video Games Market
$97
Internet Porn Industry
$97

Save the Amazon
$92
Foreign aid given by world’s major nations
$103

Online Advertising
$20

Nintendo market value
$76

Bribes received by Russian officials
$316

Manned mission to Mars
$230

Google
$175

Bill Gates
$46

Facebook
$15

Erectile Dysfunction
$4

Anti-depressants
$19

Gifts to doctors
$31

(ENLARGED SLIDE APPENDED)
Pervasive Practices

FINE (billions of dollars)

$1.42  Pfizer  SEPT 2009

$2.3  AstraZeneca  APRIL 2010

$.52  Merck  NOV 2011

$.95  Abbott  MAY 2012

$1.5  GlaxoSmithKline  JULY 2012

Groeger, 2012
“It is simply no longer possible to believe much of the clinical research that is published, or to rely on the judgment of trusted physicians or authoritative medical guidelines. I take no pleasure in this conclusion, which I reached slowly and reluctantly over my two decades as an editor of The New England Journal of Medicine.”

Marcia Angell, 2009
Ghostwriting & Ghostmanagement...

“Author TBD”
…Ghostwriting & Ghostmanagement…

Gotzsche et al, 2007

- Industry-initiated trials submitted to REB
- 40 of 44 trials had unacknowledged authors
- 64% of studies list co employees as authors
- No protocol listed clinical investigators as being part of analysis or writing
…Ghostwriting & Ghostmanagement…

Pfizer, Current Medical Directions

- 85 manuscripts on sertraline
- Uniformly positive
- Side effects under-reported
- 18 to 40% of articles on sertraline in Medline from 1998-2000
- Higher impact factor journals

Sismondo, 2007
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
CASPPER

- AJP, JAACAP (Edwards, 2009)

- “Designed to make this process as simple as possible for interested physicians”

- “Develop a topic… strengthen the product positioning”

- “benefit the sales force by expanding the database of published articles”

- “work closely with contributing physicians to ensure rapid dissemination of consistent data and messages”
A responsible consulting organization has reported the results of a continuing study by a competent medical specialist and his staff on the effects of smoking Chesterfield cigarettes.

A group of people from various walks of life was organized to smoke only Chesterfields. For six months this group of men and women smoked their normal amount of Chesterfields — 10 to 40 a day. 45% of the group have smoked Chesterfields continually from one to thirty years for an average of 10 years each.

At the beginning and at the end of the six-months period each smoker was given a thorough examination, including X-ray pictures, by the medical specialist and his assistants. The examination covered the sinuses as well as the nose, ears and throat.

The medical specialist, after a thorough examination of every member of the group, stated: "It is my opinion that the ears, nose, throat and accessory organs of all participating subjects examined by me were not adversely affected in the six-months period by smoking the cigarettes provided."

ASK YOUR DEALER FOR CHESTERFIELD... EITHER WAY YOU LIKE 'EM

CONTAINS TOBACCOs OF BETTER QUALITY & HIGHER PRICE THAN ANY OTHER KING-SIZE CIGARETTE

Buy CHESTERFIELD... Much Milder
…Ghostwriting & Ghostmanagement…

Medical Education & Communications Cos.
“gaining product adoption and usage through the systematic, planned dissemination of key messages and data to appropriate target audiences at the optimum time using the most effective communication channels…publications, journal reviews, symposia, workshops, advisory boards, abstracts, educational materials/PR.”

Sismondo, 2007
Look, half the work is done!
All you need to do is fill in the top part so we can legally say the bottom part.

DATA:

CONCLUSION: Eating chocolate will make you look younger and thinner.
**COI & study outcome**

**TABLE 1. Conflict of Interest, Industry Funding, and Outcome of Published Clinical Trials**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Studies With Conflict of Interest Present</th>
<th>Studies With Conflict of Interest Absent</th>
<th>All Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>All clinical trials</td>
<td>187</td>
<td>147</td>
<td>40</td>
</tr>
<tr>
<td>Randomized, double-blind, placebo-controlled trials</td>
<td>75b</td>
<td>67</td>
<td>8</td>
</tr>
<tr>
<td>Drug &gt; placebo</td>
<td>69c</td>
<td>63c</td>
<td>6d</td>
</tr>
<tr>
<td>Drug ≤ placebo</td>
<td>6</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

\*a Includes employees (119 of 397, 30.0%), stockholders (25 of 397, 6.3%), and consultants or speakers receiving fees (114 of 397, 28.7%).

\*b Includes employees (62 of 162, 38.3%), stockholders (12 of 162, 7.4%), and consultants or speakers receiving fees (34 of 162, 21.0%).

\*c Association between author conflict of interest and positive outcome among all studies and among industry-funded studies (p<0.001, Fisher’s exact test).

\*d Association between author conflict of interest and positive outcome among non-industry-funded studies (p=1.00, Fisher’s exact test).

- Author COI=4.9 times positive results
- Industry-supported study = 8.4 times positive results
- All clinical trials in AJP, AGP, J Clin Psych, J Clin Psychopharm
- 2001-2003

Perlis et al, 2005
Why Olanzapine Beats Risperidone, Risperidone Beats Quetiapine, and Quetiapine Beats Olanzapine: An Exploratory Analysis of Head-to-Head Comparison Studies of Second-Generation Antipsychotics

Stephan Heres, M.D.
John Davis, M.D.
Katja Maino, M.D.
Elisabeth Jetzinger, M.D.
Werner Kissling, M.D.
Stefan Leucht, M.D.

Objective: In many parts of the world, second-generation antipsychotics have largely replaced typical antipsychotics as the treatment of choice for schizophrenia. Consequently, trials comparing two drugs of this class—so-called head-to-head studies—are gaining in relevance. The authors reviewed results of head-to-head studies of second-generation antipsychotics funded by pharmaceutical companies to determine if a relationship existed between the sponsor of the trial and the drug favored in the study’s overall outcome.

Method: The authors identified head-to-head comparison studies of second-generation antipsychotics through a MEDLINE search for the period from 1966 to September 2003 and identified additional head-to-head studies from selected conference proceedings for the period from 1999 to February 2004. The abstracts of all studies fully or partly funded by pharmaceutical companies were modified to mask the names and doses of the drugs used in the trial, and two physicians blinded to the study sponsor reviewed the abstracts and independently rated which drug was favored by the overall outcome measures. Two authors who were not blinded to the study sponsor reviewed the entire report of each study for sources of bias that could have affected the results in favor of the sponsor’s drug.

Results: Of the 42 reports identified by the authors, 33 were sponsored by a pharmaceutical company. In 90.0% of the studies, the reported overall outcome was in favor of the sponsor’s drug. This pattern resulted in contradictory conclusions across studies when the findings of studies of the same drugs but with different sponsors were compared. Potential sources of bias occurred in the areas of doses and dose escalation, study entry criteria and study populations, statistics and methods, and reporting of results and wording of findings.

Conclusions: Some sources of bias may limit the validity of head-to-head comparison studies of second-generation antipsychotics. Because most of the sources of bias identified in this review were subtle rather than compelling, the clinical usefulness of future trials may benefit from minor modifications to help avoid bias. The authors make a number of concrete suggestions for ways in which potential sources of bias can be addressed by study initiators, peer reviewers of studies under consideration for publication, and readers of published studies.

(Am J Psychiatry 2006; 163:185–194)
The following table is an attempt to simplify the claims that could be obtained from these results. A ✓ is entered for those comparisons where we have a statistically significant benefit, be it with ‘all doses’ or with high dose Seroquel, and be it using observed cases or using LVCF. A ✗ marks those comparisons where a comparator has demonstrated significant superiority compared to Seroquel.

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Anxiety</th>
<th>Total BPRS</th>
<th>Factor I</th>
<th>Factor V</th>
<th>Hostility</th>
<th>Hostility Cluster</th>
<th>Mood Cluster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>-</td>
<td>✗</td>
<td>-</td>
<td>✓</td>
<td>-</td>
<td>✗</td>
<td>-</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Risperidone</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>-</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Other typicals</td>
<td>-</td>
<td>✗</td>
<td>-</td>
<td>✗</td>
<td>-</td>
<td>✗</td>
<td>-</td>
</tr>
</tbody>
</table>
Jeff and Mike,

Here's the analyses that I got from Emma. I've also attached a message that I sent to her yesterday asking for clarification.

The data don't look good. In fact, I don't know how we can get a paper out of this.

My guess is that we all (including Schulz) saw the good stuff, ie the meta analyses of responder rates that showed we were superior to placebo and haloperidol, and then thought that further analyses would be supportive and that a paper was in order. What seems to be the case is that we were highlighting the only good stuff and that our own analysis support the "view out there" that we are less effective than haloperidol and our competitors.

Once you have a chance to digest this, let's get together (or teleconference) and discuss where to go from here. We need to do this quickly, because Schulz needs to get a draft ready for APA and he needs any additional analyses we can give him well before then.

Thanks,
APA 2000 press release & presentation

• “I hope that our findings help physicians better understand the dramatic benefits of newer medications like Seroquel, because, if they do, we may be able to help ensure patients receive these medications first”

• Statistically significant advantage over haloperidol in inducing treatment response among patients with schizophrenia

• Meta-analysis of 4 studies comparing quetiapine vs haloperidol

Spielmans & Parry, 2010
Study 15

- Pts c SCZ randomized to haloperidol or quetiapine for 1 year
- Pts on haloperidol lower Sx ratings, and fewer relapses
- Data ‘cherry picked’, & trial published (Velligan et al, 2002) as “positive impact on important domains of cognitive performance that have been found to predict role function and community outcomes”

Spielmans & Parry, 2010
…Quetiapine…

Re wt gain

• Internal analysis: “moderate wt gain”, “doesn’t stop… the slope just appears to change”

• However, published review by lead AZ author (Brecher et al, 2000): “neutral effect on weight”

Spielmans & Parry, 2010
Please allow me to join the fray.

There has been a precedent set regarding "cherry picking" of data. This would be the recent Velligan presentations of cognitive function data from Trial 15 (one of the buried trials). Thus far, I am not aware of any repercussions regarding interest in the unreported data.

That does not mean that we should continue to advocate this practice. There is growing pressure from outside the industry to provide access to all data resulting from clinical trials conducted by industry. Thus far, we have buried Trials 15, 31, 56, and are now considering COSTAR.

The larger issue is how do we face the outside world when they begin to criticize us for suppressing data. One could say that our competitors indulge in this practice. However, until now, I believe we have been looked upon by the outside world favorably with regard to ethical behavior. We must decide if we wish to continue to enjoy this distinction.

The reporting of the COSTAR results will not be easy. We must find a way to diminish the negative findings. But, in my opinion, we cannot hide them.

Best regards,

John
Selective Publication…

- Turner et al, 2008
- Studies submitted to FDA
- 12 antidepressants
Data from Turner et al, 2008
...published literature...

Data from Turner et al, 2008
…SSRIs for Autism…

Carrasco et al, 2012
Comparison groups from databases to find studies (p value at 95% confidence limits)

**Completed Studies from ClinicalTrials.gov**
- Sponsored by industry vs. throughout NIH (0.001)
- Drug vs. Device (0.01)
- Interventional vs. observational studies (0.05)
- Randomized trials vs. other studies (0.01)
- Phase II vs. Phase III clinical trials (0.04)
- Phase III vs. Phase IV clinical trials (0.02)

**Reasons for Termination from ClinicalTrials.gov**
- Safety vs. other (0.4)
- Safety vs. unknown (0.8)

**Registration of the National Institutes of Health grants in ClinicalTrials.gov**
- Registered vs. not registered (0.03)

**NIH Funding by the National Cancer Institute (NIH grant database)**
- vs. National Heart, Lung and Blood Institute (0.04)
- vs. National Institute of Mental Health (0.04)
...Selective Publication

“At present, results of most clinical studies of children are unavailable to the pediatric research community and the public.”

Scott Denne, 2012
Investigator Initiated Trials

AZ e-mail:

• ...Lilly run a large and highly effective IIT program...They offer significant financial support but want control of the data in return. They are able to spin the same data in many different ways through an effective publications team. Negative data usually remains well hidden.

• Janssen have a well organized IIT plan...no IIT data is allowed to be published without going through Janssen for approval, and communication is controlled by Janssen. High expectations are set on investigators who publish favourable results but they are well rewarded for their involvement. They seem less concerned than Lilly about negative data reaching the public domain.

• BMS IIT program is growing very fast in launched markets...most proposals are modified by BMS. Strategic focus is unlicensed indications...

• Recommendations...for AstraZeneca...publications should be more creative spinning the data, aka Lilly...”

Spielmans & Parry, 2010
“Medical journals are an extension of the marketing arm of pharmaceutical companies… almost a quarter of a century editing for the BMJ to wake up to what was happening”

Richard Smith, 2005
Markets
Has He Lost That Loving Feeling?

He May Have Low Testosterone (Low T)

Take Action.
Contact your doctor and ask for a Testosterone Test (T-Test).

Low T is a medical condition that often goes undiagnosed because its symptoms are similar to other conditions.

All men can have Low T.
Those who are overweight or who have type 2 diabetes are at greater risk.

Some Symptoms of Low T Include:
- Low sex drive
- Lack of energy
- Decrease in strength and/or endurance
- Deterioration in the ability to play sports
- Falling asleep after dinner
- Deterioration in work performance
- Decrease in the enjoyment of life
- Less strong erections
- Feeling sad and/or grumpy
- Loss of height

Visit: www.lowt.ca
for more information.
"...sound as a bell"

Wise doctor.  
Wise mother.  
Fortunate youngster.

Regular physical examinations plus all the methods developed to prevent or inhibit even the once-casual diseases are now routine in American life.

The magnificent advance made in guarding health by fighting illness before it strikes is still another proud chapter in the history of the medical profession.

According to a recent Nationwide survey:

More Doctors Smoke Camels than any other Cigarette

The "T-Zone" for Taste and Throat

Your "T-Zone" is a most critical "laboratory" when it comes to cigarettes. Try the rich, full flavor of Camel's costlier tobaccos on your taste. See how your throat reacts to Camel's cool mildness. Like millions of other smokers, you too may say, "Camels suit my "T-Zone" to a T!"

- The makers of Camels take an understandable pride in the results of a nationwide survey among 111,907 doctors by three leading independent research organizations.

When queried about the cigarette they themselves smoked, the cigarette named most by the doctors was... Camel. And these doctors represented every branch of medicine—general physicians, surgeons, diagnosticians, and specialists.

Like you, doctors smoke for pleasure. The rich, full flavor and cool mildness of Camel's superb blend of costlier tobaccos are just as appealing to them as to you. Compare Camels—in your own "T-Zone."

CAMELS  Costlier Tobaccos
Expanding Markets…

Olz & bipolar

• “The company is betting the farm on Zytrexa. The ability of Eli Lilly to remain independent and emerge as the fastest growing pharma company of the decade depends solely on our ability to achieve *world class commercialization of Zytrexa*”

• 1997 document: Sales projections would increase fourfold if olz could be viewed as a “Depakote-like MOOD-STABILIZER” rather than a “Risperdal-like…Antipsychotic”

• “To be a leader in the bipolar market, Zytrexa will need to be viewed as a *true mood stabilizer*.”

• According to same document, though, the company did not yet have the data to support this.  

  Spielmans & Parry, 2010
Expanding Markets...

Our challenge

- PCPs have not been trained to recognize this patient...some afraid of the “B” word
- PCPs have traditionally not treated this patient
  - Lack of comfort with the disease state
  - Lack of comfort with the meds due primarily to safety concerns

....We can change their paradigm
…Expanding Markets…

Olz & bipolar

• “Expand our market by redefining how primary care physicians identify, diagnose and treat complicated mood disorders”

• “complicated mood… untapped growth potential”

• Fictional case vignettes that did not meet DSM criteria for BD I created for sales reps to use

• “Doctor, would you agree that you see patients who present with Sx of mood, thought and behavioral disorders who are not responding to your satisfaction”

Spielmans & Parry, 2010
...Overdiagnosis of BD...

- Goldberg et al, 2008
  - Retrospective chart review
  - 85 adults with substance abuse, admitted to inpatient unit over 1 year period
  - only 33% met DSM criteria

- Zimmerman et al, 2008
  - 700 psychiatric outpts c Dx of BD
  - <1/2 met criteria using SCID
...Trends in BD Dx...

![Graph showing trends in bipolar disorder visit rate for youth and adults over years from 1994-1995 to 2002-2003.](image)

Moreno et al, 2007
…Inappropriate prescribing…

- Essock et al 2009: 13% of youth with mental health problems in NY were prescribed 3 or more drugs concurrently.

- Pathak et al, 2010
  - Medicaid database 2001-2005
  - 11,700 <18yo on antipsychotics
  - 1,482 started in 2001, 3,110 in 2005
  - 41.3% no evidence, 17.5% weak
Expanding Markets Further

Olz & Dementia

• 2001 product plan: olz would remain the “bestselling psychotropic drug in history” by treating people suffering from “schizophrenia, bipolar disorder, and dementia”

• Case vignette of widow with early dementia used with GP

• Eli Lilly stated case represented untreated SCZ

  Spielmans, 2009

• 32% of NH residents in ON on antipsychotic (Rochon et al, 2007)

• 50% of NH residents in BC Rx’ed antipsychotic over 1 yr period (BCMOH 2011)
“We can only increase our knowledge if we doubt the extent of our existing knowledge, if we deliberately cultivate doubt — that subjective feeling of uncertainty that helps us to locate our ignorance… a constantly available antidote to the all too prevalent false certainties of contemporary medicine.”

Iona Heath, 2011
Raising questions…
### Effexor = SNRI???

<table>
<thead>
<tr>
<th></th>
<th>venlafaxine</th>
<th>citalopram</th>
<th>fluoxetine</th>
<th>fluvoxamine</th>
<th>paroxetine</th>
<th>sertraline</th>
</tr>
</thead>
<tbody>
<tr>
<td>NE reuptake block</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>5-HT reuptake block</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
</tr>
</tbody>
</table>

Virani et al, 2009
<table>
<thead>
<tr>
<th></th>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>NESRI</td>
<td>Norepinephrine Serotonin Reuptake Inhibitor</td>
</tr>
<tr>
<td>B</td>
<td>NSRI</td>
<td>Norepinephrine Serotonin Reuptake Inhibitor</td>
</tr>
<tr>
<td>C</td>
<td>SCRI</td>
<td>Selective Combined Reuptake Inhibitor</td>
</tr>
<tr>
<td>D</td>
<td>SMRI</td>
<td>Selective Multi-Reuptake Inhibitor</td>
</tr>
<tr>
<td>---------------</td>
<td>------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Depression</td>
<td><strong>Depressive reaction</strong>&lt;br&gt;Classified as a psychoneurotic disorder characterized by anxiety.</td>
<td><strong>Depressive neurosis</strong>&lt;br&gt;No longer considered a form of anxiety, it's now explained as a reaction to internal conflict or the loss of a beloved object or person.</td>
</tr>
</tbody>
</table>
Escitalopram

• Prescriptions now exceed those of citalopram in Canada

• By 2006, outdid citalopram in US, ranking 10th among all drugs (Ioannidis, 2008)
SSRI “discontinuation”?!

- Initial company estimates “at most a few percent”
- Term coined replaced ‘withdrawal’ in 1996, after an Eli Lilly-sponsored symposium on the topic
- Now estimated at “20 to 80%” Stutz, 2007

- "I don't think they're difficult to go off… The vast majority of people aren't that sensitive." Alan Schatzberg, 2006
Atypical…???

- 5-HT?
- Kd?
- Clinically
  - no advantage in tolerability when medication dose taken into account (Geddes et al, 2000)
  - Similar EPS as low-potency FGA, exception clozapine (Leucht et al 2003)
  - CATIE: d/c at 18 mo’s 64% for olz, 75% perph, similar to others (Lieberman et al, 2005)
  - CUTLASS: no diff in QOL, trend favored ‘typicals’ (Jones et al, 2006)
  - TEOSS: no superiority over molindone (Sikich et al, 2008)
  - Meta-analysis of 150 trials: no consistent diffs (Leucht et al, 2009)
  - CZP vs CPZ 9 year outcomes (Girgis et al, 2011)
"The claims of superiority for the [newer drugs] were greatly exaggerated… This may have been encouraged by an overly expectant community of clinicians and patients eager to believe in the power of new medications. At the same time, the aggressive marketing of these drugs may have contributed to this enhanced perception of their effectiveness in the absence of empirical information."

Jeff Lieberman, 2006
The rise and fall of the atypical antipsychotics  (Kendall, 2011)

“Perhaps the importance of these ‘classes’ lies not in their scientific or medical usefulness, but as an example of some of the most effective marketing in pharmaceutical history”
Answers/Solutions???

Suggestions??
Cochrane?

Re Cipriani et al (2009): “I imagine the Pfizer communications machine is now ordering hundreds of thousands of *Lancet* reprints in all major languages. **Before doing any more systematic reviews, we need to decide whether reviewing evidence that is likely to have been carefully sifted and presented by third parties is an ethical action.**”

Tom Jefferson,
Cochrane Acute Respiratory Infections Group, 2009
CPGs?

• 90% APA authors COI (Cosgrove et al, 2009)

• “It would be naive to think that clinical guidelines recommending drugs manufactured by the companies that sponsor the guidelines are any less free of bias than clinical trials” Alan Detsky (Collier, 2011)
A bitter pill?

“...given the commercial influence on medical literature we are not fulfilling our professional responsibility to our patients or ourselves if we trust at face value the sources that we have been taught to trust and are held responsible for enacting. Rather, in this climate of biased and incomplete scientific evidence we must, unfortunately, take responsibility for our own evaluation of what we choose to believe is in the best interest of our patients. This is truly a bitter pill. But refusing to face up to this burdensome responsibility means we are simply left imposing corporate bias on our patients, and that is an even more bitter pill.”

John Abramson, 2010
Detective

- apps.who.int/trialsearch/
- DIDA
- ProPublica Dollars for Docs
- Google
- Narrative

***Your judgment!***
Caution

- Supplements
- MECCs
- “free”
- Flashy / easy / simple
- COI (non-)disclosures

**Follow the money**
Resources

• Prescrire International

• Therapeutics Initiative

• Worst Pills, Best Pills
Your own critical reviews

• Avoid commercial sources
• No need to keep on top of everything – most of the literature is…
• Methods, methods, methods
• Follow the money
• Don’t hesitate to challenge widely-accepted beliefs
• Learn to tolerate uncertainty
Hippocratic Psychopharmacology

- some, not all, diseases be Tx
- Tx enhance natural healing process, not artificial cures
- Tx diseases, not Sx
- meds guilty until proven innocent

Ghaemi, 2008
Rational Prescribing

- Beyond drugs
- Strategic
- Vigilance re adverse effects
- Caution and skepticism
- Shared agenda
- Long-term, broader impacts

Schiff et al, 2011
William Osler, 1909...

“We are at the mercy of our wills much more than of our intellect in the formation of our beliefs, which we adopt in a lazy, haphazard way, without taking much trouble to inquire into their foundation..... For us, however, it must never be the blind unquestioning trust of the devotee, but the confidence of the inquiring spirit that would prove all things. But it is so much easier to believe than to doubt, for doubt connotes thinking and the expenditure of energy, and often the disruption of the status quo.”
“To have the placid faith of the simple believer, instead of the fighting faith of the aggressive doubter, has ever been our besetting sin in the matter of treatment.

In the progress of knowledge each generation has a double labour – to escape from the intellectual thralls of the one from which it has emerged and to forge anew its own fetters.”

William Osler, address to OMA, 1909