

The Prudent Prescriber

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Pharm Reps \neq Rational Prescribing

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Are Antidepressants Better than Snake Oil?

In the February 21, 2018 Lancet, Cipriani, the acknowledged king of antidepressant studies and John Ioannidis, a master statistician, *et al*/present the largest ever evaluation of antidepressant efficacy and acceptability. The study is methodologically rigorous. The authors expended significant effort to identify potential sources of bias and error.

Study methods:

- 522 double blind studies involving 116,477 patients.
- This systematic review and network meta-analysis included placebo-controlled and head-to-head trials of 21 antidepressants used for the acute treatment of adults with major depressive disorder.
- Efficacy (response rate) was measured at eight weeks
- Dropout rates at eight weeks were the proxy for acceptability (treatment discontinuations due to any cause)

Results:

- All antidepressants were more effective than placebo with odds ratios (ORs) ranging between 2.13 for amitriptyline and 1.37 for reboxetine.
- For acceptability, only agomelatine and fluoxetine were associated with fewer dropouts than placebo.

Antibiotics do NOT

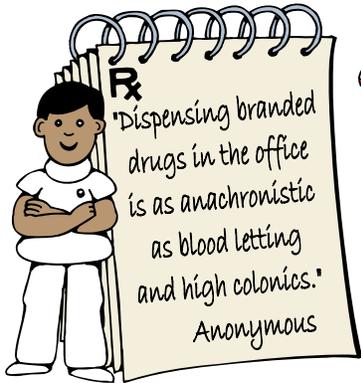


help acute bronchitis

β -blockers in post-MI save lives



Pill splitters save BIG



"Dispensing branded drugs in the office is as anachronistic as blood letting and high colonics."
Anonymous



CHE?

Think:

Ace
Aldactone
B-blocker
Dig
Diuretic



Avoid these expensive "me-too" drugs:



Intermezzo
Vimovo
Livalo
Gralise
Viibyrd
Edarbi
Daliresp

Treat patients > 60 years to 150/90



NOW AVAILABLE
ON THE
GENERIC MARQUEE

Viagra→sildenafil
Effient→prasugel
Strattera→atomoxetine
Asacol HD→mesalamine DR
Pristiq→desvenlafaxine

- In a Lancet commentary, Parikh and Kennedy indicate three drugs scored best when combining both efficacy and tolerability: agomelatine, vortioxetine (Trintellix) and escitalopram. The first is not available in the US; the second is fresh to the US market and priced at \$391/month; generic Lexapro is available for less than \$10 a month. They also posited that the most effective drugs amitriptyline and venlafaxine might be the first choices for severe depression.

My Take:

- This is a Genuine Magnus Opus and in part dispels the “it’s all placebo effect” label that I have ascribed to antidepressants.

but alas.....

- Is eight weeks long enough to predict long term outcomes?
- Cipriani indicates the fact that 78% of the studies were paid for by Big Pharma did not influence the conclusions of the study. Other authors have suggested that antidepressant studies paid for by the pharmaceutical industry are five times more likely to have positive outcomes than those **not** paid for by Big Pharma.
- I slept through the odds ratio portion of my statistics class and I have never been able to get my arms around the concept. When the overall odds ratios in the Cipriani study are converted to effect size, the effect size is ~0.3. This is on a scale where 0.2 is a small effect and 0.5 is a medium effect. **My translation is that this study suggests that antidepressants used for the acute treatment of major depression have a very modest effect.**
- Finally, I recall that some of my biggest successes with depression treatment came at the expertise of a clinical psychologist who employed cognitive behavioral therapy.

Two Myths Exposed

The World Health Organization (WHO) downgrades the status of Tamiflu: No longer an Essential Medicine.

What a debacle:

- The United States spends \$1.5 billion stockpiling Tamiflu
- The UK spends \$770 million stockpiling the drug.
- Roche suppressed five of their eight Tamiflu trials in a serious breach of research ethics.
- A meta-analysis (FamPract 2013; 358; 125-133) published in 2013 found that Tamiflu provided only a 20 hour mean reduction in symptoms and no evidence of reduction in the likelihood of pneumonia, hospitalization or death.
- A Cochrane Review (BMJ; 2014:358:g2545) with a larger set of unpublished studies confirmed the meta-analysis and pointed out Tamiflu’s harms. Nausea, Number Needed to Harm, {NNH} = 28, vomiting (NNH = 22) and psychiatric events (NNH= 94).

My take:

As Mark Ebell points out in his op-ed piece (BMJ; 2017 358:j3266), the system failed us and continues to fail us.

1. All trials should be published. Shame on you, Roche.
2. Dear US government, Beware of stockpiling any drug, particularly those shown to be minimally effective.
3. The CDC continues (as of March 2018) to promote Tamiflu for all hospitalized influenza patients, those that are pregnant and those that are under two or more than 65 years of age. This is nonsensical.
4. Some Justice: There’s a generic oseltamivir now available for \$50, half the price Roche was getting for Tamiflu. **It’s an ineffective drug at any price.**

C-PAP does NOT Reduce Major Cardiovascular Events or Prevent Deaths in Patients with Sleep Apnea

Yu in JAMA 318 (2): 156, July 11, 2017 performed a systematic review and meta-analysis of 10 randomized controlled trials of 7266 patients (follow-up 6 – 68 months) to compare positive airway pressure (PAP) with standard care or sham PAP in patients with obstructive (5683) or central (1583) sleep apnea. The composite outcome included major adverse cardiovascular events (including death) plus hospitalization for unstable angina.

Results:

Positive airway pressure was not significantly associated with the composite outcome or with cardiovascular, all cause or non-cardiovascular deaths.

Authors' Conclusions:

Based on the available evidence, it is reasonable to recommend PAP therapy for the improvement of symptoms in patients with OSA, but not for protection against vascular disease or death.

My take:

The message for both primary care physicians and cardiologists: Quit ordering sleep studies on cardiac patients or any patient who has no symptoms of sleep apnea.

Generic Viagra: Will the White pill work as well as the Blue pill?



Will the marketing director for this generic company lose her/his job for poor word choice in naming their product?

Sildenafil available now per GoodRX, best price (March 16, 2018) in Grand Junction market.

| Dosage mg | Quantity | Rx Cost \$ | Cost per 100mg dose |
|-----------|----------|------------|---------------------|
| 20mg | 30 | \$17.65 | \$2.95 |
| 20mg | 100 | \$38.50 | \$1.93 |
| 50mg | 10 | \$175 | \$35 |
| 50mg | 30 | \$507 | \$ 33.80 |
| 100mg | 10 | \$175 | \$ 17.50 |
| 100mg | 30 | \$507 | \$16.90 |

Both Safeway and City Market offer quantity price breaks on the 20mg size (Revatio for pulmonary hypertension). If you are prescribing the 20mg tablets, mark the indication for ED to avoid confusion. Insurers often will not pay for off-label use. Do not expect the price of the 50mg and 100mg size generic tablets to come down until the six months exclusivity for the single generic company disappears this summer.

You may access previous issues at <https://www.rmhp.org/i-am-a-provider/provider-resources/publications-for-providers>.

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