

“Novel” antidepressants in an era of universal screening for depression:

Challenging industry discourse and practice concerning sexual side effects

Routine screening would expose some patients to avoidable risks and would pose a significant cost burden....The Canadian Task Force on Preventive Health Care (CTFPHC) recommendation to **not** screen for depression in primary care is **consistent with available evidence.**

“There is currently **no evidence** from any well-designed and conducted RCT that screening for depression would benefit women in pregnancy or postpartum... Existing guidelines that recommend depression screening during pregnancy or postpartum should be **re-considered.**”

Source: Thombs, et al Canadian Journal of Psychiatry, 2013

USPTF Recommendations: 2016

Recommendation Summary

Population	Recommendation	Grade (What's This?)
General adult population, including pregnant and postpartum women	The USPSTF recommends screening for depression in the general adult population, including pregnant and postpartum women. Screening should be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up.	B

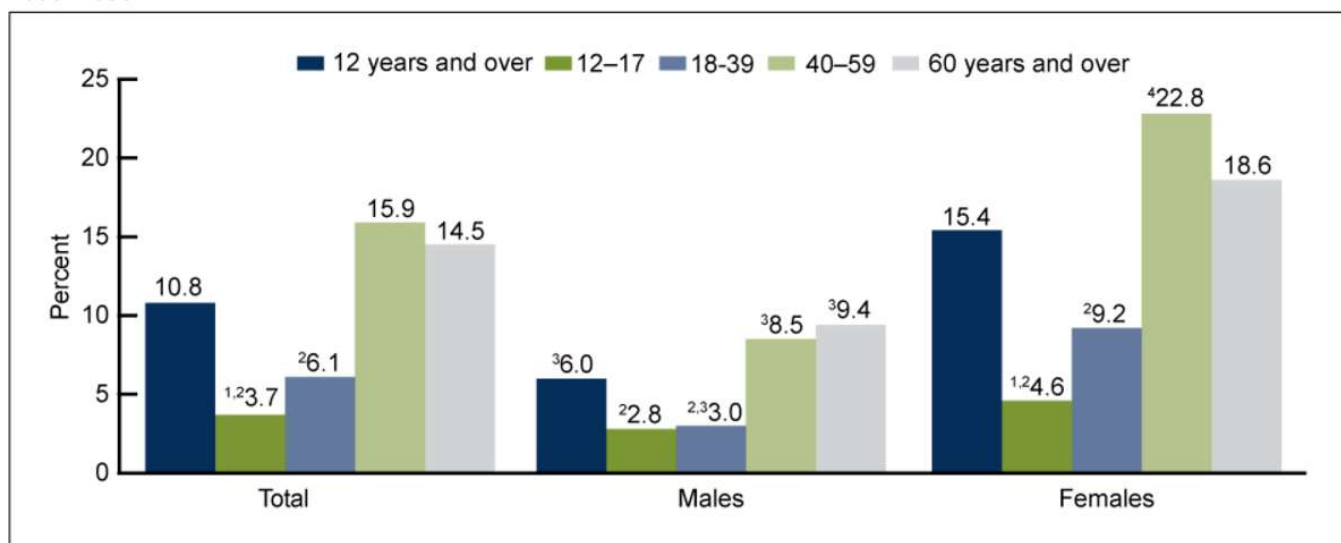
What does Grade B mean:

The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.

Offer or provide this service.

Antidepressant Use in Persons Aged 12 and Over: United States, 2005–2008

Figure 1. Percentage of persons aged 12 and over who take antidepressant medication, by age and sex: United States, 2005–2008



¹Significantly different from age group 18–39. ²Significantly different from age groups 40–59 and 60 years and over. ³Significantly different from females.

⁴Significantly different from age group 60 years and over.

NOTE: Access data table for Figure 1 at: http://www.cdc.gov/nchs/data/databriefs/db76_tables.pdf#1.

SOURCE: CDC/NCHS, National Health and Nutrition Examination Surveys, 2005–2008.

- Women in all age groups are between 2-3 times more likely to be prescribed antidepressant medication compared to men
- 22.8% of women in their 40s and 50s take antidepressants, higher than any other group (by age or sex)

Severity of Illness	Modality			
	Pharmacotherapy	Depression-Focused Psychotherapy	Pharmacotherapy in Combination With Depression-Focused Psychotherapy	Electroconvulsive Therapy
Mild to Moderate	Yes	Yes	May be useful for patients with psychosocial or interpersonal problems, intrapsychic conflict, or co-occurring Axis II disorder	Yes, for certain patients
Severe Without Psychotic Features	Yes	No	Yes	Yes
Severe With Psychotic Features	Yes, provide both antidepressant and antipsychotic medication	No	Yes, provide both antidepressant and antipsychotic medication	Yes

FIGURE 1. Recommended Modalities for Acute Phase Treatment of Major Depressive Disorder

	U.S.	U.K.	SP	ND
Lifestyle	*	X	X	X
Low-Intensity Psychological**		X	X	X
Psychotherapy	X	X	X	X
Antidepressant Medication	X			
Psychotherapy Plus Medication	X			
Other Somatic Therapies	X			

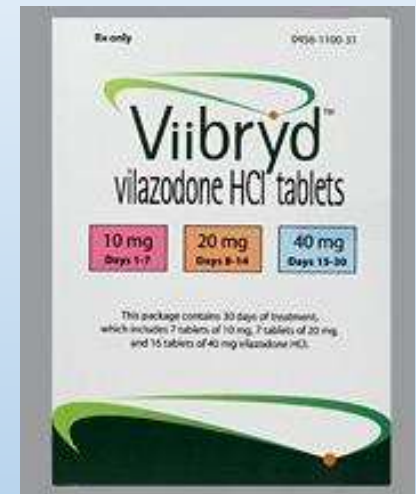
Recommendations for Mild Depression: Step 1

*CPG recommends that, "If a patient with mild depression wishes to try exercise alone for several weeks as a first intervention, there is little to argue against it" (p. 30). Exercise is not included in APA's "Recommended Treatment Modalities" figure.

e.g., guided self help; computerized CBT

Wheeler, Kosterina, & Cosgrove, 2013

Screening in Primary Care will likely lead to



“Novel” Antidepressants

- 1. “Vilazodone, a novel dual-acting serotonergic antidepressant for managing major depression.”**

Source: Khan (2009) Expert Opin Investig Drugs.

“Novel” Antidepressants

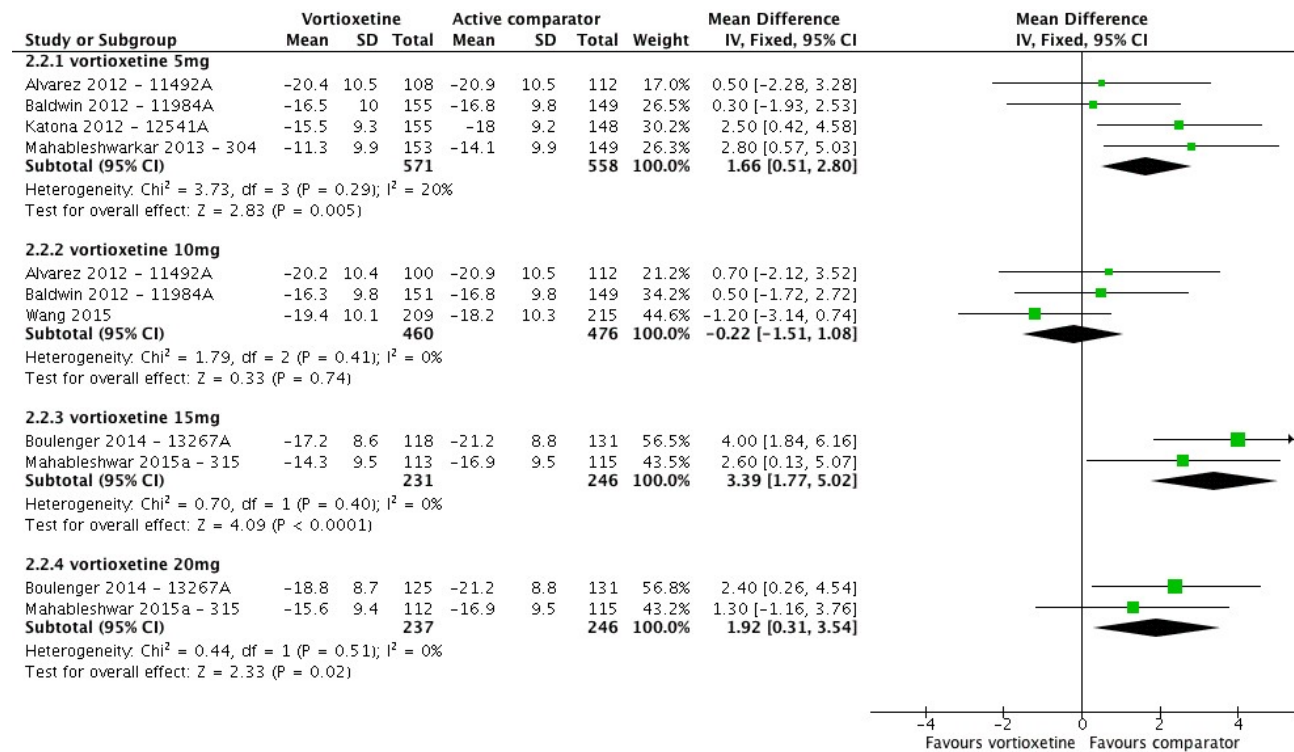
2. “Vortioxetine, a novel antidepressant with multimodal activity”

Source: Sanchez, Asin, Artigas (2015) Pharmacol Ther. 2015

How novel?

Both are SERT inhibitors and agonists of
5HT_{1A} receptor

Exploring efficacy – Meta analysis



Cosgrove et al., 2016

Both Vilazadone and Vortioxetine...

Heavily
marketed as
having a very
good sexual side
effect profile



Source: http://img.timeinc.net/time/daily/2009/0911/360_women_sex_1116.jpg

“If you don’t look properly you won’t find”

Gaming the system: How were the RCTs designed for vortioxetine?

Flawed Data Collection

- Data collection on adverse events was mainly passive via an open-ended question,
“How do you feel?”
- Such passive methods are known to lead to under-reporting.
- Probing for specific adverse effects, which is often done when they are suspected, is typical in clinical research.

Patient-Centered Outcomes

- “Given my personal characteristics, conditions, and preferences, what should I expect will happen to me?”
- “What are my options, and what are the potential benefits and harms of those options?”
- “What can I do to improve the outcomes that are most important to me?”
- “How can clinicians and the care delivery systems they work in help me make the best decisions about my health and health care?”

Arizona Sexual Experiences Scale (ASEX)

- Five-item questionnaire on a Likert scale:
 - How strong is your sex drive?
 - How are you sexually aroused (turned on?)
 - Can you easily get and keep an erection/How easily does your vagina become moist or wet during sex?

If client has had sex in past week:

- How easily can you reach an orgasm?
- Are your orgasms satisfying?

Arizona Sexual Experiences Scale (ASEX)

- ASEX goals:
 - “The ASEX was designed to be simple in order to enhance the overall accuracy in measuring sexual dysfunction by (a) minimizing patient non-compliance with rating, and (b) allowing for rapid quantification and detection of the presence of sexual dysfunction” (McGahuey et al., 2000, p. 27).
- ASEX does not measure change over time or whether a patient believes their medication is affecting their sexuality.

Arizona Sexual Experiences Scale (ASEX)

- Financial conflicts of interest
 - Study published by this team the same year on mirtazapine (Remeron) funded by Organon, (manufacturer of Remeron) using ASEX as an outcome measure:

Gelenberg, A. J., Laukes, C., McGahuey, C., Okayli, G., Moreno, F., & Delgado, P. (2000). Mirtazapine substitution in SSRI-induced sexual dysfunction. *The Journal of clinical psychiatry*, 61(5), 356-360.
 - At the time of this publication (2000), Remeron was still under patent to Organon



Sexual Dysfunction in Randomized Clinical Trials

- Only 2 RCTs for vortioxetine assessed for emergent SD (using the ASEX)
- Dysfunction is so broadly defined that the majority of patients were dysfunctional at baseline (64.5-71.2% in study 304), making it difficult to detect treatment-related effects.
- The FDA review notes that sexual dysfunction increased in a dose-related manner on vortioxetine. At 20mg/ day the frequency (29%) is similar to that on duloxetine 60mg/day (26%), and double the placebo rate (14%) in pooled short-term trials.

Spinning the data in the abstract

- The following finding was highlighted: “ASEX total scores were similar across [placebo and treatment] groups”
- This statement gives the reader the false impression not only that a conclusion about sexual side effects could be made, but also that vortioxetine had a favorable side effect profile for treatment emergent sexual side effects.
- Buried in the article was the accurate statement that “the sample number is too small to draw any conclusions” (Mahableshwarkar et al., 2015).

Vortioxetine (Brintellix™)

- The FDA approved the new antidepressant vortioxetine in 2013
- Key question: Is this newer drug better?



Caveat emptor: Buyer beware

Cost for 1 month's supply of:

Vortioxetine	Duloxetine	Venlafaxine
\$296	\$21	\$15

Source: goodrx.com