

The Prudent Prescriber

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Pharm Reps ≠ Rational Prescribing

Just How Well do Antidepressants Work? (PR) Publication Bias, Spin and Effect Size



(RP)

My spiel to patients with whom I am initiating antidepressant therapy was dealt more blows recently with Turner's, et.al (NEJM, Jan 17, 2008) and Kirsch's et.al (PLOS Med, Feb 2008) published research.

In the 1990s, I typically told patients that there was a 70% chance that my antidepressant prescription would have them feeling much better in three weeks.

In November 2006, the six year, 2876 participant, \$35 million STAR*D trial suggested that only about 1/3 of patients reached a remission with their first antidepressant in 14 weeks. For those who failed to respond, trying a second different antidepressant (and it didn't matter which one) helped another 25%.

Dr. Turner (Oregon Health and Science University) collected reviews from the FDA evaluating 12 antidepressant drugs, tested in 74 studies involving more than 12,500 patients from 1987 to 2004.

Results:

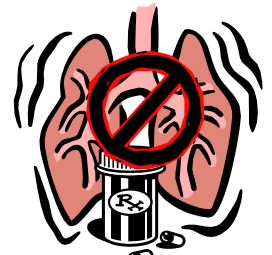
- Of the 38 studies that the FDA considered positive, all but one had been published.
- Of the 36 studies that the FDA considered either negative or questionable, 22 were not published and 11 were published with a positive conclusion (spin?).
- Ergo: Of all the published studies, 94% appeared to have positive findings while analysis revealed that only 51% of the studies were genuinely positive. Publication bias meant that the antidepressants appeared about a third more effective than if all studies had been taken into consideration.

Dr. Kirsch (University of Hull, UK) looked at some (47) of the same clinical trials presented to the FDA for six antidepressants: fluoxetine, venlafaxine, nefazodone, paroxetine, sertraline and citalopram. His study utilizes that rather strict National Institute for Health and Clinical Excellence (NICE) criteria for effect: any effect less than medium (0.5) is deemed not clinically significant.

He concludes, "Clinical efficacy reaches clinical significance only in trials involving the most extremely depressed patients."

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Antibiotics do NOT

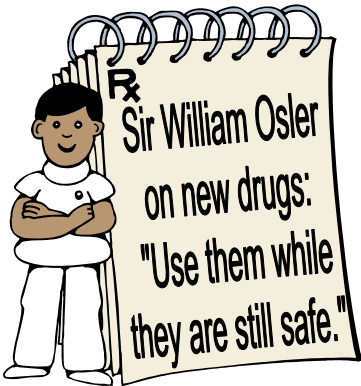


help acute bronchitis

β-blockers in post-MI save lives

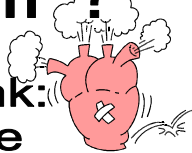


Pill splitters save big



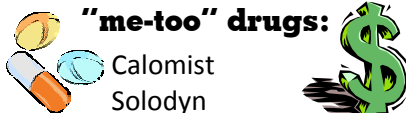
CHF?

Think:



**Ace
Aldactone
B-blocker
Dig
Diuretic**

Avoid these expensive "me-too" drugs:



Calomist
Solodyn
Soma 250
AMrix XR
Xyzal
Veramyst
Ultram ER
Ambien CR

Treat diabetics BP to 130/80



now available
on the
Generic Marquee

Fosamax → alendronate
Altace → ramipril
Norvasc → amlodipine
Ambien → zolpidem
Flonase → fluticasone nasal
Zocor → simvastatin

Just How Well do Antidepressants Work? *continued...*

My Take:

- The antidepressant efficacy “glass” is far from full, but it is not completely empty. The efficacy issue is muddled by definitions of “remission”, “response”, patient selection, dosage, and length of studies.
- I’ll tone down my fluoxetine prognostications and think more often of cognitive approaches to care.
- Recall how powerful the placebo effect of antidepressants is and also how potent is the drug called “doctor”.
- After their decision making with new drugs, the FDA needs to make all their reviews publically available on the web.

This Month’s William Shakespeare’s “Much Ado About Nothing” Award



And the winner is...

Altabax (retapamulin): new topical antibiotic ointment for the treatment of impetigo.

- ☆ Dosed twice daily for 5 days (3 times a day for Bactroban).
- ☆ Comparable efficacy with oral cephalexin in treatment of secondarily infected traumatic lesions. *Surprise!* No head to head studies with Bactroban.
- ☆ Cost: \$85 (15gm tube) vs. \$45 for 22gm tube of generic mupirocin (Bactroban).

Chantix: Be Aware!

There is growing concern about Chantix’s (\$4.32/day) association with mood changes, erratic behavior and suicidal thinking.

- Documentation of 39 completed suicides among 5 million treated patients.
- Behavioral changes are exacerbated by concomitant alcohol consumption.
- Clinical trials for Chantix excluded anyone with alcohol dependence or mental illness.
- Chantix recommendations:
 - 1) Screen patients for psychiatric illness.
 - 2) Advise abstinence from alcohol while on the drug.
 - 3) Monitor for mood changes
 - 4) Warn patients about the potential for unusually vivid dreams.



One Liners

- ☆ Actonel 150mg, once a month, just approved by the FDA (\$91/month). Recall that Fosamax now available as generic alendronate 70mg/week (~\$32/month for cash paying customers)
- ☆ Cialis (tadalafil) now available as 2.5mg tablets for daily use (\$120/month). Marketed: “Around the clock efficacy and no need to plan ahead.”

Erratum



I made a mistake in last month’s Prudent Prescriber! In the abstract reviewing the study promoting daily low dose vitamin K for stabilizing errant protimes, the correct dose of vitamin K should be 150mcg (micrograms), NOT 150mg (milligrams).

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