ANTIDEPRESSANT COMPARISON CHART [1,2,3,4,5,6,7]

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NAME: Generic / TRADE (g=generic availability)	RECEPTOR AFFINITY	SIDE EFFECTS ACH.	SED.	OTHER	COMMENTS & ADDITIONAL USES (Bold indicates official indication in Canada)		INITIAL & MAX. DOSE	USUAL ADULT DOSE RANGE	$ /Month
Citalopram CELEXA$_g$ (20, 40mg **scored** tabs) abr=**CC**	**escitalopram CIPRALEX**✗ S(+)citalopram 10^{S}-20^{S}mg od ~$60	+	+	**SSRIs SE in General** **nausea** {21%(F) - 36% (X)}, anxiety, insomnia {~14%}, agitation,anorexia,**tremor** somnolence {11-26%}, sweating, dry mouth, **headache**, dizziness, diarrhea {12% (F,P)-17% (S)}, constipation {13-18%}, EPS sexual dysfx.{>30%}[8,9],SIADH **Toxicity can**→depression **D/C Syndrome** [10]→flu-like Sx's **'FINISH'** flu,insomnia, nausea,imbalance,sensory dist., hyper.	•**fewest drug** interactions	**Therapeutic Uses**:[11,12] √ OCD (esp. **F, P,S,X**) √Panic(esp. **P,S**;F,CC,X) √ GAD (**P**); ?others √ Bulimia nervosa (**F**) √Diabetic neurop.(CC) & deter use of EtOH √ PTSD(P,S),√PMDD(F,P,S) √Social Phobia (**P**,S) √ Pediatric (F,S,X) +ve effect on headache? •**flat dose response** (majority of depressed pts respond at the **lowest effective dose**)	**10-20mg am** 60mg/d	20mg po od 40mg po od	**27** 27
Fluoxetine PROZAC$_g$ (10,20,40✗▼mg **cap** & 4mg/ml **soln**) abr=**F**	**5HT SELECTIVE SSRI's**	0	0		•**most anorexic** & stimulating •long half-life (5 wk washout) •90mg **weekly** avail. in USA		10-20mg od 80mg/d	(10mg po od) † 20mg po od am 40mg po od am	41 **30** 53
Fluvoxamine LUVOX$_g$ (50,100mg scored tabs) abr=**X**		0/+	++		•most **nauseating**, constipating & sedating SSRI; ↑ DI's		**25-50mg hs** 300mg/d	100mg po hs 150mg po hs 50mg am & 150mg hs	**30** 41 53
Paroxetine PAXIL$_g$ (10^{S},20^{S}, 30mg tab) abr=**P** {**Paxil CR** 12.5,25mg tab✗⊗ }		+	+		•most anticholinergic of SSRIs •most official **anxiety** indications •↑weight & D/C reaction possible[13]		10-20mg am 60mg/d	10-**20**mg po od am 30mg po od am 40mg po od am 12.5-25mg **CR** od am✗⊗	44-**32** 33 57 64-68
Sertraline ZOLOFT$_g$ (25,50,100mg cap) abr=**S**		0	+		•most diarrhea & male sexual dysfx of SSRIs •?benefit heart dx pts[14],**few drug** interactions[15]		**25-50mg am** 200mg/d	100mg po od cc 50mg am &100mg pm 100mg po bid cc	**34** 59 61
Nefazodone SERZONE DISCONTINUED abr=**Z**	**SARI 5HT Selective** SSRI+5HT$_2$ rec. antagonism	+	+++	As for SSRIs +: ↓ BP Rare:**hepatotoxicity**[16]	•least stimulating serotonergic •**less wt** gain;**less sex** dysfx,**DI**'s	•useful in anxiety & **insomnia**	50-100mg bid 600mg/d	100mg po bid 150mg po bid **DISCONTINUED Canada NOV03**	
Trazodone DESYREL$_g$ (50;75✗▼;100mg scored tabs) (150mg Dividose tab:50/75/100/150mg ✗▼)		**0**	++++	↓↓ **BP**, dizzy, headache, nausea; (α_1 blockade); **priapism** 1/6000, (Tx epi)	√dementia 50mg hs (**insomnia**, **sundowning**, aggression); less cardiac effects than TCAs	√ Panic, chr. pain √ **Sleep disorders:** 50-100mg hs	50mg bid 600mg/d	50mg po hs 100mg po bid pc 200mg po bid pc	14 27 **48**
Amitriptyline ELAVIL$_g$ (10, 25,50mg; 75mg✗▼tab)	**5HT & NE EFFECTS** tertiary (**3°**) amine **TCA's**	+++++	+++++	**General TCA SE**: ↑HR, ↓BP (Tx: fluid+/- Florinef), **weight gain**, sexual dysfx, sweating, rash, tremors, ECG abnormalities, seizures •fatal in overdose [17] (≥2gm) due to cardiac & neurologic toxicity.	•often 10-30^{+}mg hs for sleep, **IBS** & chronic pain •Cp	**Therapeutic Uses** [18] √ **Pain** Syndromes[19] & sleep disorders[20] (amitriptyline; but 2° TCA nortriptyline useful & less SE) √ Neuropathy √ Agitation & insomnia √ Panic→ imipramine √ **Migraine** prophylaxis[21] (esp.amitrip./nortriptyline) √ Smoke D/C→nortrip. √ ADD(ie. desipramine)	10-25mg hs 300mg/d	50 mg po hs 200mg po hs	15 **34**
Clomipramine ANAFRANIL$_g$ (10, 25, 50mg tab)		+++++	++++		•esp. effective for **OCD**$^{\geq 10yrs}$ •Most serotonergic TCA; •Cp •higher risk of seizures		10-25mg hs 300mg/d	50 mg po hs 150mg po hs 200mg po hs	22 51 **65**
Doxepin SINEQUAN$_g$ (10,25,50,75,100,150mg cap)		+++	++++		•Most histamine block; •Cp •√ psychoneurotic/anxious dep.		10-25mg hs 300mg/d	50 mg po hs 200mg po hs	15 **52**
Imipramine TOFRANIL$_g$ (10, 25, 50; 75✗▼mg tab)		+++	+++		•Cp √ Childhood enuresis (age 6+)		10-25mg hs 300mg/d	50 mg po hs 150-200mg po hs	18 40-**51**
Desipramine NORPRAMIN$_g$ (10, 25, 50, 75,100mg tab) (**50mg** tabs better price in SK)	**NE > 5HT** secondary (**2°**) amine **TCA's**	++	++		•Most NE activity •**Least ACH** side effects •Cp		10-25mg hs 300mg/d	50 mg po hs 150mg po hs (3x50mg) 200mg po hs (4x50mg)	19 43 **55**
Nortriptyline AVENTYL$_g$ (10, 25mg cap)		+++	++		•**Least hypotensive** TCA •Cp (response may be higher at low end $^{=50mg}$ of dose range[22])		10mg hs **150mg/d**	25mg po hs 50mg po hs 100mg po hs	14 **20** 35
Venlafaxine EFFEXOR (**Reg** 37.5,75mg scored tabs-Co **D/C** Jul04) (**XR** 37.5mg, 75mg, 150mg caps) (contents of XR caps may be **sprinkled**)	**SNRI 5HT & NE** (also some DA)	++	+	•**As dose↑: ↑BP**, agitation, tremor,sweating,nausea~37%, headache, sleep disturbances •caution:**withdrawal effects**	•initial nausea; "clean TCA" •side effects similar to SSRIs; •**low wt** gain; **few drug** interactions •adjust dose for ↓ renal fx	√Generalized & social anxiety disorder √for BPAD depressed; relapse ^{prevents} & ↓recurrence	18.75-37.5mg 375mg/d	37.5mg **XR** po od 75mg **XR** po od 150mg **XR** po od 225mg **XR** od (if 2-3 cap)	**37** **66** **69** 135-184
Bupropion SR WELLBUTRIN$_g$ (100mg, 150mg tab)	**NDRI DA & NE**	0	0	agitation, insomnia, tremor, ↓**appetite**, GI upset, psychos.	•↑'d risk of **seizure** ~0.4% 400mg/d •**less sex dysfx**, **low wt**. **gain**	=**ZYBAN**→D/C smoking; √ BPAD	100mg od am 450mg/d	100mg po bid 150mg po bid	47 **47**
MAOIs: non-selective & irreversible; ✓atypical/refractory depression; enzyme effect ~10days; many DIs & food cautions (tyramine-hypertensive **crisis**);phenelzine *NARDIL* 15mg tab bid-tid; tranylcypromine *PARNATE* 10mg tab bid-tid									
Mirtazapine REMERON$_g$ 15^{S},30^{S},45mg tabs⊗ (**RD** 15,30,45mg tab⊗$^{\uparrow S}$)	**NaSSA$_{5HT\ \&\ NE}$**	+++	++++	Dry mouth,sedation,DI-clonidine	↑ appetite&weight ;↓ sexual dysfx	√Anxiety,Somatization	15-45mg/day	15-30mg po hs	21-**35**
Moclobemide MANERIX$_g$ (100,150,300mg scored tabs) (2x150mg tabs **cheaper** than 300mg tab)	**RIMA** Selective & Reversible	+	0	Dry mouth, dizzy, headache, nausea, tremor, restless, **less sex dysfx**	•no dietary tyramine precaution •enzyme effect lasts ~24hrs **DI**:meperidine,sympathomimetics,DM…	√Atypical, √**Anxious-phobic**, √Co-morbid anxiety	100mg bid 600-900mg/d	150mg po bid pc 300mg am&150pm pc 300mg po bid pc	**26** 36 58

=↓ dose for renal dysfx ς=scored tab ☎ **EDS** ✗ non-formulary in SK (✆=prior approval NIHB ▼=covered by NIHB ⊗=not NIHB **COST**=total cost **5HT**=serotonin **ACH**=anticholinergic effects (dry mouth,constipation,urinary hesitancy,blurred vision) **ADD** =attention deficit disorder **BP** =blood pressure **Cp** =plasma levels avail **DA** =dopamine **DI** =drug interactions **epi** =epinephrine **GI** =gastro-intestinal **HR** =heart rate **MAOI** =monoamine oxidase inhibitors **NE** =norepinephrine **OCD** =obsessive compulsive disorder **RIMA** reversible inhibitor of MAO-A **SE** =side effects **SED** =sedation **SSRI** =selective 5HT reuptake inhibitor **TCA** =tricyclic antidepressant **Tx** =treatment **wk** =week **wt** =weight **INITIAL DOSE** -Lower initial dose rec for elderly/sensitive pts. † =initial dose lower than usual effective dose. **Pregnancy**: **C** agents: fluoxetine (**most** clinical experience), paroxetine (**inactive** metabolites) & sertraline. **B** agents: bupropion but less clinical experience.

Not in : **Duloxetine CYMBALTA** (20,30,60mg cap) 40-60mg/d Max 120mg. SE: insomnia, somnolence, headache, nausea, diarrhea, ↓appetite, fatigue, ↑sweating,↑BP, ↑LFTs,↑DI's & dry mouth. For adult depression, diabetic peripheral neuropathic pain & ? effective for stress urinary incontinence.

Augmentation→options in partial responder: some evidence (esp. with TCA's for adding lithium ~600-900mg/d or l-thyroxine ~100ug/d; for buspirone, pindolol, olanzapine & tryptophan with SSRI). **Combo's** ? bupropion or mirtazapine (with SSRI or venlafaxine).

Table 1:Adverse Effects: Management Options [23,24]

- **Dizziness** ☞check BP for **orthostatic hypotension**; mild symptoms may attenuate over several weeks; ↓ dose or switch agent; encourage adequate fluid intake & avoid excessive salt restriction; Florinef 0.1mg po od & titrate
- **Sedation/ feeling medicated/ foggy** ☞may attenuate over 1-2 weeks; give single dose 1-2 h prior to bedtime; ↓ dose or choose alternative agent
- **Peripheral anticholinergic effects** ☞ tolerance may develop over several weeks; switch to alternative agent; treatment options for some Sx:
  - **blurry vision**-pilocarpine eye drops;methylcellulose drops for dry eyes
  - **urinary hesitancy** - bethanechol 25-50mg po tid-qid
  - **abdominal cramps, nausea, diarrhea** - adjust dose
  - **dry mouth** - sugarless gum; saliva substitutes(e.g.ORAL balance Gel)
  - **constipation** - adequate hydration, activity, bulk forming laxatives
- **Weight gain**☞ modify & monitor diet & activity;switch to alternate agent
- **Sexual dysfunction** ☞ distinguish etiology (drug vs illness); switch to: (bupropion,mirtazapine,moclobemide, venlafaxine$^{\downarrow dose}$); adjust dose;

Other:
- ↓ libido→ neostigmine 7.5-15mg 30min prior to intercourse
- impaired erection → bethanechol 10mg po tid
- anorgasmia → cyproheptadine (Periactin) 4mg po qam
- antidepressant induced erectile dysfunction → sildenafil may help [25]

- **Myoclonus**☞ ?TCA toxicity; reassess dose/levels; clonazepam 0.25mg tid
- **Insomnia & anxiety (5HT related)**☞ ↓dose; administer in am; + short course of trazodone 50-100mg hs; switch to alternate agent
- **SIADH (syndrome of inappropriate antidiuretic hormone secretion)** (hyponatremia) ☞ DC causative agent; fluid restriction (1 l/d)
- **Serotonin Syndrome**[26] (eg. excitement,diaphoresis,rigidity,↑temp,tremor,clonus, ↑reflexes,↑HR,↑BP,delirium) D/C serotonergic meds;Tx: Periactin 4mg po q4h, diazepam
- **Discontinuation syndrome** with abrupt withdrawal of agents a flu-like syndrome (FINISH: flu, insomnia, nausea, imbalance, sensory disturbances & hyperactivity) may occur. Tx: **TAPER** off original antidepressants slowly over several days or give benztropine (for cholinergic rebound→nausea/vomiting, sweating), lorazepam (for agitation/insomnia), propranolol (for akathisia) as necessary.

Table 4: Individualizing Therapy Considerations[27]

Anxiety/Panic	✓SSRIs, venlafaxine, mirtazapine
Anxiety, Comorbid	✓moclobemide, mirtazapine, ? buspirone
Atypical*	✓moclobemide, MAOIs, SSRIs
Bipolar	✓mood stabilizer (+/- antidepressant) e.g. lithium, valproic acid, carbamazepine
Cardiac Condition	✓SSRIs, MAOIs, bupropion
Chronic Pain/Neuropathy[28]	✓ TCAs: amitriptyline, desipramine, nortriptyline
Drug Induced [29,30]	stop or reduce offending agent (see bottom)
Elderly [31,32]	✓SSRI(CC,P,S,X,Z);venlafaxine;RIMA;bupropion; **2°** TCA
Migraine[33]	✓amitriptyline, nortriptyline
Obsessive Compulsive	✓SSRI (high dose), clomipramine
Orthostatic Hypotension	✓venlafaxine(↑BP); nortriptyline, SSRIs (ambulation, hydration, gradual dose titration)
Phobic	✓moclobemide, MAOI, paroxetine?
Psychotic	✓+ antipsychotic (or amoxapine)
Seizure History	✓trazodone,SSRIs,moclobemide,venlafaxine
Sleep Disorders[34]	✓trazodone, amitriptyline
Smoking Cessation[35]	✓bupropion, nortriptyline
Weight Gain, Less[36]	✓bupropion, SSRIs, RIMA,venlafaxine

Table 2: Precautions [37,38,39]

TCAs: benign prostatic hypertrophy, history of urinary retention, uncorrected angle closure glaucoma, seizure history, post-MI - acute recovery phase, cardiovascular disease, cholinergic rebound upon withdrawal from high doses (dizziness, nausea, diarrhea, insomnia, restlessness, cardiac conduction delays, heart block; arrhythmias)

SSRIs: hepatic dysfunction (↑ levels & half-life), irritable bowel syndrome, CNS overstimulation (e.g. ***serotonin syndrome***) [40] especially if used in combination with other serotonergic drugs (buspirone, dextromethorphan, lithium, MAOI, meperidine, mirtazapine, MDMA, ondansetron,silbutramine,St. Johns Wort,sumatriptan,tramadol,tryptophan, TCA)[41]; withdrawal syndrome: dizziness, GI upset, headache, sleep disturbance, agitation/restlessness (usually mild & transient; less common with fluoxetine) [42]

Bleeding: assoc. by degree of serotonin reuptake inhibition & risk of bleeding$^{<0.5\%}$ [43]

MAOIs: hypertensive crisis can occur secondary to foods containing **tyramine** {e.g. HIGH → Unpasteurized cheese (cheddar, camembert, blue), yeast extract, herring, aged unpasteurized meats, broad bean pods; MODERATE→ avocado, meat extract, certain ales & beer, wine; LOW→ fruit, cream & cottage cheese, distilled spirits, chocolate}; Contraindicated: cerebrovascular/heart disease, geriatric or debilitated, pheochromocytoma, or history of severe headache.

Bupropion: avoid if hx of seizures, bulimia or anorexia nervosa

Pediatric Precautions: Safety in kids **not** well established [44,45,46,47] (Concern→ suicide & agitation.) Imipramine for enuresis in kids≥6 yrs. FDA:Fluoxetine$^{depression\ (48)\ \&\ OCD}$;clomipramine, fluvoxamine & sertraline^{OCD,49}.

Pregnancy: Consider risk vs benefit! ECT & psychotherapy are non-drug options. TCAs & SSRIs: most clinical safety data (Pregnancy category B: bupropion but less clinical experience. Some C agents may be preferable: **fluoxetine** (most experience), **paroxetine** (no active metabolites) & sertraline. Use lowest dose & try to taper off 5-10 days before delivery.[50,51,52,53,54,55] Neonates exposed late 3rd trimester may experience withdrawal.[56]

Breast feeding: consider risk vs benefit; psychotherapy; levels often <10% of maternal dose; esp. SSRI's & also nortriptyline used (**sertraline**, paroxetine & fluvoxamine:↓ levels & no reported adverse effects; fluoxetine & venlafaxine: ↑ breast milk level). [57,58,59,60]

Elderly: extra caution required; med dose: start low & go slow

Relative Seizure Risk:[61]

HIGH→ maprotiline, amoxapine, clomipramine, bupropion
LOW→amitripyline,imipramine,trimipramine,nortriptyline,desipramine,doxe
LOWEST→ trazodone, SSRI'S, MAOI'S, moclobemide, venlafaxine

***Atypical depression** defined as: mood reactivity; irritability; hypersomnia; hyperphagia; psychomotor agitation & hypersensitivity to rejection.

DRUG INTERACTIONS: Various cytochrome **P450 inhibition**[62] by SSRI's. Less DI's [63]: **citalopram, mirtazapine, moclobemide, sertraline & venlafaxine**.

Drug	CYP450 1A2	CYP450 2C9	CYP450 2C19	CYP450 2D6	CYP450 3A4
citalopram	0	0	0	+	0
fluoxetine	+	++	+ to ++	+++	+ to ++
fluvoxamine	+++	++	+++	+	++
paroxetine	+	+	+	+++	+
sertraline	+	+	+	+ to ++	+

Table 3: Switching Antidepressants: Recommended washout period (DAYS) in outpatients [64,65,66]

The more critical recommendations are in **bold**; risks of toxicity are greater with higher dosage regimens and inadequate washout period. **Some urgent cases may necessitate shorter delays in switching**.

FROM	SWITCH TO ☞ amitriptyline,clomipramine doxepin, Imipramine desipramine,nortriptyline	mirtazapine,venlafaxine	fluoxetine, fluvoxamine, paroxetine citalopram,sertraline,nefazodone,trazodone	phenelzine	tranylcypromine	moclobemide	bupropion
amitriptyline	1*	1#	1-7†	7†		1†	1-7†
clomipramine	1*	1#	**7-14†**	7†		1†	7-14†
doxepin	1*	1#	1-7†	7†		1†	1-7†
imipramine	1*	1#	1-7†	7†		1†	1-7†
desipramine	1*	1#	1-7†	7†		1†	1-7†
nortriptyline	1*	1#	1-7†	7†		1†	1-7†
mirtazapine	1#	1†	3†	7†		3†	3†
venlafaxine	1#	1†	3†	7†		3†	3†
fluoxetine	**35**!	**35**!	**1**!	**35**!		**35**!	**1**!
fluvoxamine	1-7†	7†	1#	7†		1†	1+
paroxetine	1-7†	7†	1#	**10**†		1†	1+
sertraline	1-7†	7†	1#	**10**†		1†	1+
nefazodone	1-3†	3†	1#	7†		1†	1+
trazodone	1-7†	7†	1#	7†		2†	1+
phenelzine	**10-14**	**14**	**10-14**		**14**	2##	**14**
tranylcypromine	**10-14**	**14**	**10-14**	**14**		2##	**14**
bupropion	**1-3**†	**1**†	**1**†	**7**†		**3**†	
moclobemide	**2**	**2**	**2**	**2**			**2**

* no washout required; use equivalent dose;
† taper first drug; start 2nd drug at a low dose;
# taper first drug over 3-7day prior to initiating 2nd drug;
taper if high dose; maintain dietary restriction for 10d;
! use lower doses of 2nd drug initially; longer tapering period (**8** weeks) may be required for high doses of fluoxetine

Antidepressant Drug Interactions: page 41

Drug induced depression: ACEI, acetazolamide, amphetamine & cocaine withdrawal, anticonvulsants, amantadine, barbiturates, BCPs, benzos, bromocriptine, caffeine, chemotherapy^{some}, cimetidine, clonidine, dapsone, digoxin, disulfiram, efavirenz, ethambutol, ethanol, griseofulvin, haloperidol, hydralazine, interferon, isoniazid, isotretinoin, levodopa, mefloquine, methyldopa, methylphenidate, methysergide, metoclopramide, metronidazole, nitrofurantoin, NSAIDs, opiates, physostigmine, procainamide, propranolol, reserpine, streptomycin, steroids, sulfas, tetracycline & thiazides.

[1]Jefferson J, Greist JH. Mood Disorders in Textbook of Psychiatry, 2nd Ed. Editors: Hales RE, Yudofsky SC, Talbot JA. American Psychiatric Press, Washington, 1994.
[2] Micromedix Drug Information, 2005.
[3] Geddes JR, Carney SM, Davies C, Furukawa TA, Kupfer DJ, Frank E, Goodwin GM. Relapse prevention with antidepressant drug treatment in depressive disorders: a systematic review. Lancet. 2003 Feb 22;361(9358):653-61.
[4] **Treatment Guidelines**: Drugs for Psychiatric Disorders. **The Medical Letter**: July, **2003**; p. 69-76.
[5] Remick RA. Diagnosis and management of depression in primary care: a clinical update and review. CMAJ. 2002 Nov 26;167(11):1253-60.
[6] Practice guideline for the treatment of patients with major depressive disorder (revision). **American** Psychiatric Association. Am J Psychiatry. **2000** Apr;157(4 Suppl):1-45.
[7] Trindade E, Menon D, Topfer LA, Coloma C. Adverse effects associated with selective serotonin reuptake inhibitors and tricyclic antidepressants: a meta-analysis. CMAJ. 1998 Nov 17;159(10):1245-52.
[8] Modell JG, Katholi CR, Modell JD, et. al. Comparative sexual side effects of bupropion fluoxetine, paroxetine, and sertraline. Clin Pharmacol Ther 1997;61(4):476-87.
[9] Gonzalez M, Llorca G, Izquierdo JA, et.al. J Sex Marital Ther 1997;23(3):176-94.
[10] Ditto KE. SSRI discontinuation syndrome. Awareness as an approach to prevention. Postgrad Med. 2003 Aug;114(2):79-84.
[11] Grady-Weliky TA. Clinical practice. Premenstrual dysphoric disorder. N Engl J Med. 2003 Jan 30;348(5):433-8.
[12] Pearlstein T. Selective serotonin reuptake inhibitors for premenstrual dysphoric disorder: the emerging gold standard? Drugs. 2002;62(13):1869-85.
[13] Which SSRI? Med Lett Drugs Ther. 2003 Nov 24;45(1170):93-95.
[14] Glassman AH, O'Connor CM, Califf RM, et al.; Sertraline Antidepressant Heart Attack Randomized Trial (SADHEART) Group. Sertraline treatment of major depression in patients with acute MI or unstable angina. JAMA. 2002 Aug 14;288(6):701-9. (Taylor CB, Youngblood ME, Catellier D, et al.; ENRICHD Investigators. Effects of antidepressant medication on morbidity and mortality in depressed patients after myocardial infarction. Arch Gen Psychiatry. 2005 Jul;62(7):792-8 -Observational secondary analysis)
[15] Bezchlibnyk-Butler K. Serotonergic antidepressants: Drug response and drug-drug interactions. Pharmacy Practice:National CE Program 1998;Aug:1-8.
[16] Stewart DE. Hepatic adverse reactions associated with nefazodone. Can J Psychiatry. 2002 May;47(4):375-7.
[17] Buckley NA, McManus PR. Fatal toxicity of serotoninergic and other antidepressant drugs: analysis of United Kingdom mortality data. BMJ. 2002 Dec 7;325(7376):1332-3.
[18] Furukawa TA, McGuire H, Barbui C. Meta-analysis of effects and side effects of low dosage tricyclic antidepressants in depression: systematic review. BMJ. 2002 Nov 2;325(7371):991.
[19] Maizels M, McCarberg B. Antidepressants and antiepileptic drugs for chronic non-cancer pain. Am Fam Physician. 2005 Feb 1;71(3):483-90.
[20] Houdenhove BV, Onghena P. Pain and Depression in Depression and Physical Illness. Editors: Robertson MM, Katona CLE. Wiley & Sons, New York, 1997.
[21] Pryse-Phillips WEM, Dodick DW, Edmeads JG. Guidelines for the diagnosis and management of migraine in clinical practice. Can Med Assoc J 1997;156:1273-87.
[22] Wells BG, Mandos LA, Hayes PE. Depressive Disorders in Pharmacotherapy: A Pathophysiologic Approach 3rd Ed., 1996.
[23] Tollefson GD. Antidepressant treatment and side effect considerations. J Clin Psychiatry 1991;52(5-suppl):4-13.
[24] Cole JO, Bodkin JA. Antidepressant side effects. J Clin Psychiatry 1990;51(1):21-26
[25] Nurnberg HG, Hensley PL, Gelenberg AJ, Fava M, Lauriello J, Paine S. Treatment of antidepressant-associated sexual dysfunction with sildenafil: a randomized controlled trial. JAMA. 2003 Jan 1;289(1):56-64.
[26] Boyer EW, Shannon M. The serotonin syndrome. N Engl J Med. 2005 Mar 17;352(11):1112-20.
[27] Bhatia SC, Bhatia SK. Major Depression: Selecting Safe and Effective Treatment. Am Family Physician 1997;55(5):1683-1694.
[28] Watson CPN. Antidepressant Drugs as Adjuvant Analgesics. J Pain Symptom Manage 1994;9:392-405.
[29] The Medical Letter: Drugs that may cause Psychiatric Symptoms. July 8, 2002; (1134) pp. 59-62.
[30] Birrer RB, Vemuri SP. Depression in later life: a diagnostic and therapeutic challenge. Am Fam Physician. 2004 May 15;69(10):2375-82.
[31] Finkel SI. Efficacy and tolerability of antidepressant therapy in the old-old. J Clin Psychiatry 1996;57(suppl 5):23-8.
[32] Menting JEA, Honig A, Verhey FRJ, et. al. Int Clin Psychophamacology 1996;11:165-175.
[33] Pryse-Phillips WEM, Dodick DW, Edmeads JG. Guidelines for the diagnosis and management of migraine in clinical practice. Can Med Assoc J 1997;156:1273-87.
[34] Reite M, Ruddy J, Nagel K. Evaluation and management of sleep disorders, 2nd Ed. Am Psychiatric Press, Washington, 1997.
[35] Hughes J, Stead L, Lancaster T. Antidepressants for **smoking cessation**. Cochrane Database Syst Rev. 2004 Oct 18;(4):CD000031. Review.
[36] Drugs and Therapy Perspectives 1998;12(7):14-15.
[37] AHFS (American Hospital Formulary System) Drug Information: Antidepressants. 2005.
[38] Gunnell D, Saperia J, Ashby D. Selective serotonin reuptake inhibitors (SSRIs) and suicide in adults: meta-analysis of drug company data from placebo controlled, randomised controlled trials submitted to the MHRA's safety review. BMJ. 2005 Feb 19;330(7488):385.
[39] Gibbons RD, Hur K, Bhaumik DK, Mann JJ. The relationship between antidepressant medication use and rate of suicide. Arch Gen Psychiatry. 2005 Feb;62(2):165-72.
[40] Birmes P, Coppin D, Schmitt L, Lauque D. Serotonin syndrome: a brief review. CMAJ. 2003 May 27;168(11):1439-42.
[41] Hansten, PD and Horn JR. Drug Interactions Analysis and Management. Applied Therapeutics Incorporated. Vancouver, WA. 2005.
[42] Stahl MM, Lindquist M, Pettersson M, et.al. Withdrawal reactions with selective serotonin re-uptake inhibitors as reported to the WHO system. Eur J clin Pharmacol 1997;53(3-4):163-9.
[43] Meijer WE, Heerdink ER, Nolen WA, et al. Association of risk of abnormal bleeding with degree of serotonin reuptake inhibition by antidepressants. Arch Intern Med. 2004 Nov 22;164(21):2367-70.
[44] Jureidini JN, Doecke CJ, Mansfield PR, Haby MM, Menkes DB, Tonkin AL. Efficacy and safety of antidepressants for children and adolescents. BMJ. 2004 Apr 10;328(7444):879-83.
[45] Gunnell D, Ashby D. Antidepressants and suicide: what is the balance of benefit and harm. BMJ. 2004 Jul 3;329(7456):34-8.
[46] Whittington CJ, Kendall T, Fonagy P, Cottrell D, et al. Selective serotonin reuptake inhibitors in **childhood** depression: systematic review of **published versus unpublished** data. Lancet. 2004 Apr 24;363(9418):1341-5.
[47] The American Academy of Child and Adolescent Psychiatry http://www.aacap.org/Announcements/pdfs/physiciansmedguide.pdf
[48] Treatment for Adolescents with Depression Study (TADS). Fluoxetine, Cognitive-Behavioral Therapy, & their Combination for Adolescents with Depression. JAMA. 2004 Aug 18;292(7):807-820.
[49] Pediatric OCD Treatment Study (POTS) Team. Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial. JAMA. 2004 Oct 27;292(16):1969-76.
[50] Kulin AK, Pastuszak A, Sage SR, et.al. Pregnancy outcome following maternal use of the new selective serotonin reuptake inhibitors: a prospective controlled multicenter study. JAMA 1998;279:609-610.
[51] Briggs GG, Freeman RK, Yaffe SJ. Drugs in Pregnancy and Lactation 6th Ed. Williams & Wilkins, Media, Pennsilvania, 2002.
[52] Simon GE, Cunningham ML, Davis RL. Outcomes of prenatal antidepressant exposure. Am J Psychiatry. 2002 Dec;159(12):2055-61.
[53] Ward RK, Zamorski MA. Benefits and risks of psychiatric medications during pregnancy. Am Fam Physician. 2002 Aug 15;66(4):629-36.
[54] Altshuler LL, Cohen LS, Moline ML, et al. Expert Consensus Panel for Depression in Women. The Expert Consensus Guideline Series. Treatment of depression in women. Postgrad Med. 2001 Mar;(Spec No):1-107.
[55] Nordeng H, Spigset O. Treatment with selective serotonin reuptake inhibitors in the third trimester of pregnancy: effects on the infant. Drug Saf. 2005;28(7):565-81.

[56] Emilio J Sanz, Carlos et al. Selective serotonin reuptake inhibitors in pregnant women and neonatal withdrawal syndrome: a database analysis Lancet 2005; 365: 482-87 **& ALSO** Moses-Kolko EL, Bogen D, Perel J, et al. Neonatal signs after late in utero exposure to serotonin reuptake inhibitors: literature review and implications for clinical applications. JAMA. 2005 May 18;293(19):2372-83.(InfoPOEMs: Late third trimester exposure to maternal use of SSRIs increases the risk of neonatal behavioral abnormalities. Since the symptoms and signs were relatively benign and short lived, it makes sense to individualize the risks and benefits of continuing SSRI treatment throughout pregnancy. (LOE = 2a-))

[57] Misri S, Burgmann A, Kostaras D. Are SSRIs safe for pregnant and breastfeeding women? Can Fam Physician. 2000 Mar;46:626-8, 631-3.

[58] Spencer JP, Gonzalez LS 3rd, Barnhart DJ. Medications in the breast-feeding mother. Am Fam Physician. 2001 Jul 1;64(1):119-26.

[59] Wisner KL, Parry BL, Piontek CM. Clinical practice. Postpartum depression. N Engl J Med. 2002 Jul 18;347(3):194-9.

[60] Altshuler LL, Cohen LS, Moline ML, Kahn DA, et al; Expert Consensus Panel for Depression in Women. The Expert Consensus Guideline Series. Treatment of depression in women. Postgrad Med. 2001 Mar;(Spec No):1-107.

[61] Skowron DM, Stimmel GL. Antidepressants and the risk of seizures. Pharmacotherapy 1992;12(1):18-22.

[62] **Clinical Guidelines** for the Treatment of Depressive Disorders. The Canadian Journal of Psychiatry **June 2001**. (Prescribing Antidepressants for Depression in **2005**: Recent Concerns & Recommendations http://www.cpa-apc.org/Publications/Position_Papers/2004-23s-en.pdf)

[63] Clinically significant drug interactions with antidepressants in the elderly. Spina E, Scordo MG. Drugs Aging 2002;19(4):299-320.

[64] Product monographs 2004

[65] Bezchlibnyk-Butler K, Jeffries JJ, eds. Clinical handbook of psychotropic drugs, 13th ed. Toronto: Hogrefe & Huber, 2003.

[66] Bezchlibnyk-Butler K. Serotonergic antidepressants: Drug response and drug-drug interactions. Pharmacy Practice:National CE Program 1998;Aug:1-8.

Additional references:

Brown GK, Ten Have T, Henriques GR, Xie SX, Hollander JE, Beck AT. Cognitive therapy for the prevention of suicide attempts: a randomized controlled trial. JAMA. 2005 Aug 3;294(5):563-70.

Chun-Fai-Chan B, Koren G, Fayez I, et al. Pregnancy outcome of women exposed to bupropion during pregnancy: A prospective comparative study. Am J Obstet Gynecol 2005; 192:932-36. (InfoPOEMs: Bupropion is not associated with increased rates of major malformations. It may be associated with an increase in spontaneous abortions. (LOE = 1b))

Gamble J, Creedy D, Moyle W, Webster J, McAllister M, Dickson P. Effectiveness of a counseling intervention after traumatic childbirth: A randomized trial. Birth 2005; 32:11-19. (InfoPOEMs: Women with trauma symptoms who receive face-to-face counseling during their hospital stay and phone counseling at 4 to 6 weeks postpartum are less likely to have persistent trauma symptoms or postpartum depression at 3 months. (LOE = 1b-))

Mariappan P, Ballantyne Z, N'dow J, Alhasso A. Serotonin and noradrenaline reuptake inhibitors (SNRI) for stress urinary incontinence in adults. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD004742.

Medical Letter, **Duloxetine** for Diabetic Neuropathic pain. Vol 47 (Issue 1215/1216) Aug 15/29,2005. p.67-68.

Moja P, Cusi C, Sterzi R, Canepari C. Selective serotonin re-uptake inhibitors (SSRIs) for preventing migraine and tension-type headaches. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD002919. CONCLUSIONS: Over 2 months of treatment, SSRIs are no more efficacious than placebo in patients with migraine. In patients with chronic TTH, SSRIs are less efficacious than tricyclic antidepressants. In comparison with SSRIs, the burden of adverse events in patients receiving tricyclics was greater. These results are based on short-term trials and may not generalise to longer-term treatment.

Vignatelli L, D'Alessandro R, Candelise L. Antidepressant drugs for narcolepsy. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD003724.