BEHAVIOURAL & PSYCHOLOGICAL SYMPTOMS OF DEMENTIA (BPSD): Treatment Chart [1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22]

Brent Jensen BSP Jun 13

GENERIC/TRADE (Strength & formulations)	THERAPEUTIC USE/ COMMENTS	ADVERSE EVENTS AE /DRUG INTERACTIONS DI [3,23,24]	INITIAL, USUAL Elderly & MAXIMUM DOSE	$ /MONTH
ACETYLCHOLINESTERASE INHIBITORS (ChEI): differing activity contributes to AE>benefit[43]				
Relative CIs ↓HR, sick sinus syndrome, active peptic ulcer, severe asthma/COPD, anesthesia ↑ succinylcholine effect, **anticholinergic meds** antagonistic effects (see RxFiles Anticholinergics List), Parkinson's ↑EPS, epilepsy ?↓sz threshold & beta-blockers ?↓HR ☎ = **EDS** *in SK* **New pts**: a) dx of probable Alzheimer's b) MMSE score of 10-26 within 60 day before coverage c) Functional Activities Questionnaire (FxAQ) within 60 days before coverage d) Stop all anticholinergic meds 14 days before MMSE & FxAQ e) if intolerant: may switch to another ChEIs. **To continue coverage** must **not** have **both** >2point ↓MMSE & 1point ↑ FxAQ in a 6month period. **MMSE** must **always** be **≥10**. Patients who do not meet criteria to continue can be reevaluated within 3 months to confirm deterioration before coverage is discontinued. **Re-evaluate q 6 months**.				
DONEPEZIL ARICEPT [25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42] 5ᶜ, 10ᶜ mg tablet ☎ ✆ RDT rapid dissolve tablet 5, 10mg χ⊗ acetylcholinesterase activity "central effects" - possibly↑ tolerability? t½ ~75hr approved 1997	✓**Mild to moderate** Alzheimers (MMSE 10-26) **DONEPEZIL** ✓mod-**severe** FDA approved Oct/06 Alzheimer's [43,44]; **Not** better than placebo for **agitation** Howard NEJM/07 **GALANTAMINE** To reverse neuromuscular blockers **RIVASTIGMINE** ✓Parkinson's dementia (benefit vs AE) Almaraz'09 & ? Lewy Body Dementia	**AE** ↑ with ↑ dose: N/V, diarrhea ~10%; anorexia, muscle cramps, insomnia, fatigue, wt loss~3%, other cholinergic effects (**incontinence**, stomach, ↓**HR** esp with high dose, syncope, falls, nightmares) & agitation initially **DI** ↑ level by erythromycin, grapefruit juice, ketoconazole, paroxetine & quinidine ; ↓ level by CYP 2D6 & 3A4 e.g. carbamazepine, dexamethasone, phenytoin, phenobarbital & rifampin	**Initial:** 2.5-5mg po daily **Usual:** 5 -10mg po **OD** in **am** (cc may ↓ AE) **Maximum:** 10mg po daily ♦↑ dose q 1 month if needed; trial ~6 month; taper over ~1 wk, if d/c therapy CCCDTD4	$166 $166 $166
GALANTAMINE REMINYL, g ☎✆ [49,50,5152,53,54,55,56,57,58,59,60] 8,16,24 ER capsule (4,8,12ᶜ mg tab - **d/c** June 2006) acetylcholinesterase & nicotinic activity presynaptic receptor binding ↑ [acetylcholine] t ½ ~6hr	♦**May**[45] temp. **stabilize dementia** & behaviour (& **may** help **apathy**, anxiety, depression, hallucinations & delusions) ♦May help ↓ visual sx's of Lewy Body dementia [46,47] ♦**May ↓rate of functional loss** ♦Does not delay institutionalisation [36] AD2000 ♦Not effective for mild cognitive impairment. [120,48] NNT **12** minimal benefit [12] NNT **42** marked benefit [12] NNH **16** AE-dropout [12]	**AE** ↑ with ↑ dose: N/V, diarrhea ~10%; anorexia, wt loss~3%, insomnia, abdominal pain other cholinergic effects (incontinence, stomach, ↓HR, syncope, falls, nightmares), agitation initially; ↑ mortality 1.3 vs 0.1% [61] **DI** ↑ levels with: antidepressants (~30%) e.g. amitriptyline, fluoxetine, fluvoxamine, paroxetine & CYP 2D6 & 3A4 e.g. cimetidine 16%, ketoconazole 30% & quinidine 30%	**Initial:** 4-8mg ER cap po daily **Usual:** 8-24mg ER cap po OD cc in am **Maximum:** 24-32mg po daily ♦ ↑ dose q 1 month if needed; trial ~6 month; taper over ~1 wk, if d/c therapy CCCDTD4; ↓ dose in hepatic/renal dysfx.	$122 $122 $122
RIVASTIGMINE EXELON, g ☎✆ [62,63,64,65,66,67,68,69] 1.5, 3, 4.5, 6 mg capsule 2mg/mL solution (stable for **4hrs** when mixed with juice/soda) EXELON 5 (4.6mg/d), 10 (9.5mg/d) patch χ⊗ acetyl & butyrylcholinesterase activity "peripheral effects" - ↓tolerability t ½ ~2hr	♦↑ADAS-Cog ~2-3 points vs placebo [8] (~20%↑4 points; ~10%↑7 points) ♦↑ MMSE ~1 point vs placebo [8,36] ♦Takes ~**3-6 months** treatment for fairly modest benefit ♦If ChEI tx stopped & then restarted, some pts may not return to baseline fx level; but outcome in cohort not compromized Pariente'12. If **restarted** ≥3days later, use low dose.	**AE** ↑ with ↑ dose (? ↓ with patch): N/V, diarrhea ~>10%; anorexia, cramps muscle, insomnia, fatigue, sweat, wt loss ~3%, asthenia, headache, confusion, other cholinergic effects (incontinence, stomach, ↓**HR**, syncope, falls, nightmares), agitation initially Patch administration errors: >1patch cut → death reported) Patch:↓N/V, avoid heat. **DI low** risk of DIs ↓↓ DI's but smoking↓levels. Delirium pts: ↑mortality Van Eijk'10	**Initial:** 1.5mg po BID **Usual:** 1.5-6mg po BID cc 4.5 mg po (2.25mL) BID **Maximum:** 12mg po daily **Patch:** 4.6mg/day, may ↑ to 9.5mg/day after a minimum of 4 weeks ♦ ↑ dose **q 1 month** if needed; trial ~6 month, taper over ~1 wk, if d/c therapy.	$67 $67 $210 soln $67 $155
NMDA ANTAGONIST				
MEMANTINE EBIXA, g χ ⊗ NAMENDA (USA) 10ᶜ mg tablet [70,71,72.] t½ ~80hr	✓Moderate (if not tolerate ChEIs) to severe Alzheimer's ♦Option: combo with ChEIs DOMINO NS ♦ May help agitation/aggression Herrmann'13 NS, irritability, disinhibition & psychosis case reports, only post-hoc RCT ♦Not effective for Down's syndrome MEADOWS or in Frontotemporal Dementia Boxer'13	**AE** dizzy, drowsy ↓5mg BID, confusion, insomnia, headache, restlessness inner & motor, akathisia, nausea, ?cornea changes, seizures, ↑BP, ?↑LFTs, & over excitation; Caution: seizures & heart disease. **DI** ↓ DI risk: renally excreted → trimethoprim, SSRI?; amantadine, dextromethorphan & ketamine since also NMDA antagonists; NaHCO3 & acetazolamide.	**Initial:** 5mg po daily **Usual:** 5-10mg po BID **Maximum:** 20mg po daily possible ♦↑ dose **q1-2wk** if needed	$36 $50-100 $100
ANTIPSYCHOTICS: Start low dose, go slow				
HALOPERIDOL [73] HALDOL, g 0.5ᶜ, 1ᶜ, 2ᶜ, 5ᶜ, 10ᶜ mg tablet (2mg/mL soln χ▼); DEPOT 250 & 500/5ml vials, 100mg/1mL amp χ ⊗; 5mg/mL amp	♦ Helps delusions, hallucinations, hostility & aggression. ♦ Aim for **improvement**, not resolution ♦ Minimal improvements with olanzapine, risperidone & quetiapine in general, **offset with AE** Catie-AD [74] ♦In Lewy body dementia cause significant ↑ in EPS AE (if tx required & Parksinon's or Lewy Body dementia, quetiapine or clozapine {12.5-50mg daily & watch WBC} are options) **HALOPERIDOL** For acute delirium 0.5mg q30min prn day 1→ 0.5mg TID x 3-4days	**HALOPERIDOL AE** ↑EPS, ↑ALT ≤16%, **weight gain ≤ 1 kg**	**Initial**: 0.25mg BID-TID **Usual**: 0.25-1mg BID **Maximum:** 5mg daily	$12 $12 $12
OLANZAPINE ZYPREXA, g ☎▼ [77,78,79,80,81,82,83,84,85,86] 2.5, 5, 7.5, 10, 15mg tablet ZYDIS 5, 10, 15mg tablet 10mg IM χ ⊗ vial use SWFI; don't mix in same syringe with diazepam, haloperidol or lorazepam	**RISPERIDONE** ✓Official BPSD indication (others used off-label) **SHARED AE** Delirium, confusion, anticholinergic, **sedation**, constipation, ↓BP, ↑weight, EPS esp. **parkinsonian (least with quetiapine & clozapine)**, akathisia, falls [75], NMS & tardive dyskinesia, diabetes esp. with **clozapine** & olanzapine. [76] ♦Health Canada: as of Nov'08 received 69 total reports of agranulocytosis / **neutropenia** for olanzapine, quetiapine & risperidone. ♦CDN & FDA warning: atypical antipsychotics may, in BPSD pts, ↑ mortality 4.5 vs 2.6% placebo, mainly by cardiovascular or pneumonia or **DVT** causes. Haloperidol may ↑ mortality most. M **ECG to** assess cardiac abnormalities.	**OLANZAPINE AE** somnolence, dry mouth, dizzy, headache, asthenia, **falls**, constipation, blurred vision, urinary incontinence, dyspepsia, ↑ALT ≤ 6%, **diabetes**, postural ↓BP, seizures 0.9%, **anticholinergic**, ? ↑ stroke/death, ↑ triglyceride, ↑ cholesterol, **↔↑ prolactin effect, weight ↑, akathisia>10%**	**Initial**: **1.25**-5mg po daily **Usual:** 2.5-7.5mg po daily **Maximum:** 10-20mg po daily	$28 $28-69 $69
QUETIAPINE SEROQUEL, g 25, 50, 100, (150χ▼) 200, 300mg tab [87,88]; XR 50,150,200,300,400mg tablet ⊗		**QUETIAPINE AE somnolence**, dizzy, drowsy, constipation, dry mouth, **falls**, **lens changes** in beagles-annual slit lamp exam, ↓BP, seizures ≤0.8%, dyspepsia, headache, urinary incontinence, diabetes, ↑ALT ≤ 9%, ↑ triglyceride 17%, ↑ cholesterol 11%, hypothyroidism 0.4%, ? ↑stroke/death, QT, **low EPS** effect (option in **Lewy Body Dementia & Parkinson's**), **↔ prolactin effect, weight ↑, akathisia >2%**	**Initial**: 12.5mg po daily **Usual:** 25-100mg po HS 50-100mg po XR HS **Maximum:** 200-750mg po daily	$15 $39-72 $72
RISPERIDONE RISPERDAL, g [89,90,91,92,93] 0.25, 0.5ᶜ, 1, 2ᶜ, 3ᶜ, 4ᶜ mg tablet M-TAB 0.5,1,2,3,4mg tablet 1mg/mL soln (do **not** mix with cola/tea) DEPOT CONSTA 12.5,25,37.5,50mg vial ☎⊗		**RISPERIDONE AE** sedation, headache, dry mouth, constipation, blurred vision, urinary incontinence, insomnia, asthenia, ↓**BP**, ↓appetite, TTP, seizures ≤0.3%, photosensitive, ?↑stroke/death, ↑ **EPS at doses ≥ 2-4mg/day, ↑ prolactin effect , weight ↑, akathisia >10%** **DI**? Furosemide ↑ associated mortality	**Initial**: **0.25**-1mg po daily **Usual:** 0.5-2mg po HS 1-2mg M-TAB po HS **Maximum:** 2-6mg po daily	$21 $20-34 $41-74 $74

GENERIC/TRADE (Strength & formulations)	THERAPEUTIC USE/ COMMENTS	ADVERSE EVENTS AE /DRUG INTERACTIONS DI [3,116,117]	INITIAL, USUAL Elderly & MAXIMUM DOSE	$ /MONTH
All antidepressants may help depression (mood, appetite, sleep or energy) & apathy (rare potential for worsening) which often occurs early in dementia. May help behaviour/disinhibition in frontotemporal dementia.				
SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs): limited efficacy for specific phobias				
CITALOPRAM [118,119,120] =CC CELEXA, g 10 ✗ ▼,20ç, 40mgç tablets	**DOSING STRATEGY:** ♦ **Start low, slow but go** ♦Elderly may need **> 8week trial** ♦A small number of people with dementia & neuropsychiatric sx experience clinically significant worsening when antidepressants are **stopped** DESEP Serotonin Antagonist and Reuptake Inhibitor: **Trazodone**: 25-50mg HS ♦similar to SSRIs ♦Helps sleep, sun downing & depression ♦**Flat dose response curve for depression**; however titration to ↑ doses sometimes required for anxiety	**SHARED AE (GI & CNS):** nausea {21%(F) - 36% (X)}, anxiety, insomnia {~14%}, agitation, anorexia, tremor, somnolence {11-26%}, sweating, dry mouth, headache, dizziness, falls, diarrhea {12% (F,P)-17% (S)}, constipation {13-18%}, sexual dysfx.[121,122], d/c Syndrome (esp with P) **Serotonergic syndrome** with MAOI's ♦↓BP, tremor, agitation, hypomania **SHARED DIs** Many (see RxFiles Antidepressant DI Chart p. 106)	AE may ↑ QT if >40mg /day DI fewer DIs	**Initial:** 10-20mg am po daily; **Usual:** 20-40mg po daily **Maximum:** 20mg po daily ?safety of 40mg	$25-38 $25
ESCITALOPRAM CIPRALEX ✗▼ 10ç,20ç mg tablets CIPRALEX MELTZ⊗ 5, 10 , 15, 20mg ODT			AE may ↑ QT if >20mg /day	**Initial:** 5-10mg po daily **Usual:** 10-20mg po daily **Maximum:** 10mg po daily ? 20mg daily may be safe	$65 $65 $65
FLUOXETINE [123] =F PROZAC, g 10,20,40✗ ▼mg capsules & 4mg/mL soln			AE most anorexic and stimulating (↑t½, thus 5 week washout)	**Initial:** 10-20mg po OD; **Usual:** 20-40mg am OD **Maximum:** 60-80mg po daily	$28-50 $70
FLUVOXAMINE [124] =X LUVOX, g 50ç, 100ç mg tablets			AE most nausea, contipation & sedation	**Initial:** 25-50mg po HS;**Usual:** 100-150mg po HS **Maximum:** 300mg po daily	$17-33 $59
PAROXETINE [125,126] =P PAXIL, g 10ç, 20ç, 30mg tablets			AE most anticholinergic AE; ↑weight & a discontinuation reaction possible	**Initial:** 10-20mg am OD; **Usual:** 20-40mg am OD **Maximum:** 60mg po daily	$18-50 $50
SERTRALINE [127,128] =S ZOLOFT, g 25, 50, 100mg capsules			AE↑diarrhea & sexual dysfx DI fewer DIs	**Initial:** 25-50mg am po daily **Usual:** 100mg OD-BID cc DIADS-2 **NS**, HTA-SADD **NS 95mg OD** **Maximum:** 200mg po daily	$26 $26-46 $46
SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITOR (SNRI): serotonin (5HT), norepinephrine (NE) & some dopamine action					
VENLAFAXINE EFFEXOR, g (**Reg** 37.5, 75mg tablets-Co **D/C** Jul04) XR, g 37.5, 75, 150mg capsules (contents of XR may be sprinkled)	**DULOXETINE:** ✓depression (adult & maintenance) ⊗, GAD ⊗, diabetic neuropathic pain ✆, fibromyalgia & ? stress incontinence ⊗	**SHARED AE** similar to SSRIs Caution: d/c Syndrome (e.g. agitation, nausea, fatigue, dizziness, headache, etc.) **SHARED DIs** Many (see RxFiles Antidepressant DI Chart p. 106)	AE **As dose↑**: ↑BP, agitation, tremor, less weight ↑, sweating, nausea {~37%}, sleep disturbances, headache, "clean TCA" DI fewer DIs	**Initial:** 37.5mg XR po daily **Usual:** 75-150mg XR po daily **Maximum:** 225-375mg XR po daily	$13 $20 $40-60
DESVENLAFAXINE ER PRISTIQ ✗⊗ 50, 100mg extended release tablets			DI Cyp 3A4 (?clarithromycin)	**Initial:** 50mg po daily; **Usual:** 50-100mg po OD **Maximum:** 400mg po daily	$95 $335
DULOXETINE CYMBALTA 30, 60mg capsules			AE nausea, insomnia, somnolence, headache, diarrhea, ↓appetite, fatigue, ↑sweat, ↑BP, ↑LFTs, dry mouth, urinary retention DI CYP 1A2, 2D6	**Initial:** 30mg po daily **Usual**: 30-60mg po daily **Maximum**: 120mg po daily	$69 $69-132 $254
TRICYCLIC ANTIDEPRESSANTS (TCAs):					
DESIPRAMINE=D NORPRAMIN, g 10, 25, 50, 75, 100mg tablets	♦Trough plasma level available ♦ ~2-3 months for maximum effect	AE **CNS**: agitation initially, confusion, drowsiness, headache, tremors, seizures, **anticholinergic (least with D)**: dry mouth, blurred vision, constipation etc.; nausea, sweating, rash, **cardiovascular**: ↑ heart rate, arrhythmias, ↓ BP; anorgasmia, Fatal (≥2g) **overdose** → to heart & CNS; **Nortriptyline: ↑ tolerated vs** other TCA's DI May ↑ effect of anticholinergic & CNS meds.	**Initial:** 10-25mg po HS; **Usual:** 50-75mg po HS **Maximum:** 150-300mg po HS	$20-36 $58-95
NORTRIPTYLINE=N AVENTYL, g 10, 25mg capsules [129]			**Initial:** 10-25mg po HS **Usual:** 25-50mg po HS **Maximum:** 150mg po HS	$15-24 $28
NORADRENERGIC AND SPECIFIC SEROTONERGIC ANTIDEPRESSANT (NaSSA): 5HT & NE					
MIRTAZAPINE REMERON, g 15ç,30ç,45mg tabs; RD, g 15,30,45mg tab ♦RD form useful if difficulty swallowing	♦**Useful** if anxiety, anorexia, somatization, or difficulty sleeping ♦ t½ =20-40hr	AE Dry mouth, **sedation**, edema, arthralgias, dizzy, rare neutropenia. May ↑appetite & **weight**, but may have ↓ sexual dysfx DI Clonidine & many others (see RxFiles Antidepressant DI Chart p. 106)	**Initial:** 7.5-15mg po daily **Usual:** 15-30mg po daily HTA-SADD **NS** **Maximum:** 60mg po daily Star*D	$12RD-15 $12RD -22 $25RD-36
AZAPIRONE 5HT$_{1A}$ AGONIST:					
BUSPIRONE BUSPAR, g (5✗), 10ç mg tablets ⊗ ♦ Onset 1wk; Max effect 6 wks	✓ Anxiety in benzodiazepine naive pt & for alcohol withdrawal ♦Non-addicting	AE Nausea, headache, dizziness DI Many (see RxFiles Antidepressant DI Chart p. 106)	**Initial:** 5mg TID-QID ↓$ if taken as ½ of 10mg tablet **Usual:** 5-10mg po TID-QID **Maximum:** 60-90mg po daily	$25-46 $25-56 $80-117
BENZODIAZEPINES: may help severe anxiety (use short term/with caution if at all)					
CLONAZEPAM RIVOTRIL, g 0.25✗ ▼,0.5ç, 1, 2ç mg tablets	✓ Anticonvulsant, Panic attack; Other: **sedative,** social phobia & akathisia, acute mania & neuralgic pain	AE Drowsiness (tolerance develops), dizziness, falls, ↓ concentration, anterograde amnesia, ↑ traffic accidents, physical dependence & paradoxical anger/hostility Disinhibition: inappropriate sexual behaviour, physical/verbal outbursts ♦Taper off slowly to ↓ rebound anxiety ♦clonazepam is long-acting & lorazepam is a short-acting DI Lorazepam ↓DI's versus other therapeutic options	**Initial:** 0.25mg po daily-BID **Usual:** 0.5mg po TID-1mg po BID **Maximum:** 10-20mg po daily	$10 $15 $27-46
LORAZEPAM ATIVAN, g 0.5, 1ç, 2ç mg tablets (0.5,1,2mg SL▼tablets; 4mg/mL **ampule**⊗✗	✓ Anxiety, Preanesthetic, Status epilepticus; **Other**: **sedative;** muscle relaxant;delirium (from alcohol withdrawal, Parkinson's or NMS)		**Initial:** 0.5mg daily **Usual:** 0.5mg TID-1mg po TID **Maximum:** 10mg daily	$10 $10 $20

=↓dose for renal dysfunction =↓dose for liver dysfunction ç=scored tab g=generic ✗=Non-formulary Sask ☎=Exceptional Drug Status Sask. ⊗=not covered by NIHB ▼=covered by NIHB ✆=prior by NIHB $=cost **ADAS-cog**=cognitive section of the 70 point Alzheimer's Disease Assessment Scale **am**=morning **Bz**=benzodiazepine **BP**=blood pressure **cc**=with meal **COPD**=chronic obstructive pulmonary disorder **CV**=cardiovascular **CYP**=cytochrome **d/c**=discontinue **DI**=drug interaction **DM**=diabetes mellitus **DVT**=deep vein thrombosis **dx**=disease **EDS**=exception drug status **EPS**=extrapyramidal symptoms **ER**=extended release **FxAQ**=Functional Activities Questionnaire **GAD**=generalized anxiety disorder **hr**=hour **HR**=heart rate **HS**=at bedtime **LFT**=liver function test **M**=monitor **MMSE**=Mini-mental state examination (Scale 0-30) **NaHCO3**=sodium bicarbonate **NNH**=number needed to harm **NNT**=number needed to treat **NMDA**=N-methyl-D-aspartate **NMS**=neuroleptic malignant syndrome **NS**=not significant **N/V**=nausea & vomiting **OD**=once daily **ODT**=oral dissolvable tablet **Pt**=patient **SWFI**=sterile water for injection **sx**=syndrome **sz**=seizure **TG** =triglycerides **t½**=half life **tx**=treatment **WBC**=white blood cell **wk**=week **wt**=weight **XR**=extended release

OTHER MEDS See RxFiles Charts: Mood Stabilizers (p. 103), Antidepressants (p. 105) & Behavior Management in Dementia Newsletter; Alzheimer's Association www.alz.org

Not an Option: ASA 75mg daily x 2yr[131], estrogen[130], NSAID[131, ADAPT NS], or ginkgo[132 GEM, GuidAge].
Uncertain: ?statin[133 Leadé & Sano'11 NS], ?Vit E[134] not for mild cognitive impairment, ↑mortality if >400IU/day, ?B_{12}[135] & vegetables.
PREVENTION ↓ CV risk (↓BP [136], ↓cholesterol, **stop smoking**, ↑exercise & ASA in ↑risk pts). Cognitive rehab may ↑ cognitive function (mnemonics, association strategies, & computer-assisted training programs).[140] If mild cognitive impairment, 5-10% progress to dementia annually. Assess risk for postop delirium.
EPIDEMIOLOGIC 1.5% @ 65yrs; doubles q4yr; 30% @80yrs; average survival 8yr from diagnosis.
NON DRUG involve family/caregivers in enviro & behavioural tx; advance health care directive & discourage driving.

DEMENTIA Type Alzheimer's ~50% (short term **memory**, word & way finding), vascular ~25% (often stepwise evolution, apathy, dys-executive sx), combo, Lewy body ~15% (fluctuations in cognition, hallucinations visual & spontaneous motor features of Parkinsonism), Frontotemporal ~5% (disinhibition, behavioural & social tactlessness, language changes, often onset <60yr) & hydrocephalus normal pressure (rapid progressing, early gait abnormalities & incontinence). Progessive deterioration req. interventions to ↓ progression, ↓ sx (cognitive, behavioural & psychological) & ↓ caregiver burden. Comorbidity with diabetes & HTN ↑ mortality.
DRUG INDUCED DELIRIUM antiemetics (eg. dimenhydrinate, meclizine), antihistamines sedating (eg. chlorpheniramine & diphenhydramine), anticholinergics (antipsychotics like chlorpromazine, clozapine & olanzapine; benztropine, oxybutynin, procyclidine, scopolamine, TCAs like amitriptyline & imipramine; tolterodine), antiparkinsonian meds, benzodiazepines, digoxin, disopyramide, muscle relaxants, narcotics (eg. meperidine, pentazocine, propoxyphene) & NSAIDs (rarely eg. high-dose aspirin, indomethacin, sulindac).

MANAGEMENT OF BEHAVIORAL & PSYCHOLOGICAL SYMPTOMS OF DEMENTIA BPSD[137]

Brent Jensen © www.RxFiles.ca Jun 2013

Background: very common (≤90% in dementia); major cause of distress to pts/families/caregivers; harm to self & others; ↑cost (e.g. institutionalization). Not just agitation but non-agitated sx (apathy, withdrawal, daytime somnolence {circadian rhythm disturbances}, depression, disinhibition, etc.)

Diagnosis: (Evaluate behaviour→ABC's **A**ntecedents (causes:Physical Intellectual Emotional Cultural Environmental Social), **B**ehaviours & **C**onsequences),→Assess hx (unique factors like Down's sx), physical exam, cognitive tests Feldman'08 & nurse/collateral family info! Behavioural Vital Signs tool www.cagp.ca

Lab Tests: Recommend CBC, electrolytes, Ca^{++}, B_{12}, glucose & TSH; Optional: BUN & SCr, ferritin, magnesium, LFTs, arterial blood gases, ECG, CT/MRI if suggestion of structural lesion (eg. renal failure, brain tumor, normal pressure hydrocephalus,subdural hemorrhage) ◆Eliminate delirium source Young BMJ'07 (eg.meds eg. opiates, benzos, anticholinergics) /withdrawal rxs/DI's,dehydration & infections (if indicated: urinalysis/ C&S, chest x-ray, lumbar puncture if suspicion of meningitis)

Step 1: **Assess for & treat any comorbitities** (eg. **infection, pain, constipation**, depression, psychosis}

Step 2: **Explore environmental, exercise, music & behavioural measures** COPE Reserve **drug tx** where non-drug tx has been fully explored & implemented or if **significant dangerous risk**. Specify problem behaviour (eg."agitation" is less useful than "screaming", "hitting when bathed"). Identify triggers & what makes it go away. Identify whom the behavior is bothering (pt, caregiver/staff or other pts). Human interactions eg. Activity www.enasco.com/senioractivities, adequate staff eg. nursing home & proper environment most critical.

Step 3: **Drug tx** consider if sx having no physical cause, are unrelated to other drugs or unresponsive to non-pharmacological interventions, generally start with **1/3 to 1/2 of usual adult** dose & titrate up slowly; individualize dose

Step 4: **Reevaluate drug regimen after 3 months**; may attempt to **taper/withdraw** meds after **3 months of behavioural stability**

MAJOR DEPRESSION
↓ mood, apathy, amotivation

Mild→non pharmacologic

Moderate to *severe*→**ANTIDEPRESSANT Medication**

Anxiety often coexists thus use antidepressants with anxiolytic properties e.g.citalopram,sertraline,venlafaxine

CANMAT 09 suggests: (See also RxFiles Charts book pg 104-5).
SSRI's, venlafaxine, mirtazapine, duloxetine, moclobemide, bupropion.

In general →may be good for depression, depression assoc. agitation, emotionality & irritability. May help behaviours/disinhibition (May worsen apathy in some pts)

Allow >6 week for adequate trial at an adequate dose

⇩ ***Start Low, Go Slow, But go!***

SSRIs: AE N/V, restlessness, falls, insomnia, ↓weight, agitation initially, hyponatremia & bleeding<0.5%
Citalopram 10-20mg/d, **escitalopram**χ⊗ 10mg/d, **sertraline** 25-100mg OD, fluvoxamine 25-150mg OD, paroxetine 10-30mg OD etc.

Venlafaxine: 37.5-225mg XR OD {Similar AE as SSRI, but ↑ GI AE & may ↑ BP); XR cap: can sprinkle on food.

Bupropion: 100-150mg BID or 150-300mg XL to activate pt with withdrawal or psychomotor retardation

TCA's: Avoid anticholinergics →↓with **nortriptyline** 10-75mg HS & desipramine 25-150mg OD; AE ↓BP, blurred vision, urinary hesitancy, cardiac conduction changes

Mirtazapine: consider if anorexia/anxiety/sleep problem; RD rapid dissolve form if difficulty swallowing; ≤7.5-45mg OD

Moclobemide: role in anxiety & mood dx but may ↑ stimulation; 100mg OD-300mg BID

Trazodone: ↓ doses for sedation & some anxiolytic effect; monitor for ↓BP, serotonin syndrome & rare ♂ priapism. Consider **ECT** in tx resistant or severe depression.

PSYCHOSIS/AGITATION
delusions, hallucinations; agitation, aggression

-use non-drug validation, environment…when possible!

Psychosis:Positive sx delusions, hallucinations or paranoia
Negative sx poverty of thought, apathy, social withdrawal

Agitation: aggression, shouting, pacing, psychomotor

Start Low, Go Slow… Then Taper!

ANTIPSYCHOTIC Medication

-first designate target sx (**not wandering or mild sx**); try to ↓ **sedation**, ↑ confusion,hypotension & **EPS;** titrate no more frequent then q1-2wks

-**target sx** (hallucinations, delusions, hostility, aggression, severe agitation, & violent/high risk behaviour)

risperidone 0.25-2mg OD
quetiapine 12.5-200mg OD
olanzapine ☎ ▼1.25-10mg OD
haloperidol 0.25-2mg OD (especially useful in delirium)
⇨monitor for AE; may attempt to taper or d/c q3 months

[**aripiprazole** ☎ ✆ & **ziprasidone** ✆: caution stimulating agents]

◆Newer agents, as effective, ↑ tolerated. Monitor for AE sedation, ↓BP, falls [138], EPS (drooling, rigidity & akinesia), anticholinergic AE dry mouth, delirium, constipation, ??ECG, ↑weight/lipids/diabetes , ? ↑stroke OR 2.5-3/death OR 1.5-1.8 Class effect & tardive dyskinesia→need to **reevaluate ongoing use**.

◆Pts with **Lewy bodies** (often visual hallucination sx) have ↑ sensitivity to neuroleptics (option: quetiapine ↓ dose)

ANXIETY
pacing, chanting, psychomotor agitation, etc.

-use non-pharmacological intervention
-minimize provocation
-consider **antidepressant** therapy if anxiety is secondary to depression or very chronic in nature

ANTIANXIETY Medication - consider **short term as needed**
lorazepam 0.5-2mg OD
oxazepam 5-30mg OD
clonazepam 0.125-2mg OD (Caution long-acting!)

Benzodiazepines-caution!
AE sedation, ataxia, altered sleep architecture, motor & **cognitive** impairment & possible withdrawal sx when d/c. Paradoxical excitation, **disinhibition** & **falls** may occur. An intermediate acting such as temazepam/oxazepam /lorazepam can be best used short term, if possible for sleep/anxiety states or before planned anxiety provoking situations eg.bathing,dental work

Trazodone 12.5-100mg OD considered option by some 50-100mg po HS

Buspirone ✆ 10-30mg OD; ↓sedation, ↓DI's, ↓ withdrawal & ↓ impairment of motor fx;option→chronic anxiety but slow onset ~3wk

APATHY tx with external activity & environmental measures.
Possible drug options (not without concern): methylphenidate, dopamine agonists or cholinesterase inhibitors.

Sexually Inappropriate Behaviour assess for **medical reason eg. UTI & any drug causes eg. lorazepam, dopamine agonists.** Remove disinhibiting drugs including benzo's & alcohol.
Behavioural interventions: First redirection, distraction, avoiding stimulants, ↓data on drug tx antidepressants, antipsychotics, cholinesterase inhibitor (see also RxFiles Hypersexuality Chart, pg 107).

Sleep Disturbances assess for **medical reason eg. heart failure, sleep apnea, drug cause eg. stimulants, Options**: **behavioural, trazodone 25-50mg HS, zopiclone χ⊗ 3.75-5mg HS, Limit to 3-4 weeks.**

Pain consider trial of regularly scheduled **acetaminophen ≤ 3.25g OD (e.g. 650mg po QID; or long-acting 1300mg BID AM & HS) to** reduce **agitation & pain** Husebo'11; opioids may be appropriate alternative in select patients.

Cholinesterase Inhibitors (ChEIs) modest cognitive, functional & behavioural benefit; may help apathy, hallucination & delusion?-post hoc analyses; **unlikely ↓ agitation & aggression** - not better than placebo for agitation Howard'07, may help **Lewy Body dementia**↓ visual sx's. **Consider cholinesterase inhibitors in Alzheimer's** (**donepezil**, **galantamine**, **rivastigmine**) ☎ ✆; but AE N/V, fatigue, anorexia, ↑HR, urinary incontinence

Memantine ✗ ⊗NMDA receptor antagonist, may help agitation, aggression, irritability, disinhibition & psychosis-case reports, only post-hoc analysis of RCT. Option: combo with ChEIs in mod-severe AD.

Anticonvulsants some use short term (<6weeks) in agitation, aggression, hostility, sleep-wake disturbance cycle & mania ◆ **carbamazepine** 100-600mg OD ≤400mg OD in BPSD AE sedation, ataxia, falls, rash, headache, leukopenia & ↑ liver tests & Dis.
✓Good for impulsivity or if brain injury. ◆ **? topiramate 25-50mg OD** cognitive difficulties ◆ **valproate no longer recommended** dose required associated with sedation, diarrhea, tremor, nausea, hair loss, ↑ liver tests; CCCDTD4; **useful if manic**
◆ **other agents (gabapentin, lamotrigine-rash, levetiracetam) benefit unknown; concerns re: worsening existing behaviour (eg. gabapetin-worsening agitation if Lewy Body dementia)**

Beta Blocker **propranolol** 10-80mg OD; possible ↓ aggression but diminishes over time; AE ↓ HR &↓BP Caution: asthma, PVD & possibly depression Hx

☎=Exception Drug Status Sask. ✗ =non-formulary in Sask. ⊗=not covered by NIHB ▼=covered by NIHB ✆=prior approval NIHB **AD**=Alzheimer's **AE**=adverse effect **BP**=blood pressure **BPSD**=behavioural & psychological symptoms of dementia **BUN**=blood urea nitrogen **Ca^{++}**=calcium **CBC**=complete blood count **C&S**=culture & sensitivity **CT**=computed tomography **d/c**=discontinued **DI**=drug interaction **dx**=disorder **ECG**=electrocardiogram **ECT**=electroconvulsive therapy **EPS**=extrapyramidal symptoms **fx**=function **GI**=gastrointestinal **HR**=heart rate **hx**=history **LFTs**=liver function tests **MRI**=magnetic resonance imaging **NMDA**=N-methyl-D-asparate **N/V**=nausea/vomiting **pt**=patient **PVD**=peripheral vascular disease **RCT**=randomized controlled trial **SCr**=serum creatinine **sx**=symptom **SSRI**=selective serotonin reuptake inhibitors **TSH**=thyroid stimulating hormone **tx**=treatment **UTI**=urinary tract infection

Behavioural & Psychological Symptoms of DEMENTIA (BPSD) Treatment Chart

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Useful Web sites:

Alzheimer Society Canada www.alzheimer.ca
Alzheimer Association USA www.alz.org
Alzheimer Society UK www.alzheimers.org.uk