

Sexual Dysfunction and Antidepressant Therapy

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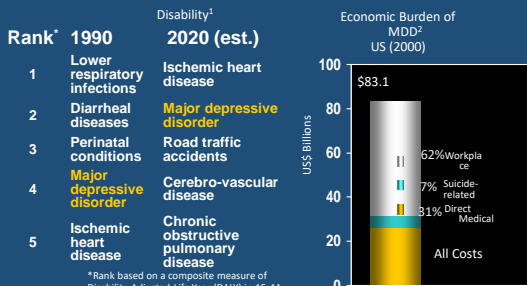


Disclosures

Professor Hopwood has the following relationships to disclose:

- Speaker's Fees / Honoraria**
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- Advisory Board**
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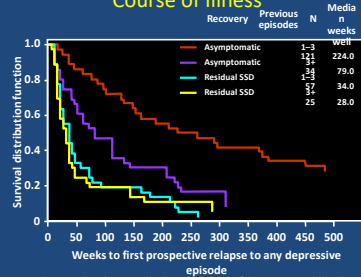
MDD is Disabling and an Economic Burden Worldwide



* Rank based on a composite measure of Disability-Adjusted Life Year (DALY) in 15-44 year olds

1. Murray CJ, et al. Science. 1996;274(5288):745-749
2. Greenberg PE, et al. J Clin Psychiatry. 2003;64(12):1405-1415

Residual Symptoms and Number of Episodes in MDD May Influence the Course of Illness

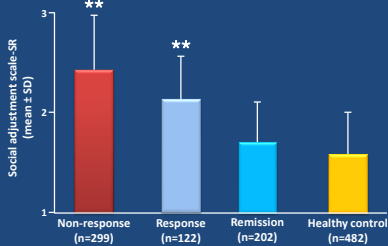


MDD=major depressive disorder; SSD=subsyndromal symptoms of depression; Survival distribution function=cumulative proportion of cases surviving to given time interval.

Judd LL, et al. J Affect Disord. 1998; 50:97-108. Copyright © 1998, by permission from Elsevier.

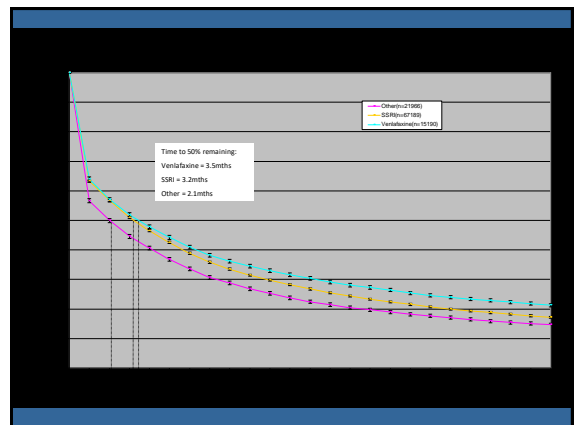
Impairment in work and relationships "normalizes" only with remission

Psychosocial functioning before and after treatment with sertraline or imipramine



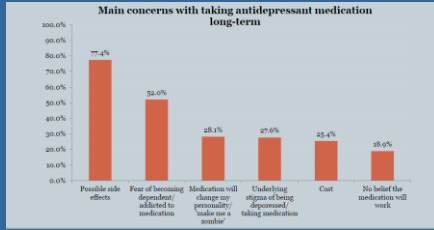
** p<0.05 compared with remission group

Miller et al. J Clin Psychiatry 1998 59(11): 608-19



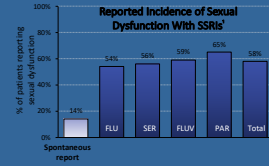
Results-Patient Attitudes/Concerns

- Over half the patients audited (54.9%) had concerns about starting antidepressant treatment.



<https://thinkapp.com.au/education/clinical-audit-tailor-target-antidepressant-initiation-choice-unlock-positive-patient> (accessed 10/01/2018)

Patients respond to questioning on sexual function



A prospective, observational, open, multicenter study to assess antidepressant-associated sexual dysfunction

344 patients (192 women, 152 men)

Greater incidence of sexual dysfunction when patients were directly questioned as compared to incidence when spontaneously reported as an adverse effect

0.83%

Incidence of spontaneous reports of sexual disorders associated with SSRIs in the French Pharmacovigilance Database (98/11,863 adverse drug reactions)²

FLU: Fluoxetine; SER: Sertraline; FLUV: Fluvoxamine; PAR: Paroxetine.
1. Montepío-González AL, et al. J Sex Marital Ther. 1997;23(3):176-194.
2. Trouque T, et al. Drug Saf. 2013;36(7):515-519.

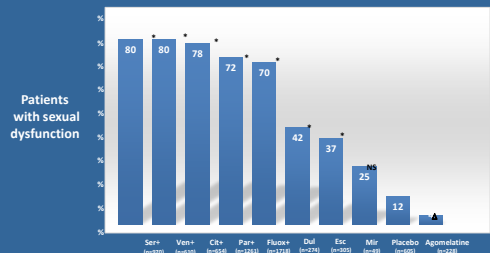
Key side effects of antidepressant classes¹

	Weight gain	Sexual dysfunction	CNS effect (e.g., sedation, fatigue or agitation)	Anticholinergic effect (e.g., dry mouth, tremor)	GI distress
SSRI	+	+++	++	++	++
SH	+	++	+	+	+++
NARI	++	+	+	+	++
NaSSA	++	++	+++	++	+
Melatonergic agonist	+	+	+	+	+
NIDRI	++	+	++	++	+
SNRI	+	+++	++	++	++
TCA	++	+	+++	+++	+
MAOI ²	+	+	+	+	+
SARI	+	+	+++	+	++

1. Adapted from Mahi et al 2015¹¹

KEY: ++=30%, +++=30-50%, +++=50%. SM, serotonin modulator. 1. Some combinations of MAOIs with other drugs can be fatal. Dietary restrictions are necessary to prevent hypertensive crisis.

Sexual dysfunction in patients with depression – meta analysis¹



Studies up to 12 weeks duration:

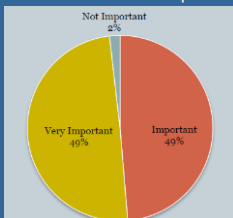
* Sexual dysfunction greater than placebo, p<0.00001. † Sexual dysfunction less than placebo, p=0.0004. ‡ Significant variation across studies.

Rates of sexual dysfunction can vary according to the scale used.

1. Serretti and Chiesa J Clin Pharmacol 2005

Results-patient expectations²

- 98% of patients felt it was 'important' or 'very important' that their GP discussed their treatment preferences with them.



<https://thinkapp.com.au/education/clinical-audit-tailor-target-antidepressant-initiation-choice-unlock-positive-patient> (accessed 10/01/2018)

Sexual Dysfunction-Management

- Careful History
 - Time course
 - ?Relationship to Underlying Depression
 - ?Relationship to Physical Health
 - ?Relationship to Substance Use
 - ?Relationship to relationship
- Nature of Sexual Dysfunction

Sexual Dysfunction-Treatment Alternatives

- Drug Holiday
- Sildefanil
- "Antidote therapy"
 - Psychostimulants
 - dopamine (DA) agonists; amantadine, pramipexole and Dextedrine,
 - norepinephrine (NE)/DA agents such as bupropion
 - serotonin (5-HT)₂ receptor antagonists such as nefazodone
 - α 2-adrenergic receptor antagonists such as yohimbine

The JAMA Network

From: Sildenafil Treatment of Women With Antidepressant-Associated Sexual Dysfunction: A Randomized Controlled Trial
 JAMA. 2008;300(4):395-404. doi:10.1001/jama.300.4.395

Table 2. Sexual Function*

Outcome	Mean (SD)				Change From Baseline (95% Confidence Interval) ^b	P Value ^c
	Placebo (n = 49)		Sildenafil (n = 49)			
Primary						
Clinical Global Impression scale	4.7 (0.9)	3.6 (0.9)	4.8 (0.7)	3.6 (1.1)	0.8 (0.6 to 1.0)	.001
ITIP	4.7 (0.9)	3.6 (1.2)	4.8 (0.7)	3.2 (1.4)	0.6 (0.3 to 0.8)	.03
Secondary						
SFQ domains ^d						
Desire	13.6 (4.7)	16.4 (5.2)	13.0 (4.7)	17.3 (5.1)	1.4 (-0.9 to 3.6)	.22
Arousal-sensation	6.4 (3.4)	10.4 (4.2)	7.1 (3.6)	10.3 (4.2)	1.1 (-0.8 to 2.9)	.24
Arousal-satisfaction	9.9 (2.0)	9.6 (2.3)	8.8 (1.7)	9.2 (2.2)	0.6 (-0.3 to 1.5)	.26
Orgasm	7.9 (2.9)	6.6 (3.0)	5.9 (3.4)	6.6 (3.9)	2.1 (0.9 to 3.6)	.01
Enjoyment	14.3 (5.3)	16.9 (5.4)	13.0 (5.2)	16.0 (5.7)	2.4 (0.1 to 4.7)	.05
Pain	14.1 (5.6)	13.9 (1.6)	13.8 (2.4)	14.1 (5.9)	0.3 (-0.2 to 1.3)	.21
Partner	7.5 (2.0)	7.9 (2.0)	7.0 (1.9)	8.2 (1.6)	0.9 (0.3 to 1.6)	.007
ADQ ^e items						
Sexual drive	4.7 (1.1)	4.2 (1.2)	4.9 (1.2)	4.2 (1.2)	0.2 (-0.2 to 0.6)	.40
Arousal	4.2 (1.0)	4.1 (1.1)	4.5 (0.9)	4.1 (1.1)	0.0 (-0.4 to 0.5)	.81
Lubrication	3.9 (1.1)	3.5 (1.3)	3.8 (1.1)	3.3 (1.1)	0.1 (-0.3 to 0.5)	.64
Ability to reach orgasm	4.8 (0.8)	4.6 (1.0)	5.2 (0.8)	4.3 (1.2)	0.5 (0.1 to 1.0)	.01
Orgasm satisfaction	4.0 (1.4)	3.6 (1.3)	4.5 (1.5)	3.6 (1.4)	0.6 (0.2 to 1.0)	.06
Total score	21.9 (3.6)	20.0 (4.2)	22.9 (3.5)	19.5 (4.6)	1.5 (-0.1 to 3.1)	.06
UNM-QRI items ^f						
Desire	5.0 (1.7)	4.3 (1.6)	5.1 (1.4)	4.1 (1.5)	0.4 (-0.2 to 1.0)	.16
Sexual arousal	5.0 (1.4)	4.4 (1.5)	5.0 (1.3)	4.3 (1.5)	0.2 (-0.5 to 0.6)	.81
Lubrication	4.3 (1.5)	3.6 (1.6)	4.1 (1.4)	3.4 (1.4)	0.3 (-0.3 to 0.6)	.30
Ability to reach orgasm	5.6 (1.2)	5.0 (1.4)	5.9 (1.1)	4.6 (1.6)	0.7 (0.1 to 1.3)	.01
Overall satisfaction	4.9 (1.3)	4.4 (1.5)	5.1 (1.2)	4.0 (1.5)	0.6 (-0.03 to 1.2)	.07
Total score	24.8 (5.6)	22.0 (6.1)	25.2 (4.7)	20.2 (6.4)	2.3 (-0.1 to 4.7)	.06
Harmonization depression scores	4.1 (0.5)	3.6 (0.6)	4.1 (0.4)	3.6 (0.5)	0.2 (-0.5 to 1.0)	.90

Summary

- Sexual Dysfunction is Common in Depressed patients
- Antidepressants can also Variably Induce Sexual Dysfunction
- Patients will regularly NOT Spontaneously Report these concerns
- Management is built Around Awareness, Careful Evaluation and Shared Decision Making
- PDE Inhibitors and other "Antidotes" may have a role
- Consideration of Change in Antidepressant may be Appropriate

THANK YOU

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