Sexual Dysfunction and Antidepressant Therapy

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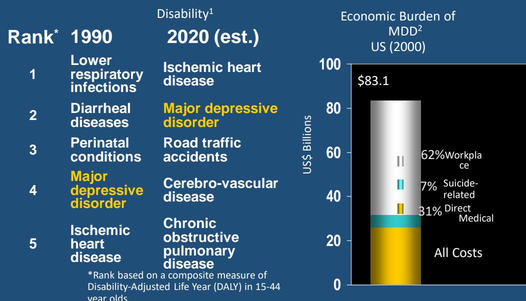
Disclosures

Professor Hopwood has the following relationships to disclose:

- **Speaker's Fees / Honoraria**
  Janssen-Cilag, Lundbeck, Servier, Wyeth
- **Advisory Board**
  Bionomics,Defence Health Foundation, Lundbeck, Phoenix Australia, Summer Foundation, Wintringham
- **Travel Support**
  Eli-Lilly, Janssen-Cilag, Lundbeck, Servier
- **Clinical trials/Research support**
  ISSCR, Lundbeck, NHMRC, Servier, US Department of Defence, VNI

MDD is Disabling and an Economic Burden Worldwide



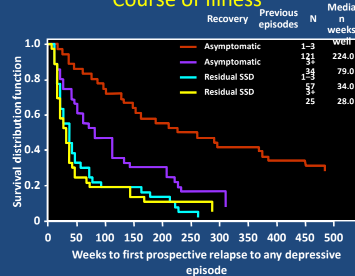
Disability[1]

Rank*	1990	2020 (est.)
1	Lower respiratory infections	Ischemic heart disease
2	Diarrheal diseases	Major depressive disorder
3	Perinatal conditions	Road traffic accidents
4	Major depressive disorder	Cerebro-vascular disease
5	Ischemic heart disease	Chronic obstructive pulmonary disease

*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):740-743
2. Greenberg PE, et al. *J Clin Psychiatry*. 2003;64(12):1465-1475

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

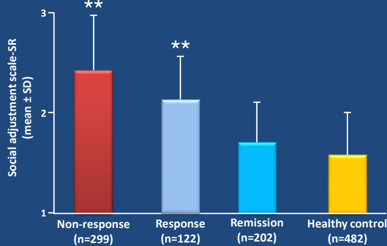


MDD=major depressive disorder; SSD=subsyndromal symptoms of depression; Survival distribution function=cumulative proportion of cases surviving to given time interval.

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

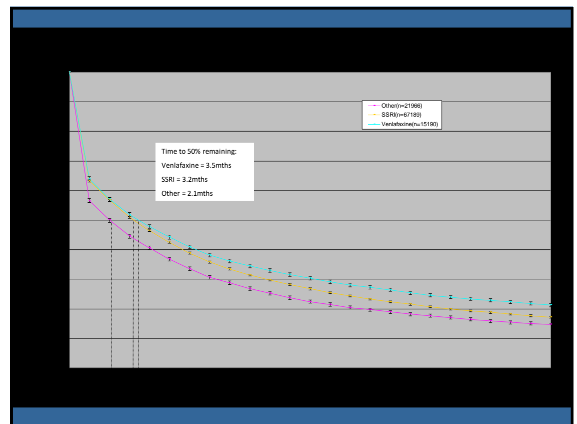
Impairment in work and relationships "normalizes" only with remission

Psychosocial functioning before and after treatment with sertraline or imipramine



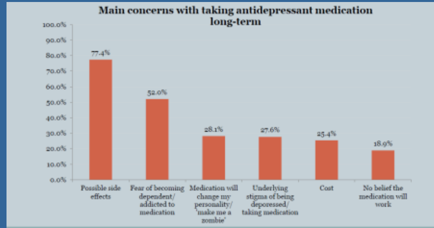
** *p*=0.05 compared with remission group

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



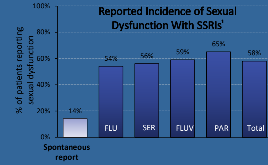
Results-Patient Attitudes/Concerns

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



https://thinkgp.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. Montejo-Gonzalez AL, et al. J Sex Marital Ther. 1997;23(3):176-194.
2. Trenque T, et al. Drug Saf. 2013;36(7):515-519.

Key side effects of antidepressant classes[1]

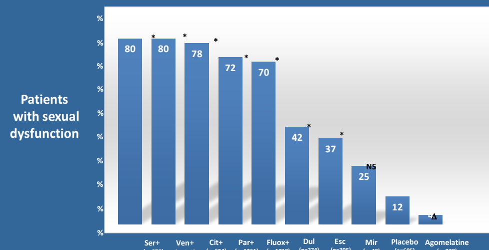
	Weight gain	Sexual dysfunction	CNS effect (e.g., sedation, fatigue or agitation)	Anticholinergic effect (e.g., dry mouth, tremor)	GI distress
SSRI	+	+++	++	++	++
SM	+	++	+	+	+++
NARI	++	+	+	+	++
NaSSA	++	++	+++	++	+
Melatonergic agonist	+	+	+	+	+
NDRI	++	+	++	++	+
SNRI	+	+++	++	++	++
TCA	++	+	+++	+++	+
MAOI[1]	+	+	+	+	+
SARI	+	+	+++	+	++

1. Adapted from Malhi et al 2015[13]

KEY: + <10%, ++ 10-30%, +++ >30%. 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 analysis[1]

Patients with sexual dysfunction



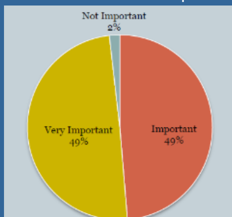
Studies up to 12 weeks duration:
* Sexual dysfunction greater than placebo, p<0.00001 Δ Sexual dysfunction less than placebo, p=0.0004 + Significant variation across studies.

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

1. Serretti and Chiesa J Clin Pharmacol 2009

Results-patient expectations

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



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Sexual Dysfunction-Managemnt

- 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 Dexedrine,
  - norepinephrine (NE)/DA agents such as bupropion
  - serotonin $(5\text{-HT})_2$ 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 DysfunctionA Randomized Controlled Trial**

JAMA. 2008;300(4):395-404. doi:10.1001/jama.300.4.395

Table 2. Sexual Function[a]

Outcome	Placebo (n = 49) Mean (SD)		Sildenafil (n = 49) Mean (SD)		Change From Baseline	
	Baseline	Study End	Baseline	Study End	Mean (95% Confidence Interval)[b]	P Value[c]
Primary						
Clinical Global Impression scale						
ITT[d]	4.7 (0.9)	3.6 (0.9)	4.8 (0.7)	2.8 (1.1)	0.8 (0.6 to 1.0)	.001
ITT-BCF[e]	4.7 (0.9)	3.8 (1.2)	4.8 (0.7)	3.2 (1.4)	0.6 (0.3 to 0.8)	.03
Secondary						
SFQ domains[f]						
Desire	13.6 (4.7)	16.4 (5.2)	13.0 (4.7)	17.3 (5.1)	1.4 (−0.9 to 3.8)	.22
Arousal-sensation	8.4 (3.4)	10.4 (4.2)	7.1 (3.6)	10.3 (4.2)	1.1 (−0.8 to 2.9)	.24
Arousal-lubrication	4.9 (2.0)	5.6 (2.3)	4.9 (1.7)	6.2 (2.2)	0.6 (−0.3 to 1.5)	.20
Orgasm	7.9 (2.9)	8.6 (3.0)	6.9 (3.4)	8.6 (3.9)	2.1 (0.5 to 3.6)	.01
Enjoyment	14.3 (5.5)	16.9 (5.4)	13.0 (5.2)	18.0 (5.7)	2.4 (0.01 to 4.73)	.05
Pain	14.1 (1.6)	13.9 (1.8)	13.8 (2.4)	14.1 (1.9)	0.5 (−0.3 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
ASEX 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	4.5 (1.0)	4.1 (1.1)	4.6 (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)	4.5 (1.0)	5.2 (0.8)	4.3 (1.2)	0.5 (0.1 to 1.0)	.01
Orgasm satisfaction	4.0 (1.4)	3.8 (1.3)	4.5 (1.5)	3.6 (1.4)	0.6 (0.0 to 1.3)	.05
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-SFI items						
Desire	5.0 (1.7)	4.3 (1.6)	5.1 (1.4)	4.1 (1.5)	0.4 (−0.2 to 1.0)	.18
Sexual arousal	5.0 (1.4)	4.4 (1.5)	5.0 (1.3)	4.3 (1.5)	0.2 (−0.5 to 0.8)	.61
Lubrication	4.3 (1.5)	3.9 (1.6)	4.1 (1.4)	3.4 (1.4)	0.3 (−0.3 to 0.8)	.32
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
Hamilton depression score	4.1 (2.5)	3.9 (3.6)	4.1 (2.4)	4.0 (3.5)	0.2 (−1.6 to 1.9)	.86

Abbreviations: ANOVA, analysis of variance; ASEX, Arizona Sexual Experience scale; BCF, baseline carried forward; ITT, intent to treat; LOCF, last observation carried forward; SFQ, Sexual Function Questionnaire; UNM-SFI, University of New Mexico Sexual Function Inventory.

[a] Thirty-seven of 49 women (75.5%) in the placebo group and 39 of 49 women (79.6%) in the sildenafil group completed all 8 end point assessments.

[b] Differences in the change from baseline to each patient's own end point for the change in sexual functioning measured by Clinical Global Impression of Sexual Function improvement.

[c] Calculated as part of the repeated measures ANOVA and using the last-observation-carried-forward algorithm.

[d] The intent-to-treat analysis using the last observation carried forward measured by the mean difference in baseline to study end improvement in placebo-treated group was 1.1 (95% confidence interval [CI], 0.8-1.5) vs sildenafil-treated group 1.9 (95% CI, 1.6, 2.3). The effect size was 0.7 (95% CI, 0.5-0.9).

[e] For patients not completing trial the mean difference in baseline to end point in placebo-treated group was 0.9 (95%CI, 0.6-1.3) vs sildenafil-treated 1.5 (95% CI, 1.1-1.8). The effect size was 0.5 (95%CI; 0.3,0.7).

[f] See the "Methods" section for the 7 SFQ domain scoring ranges. All randomized women providing responses to all domain questions at baseline or study end of treatment, or time of discontinuation, were included in analysis of that domain. Nonapplicable responses were treated as missing.

Date of download: 3/1/2018

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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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