

# Psychotropic Drugs in the Elderly

## Treatment Considerations

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Saskatchewan residents over 65 years of age (16% of population) consume 47% of all prescription medications. The elderly are especially susceptible to drug-induced cognitive impairment partly due to polypharmacy and renal/hepatic dysfunction. Pre-existing cognitive problems make it difficult to detect the role of drugs in causing new symptoms or making old ones worse.<sup>1</sup>

♦ See also additional *RxFiles Psychotropic Comparison Charts!*

Common Reactions	Agents & Comparisons
<b>Anticholinergics</b> confusion, delirium, memory impairment, obtundation, dry mouth & constipation	Benztrapine, chlorpheniramine, dicyclomine, diphenhydramine, hyoscine, oxybutynin, propantheline, scopolamine, solifenacin, tolterodine, trihexyphenidyl, trospium
<b>Mood Stabilizers / Antiepileptics</b> delirium, confusion, ↓ cognition & amnesia	↓ Cognition possible; ↑ drug interactions; (in general, aim for lower levels in elderly); Lithium poorly tolerated in some elderly; <b>divalproex</b> reasonably well tolerated
<b>Antipsychotics</b> delirium, confusion, neuroleptic malignant syndrome, anticholinergic effects, sedation, hypotension, weight gain, diabetes, ↑ lipids, EPS (extrapyramidal side effects) especially parkinsonian & tardive dyskinesia	1. <b>Anticholinergic</b> highest activity with chlorpromazine & clozapine; lowest with <b>risperidone &amp; quetiapine</b> 2. <b>Sedation</b> highest with clozapine*, olanzapine, chlorpromazine & methotrimeprazine; lowest with <b>haloperidol &amp; risperidone</b> 3. <b>EPS</b> side effects highest with haloperidol; lowest with <b>clozapine* &amp; quetiapine</b> 4. <b>Hypotension</b> highest with chlorpromazine & clozapine*; lowest with <b>haloperidol &amp; olanzapine</b>
<b>Benzodiazepines</b> cognitive impairment, amnesia, excessive sedation, lack of coordination → falls, disinhibition, withdrawal syndrome with delirium, hallucinations, caution if respiratory dysfx	Long-acting <sup>Clonazepam, Diazepam</sup> & high doses increase risk of toxicity  <b>Short-acting</b> <sup>Lorazepam, Oxazepam</sup> increase risk of withdrawal but less accumulation in the elderly  Ultra short acting <sup>Triazolam</sup> can ↑ amnesia & behavioural disturbances
<b>SSRI antidepressants &amp; venlafaxine</b> falls, ↓ concentration, confusion, SIADH & rarely EPS	<b>SSRI:</b> Fewer cognitive / anticholinergic side effects than with TCA's; (weight loss may also be a particular problem with fluoxetine in the elderly; potential also for sexual dysfunction with any SSRI)
<b>TCA antidepressants</b> delirium, confusion, memory impairment	1 <b>Anticholinergic &amp; Sedation:</b> most with amitriptyline, doxepin, imipramine; least with <b>desipramine, nortriptyline</b> 2 <b>Hypotension</b> with antidepressants: most with trazodone; least with <b>nortriptyline</b>

\*note **clozapine** requires weekly CBC monitoring initially due to neutropenia; also associated with hypersalivation & high cost; **seldom indicated in elderly**

### ANTIDEPRESSANTS:

- ♦ Caution: TCAs with high anticholinergic, sedative & hypotensive effects (i.e. amitriptyline, imipramine, doxepin, trimipramine); if low doses of these TCAs used (for **pain/sleep**) monitor for delirium, urinary retention, etc.
- ♦ **Nortriptyline or desipramine** are suggested TCA options, with less anticholinergic effects (e.g. for pain/migraine control)
- ♦ **Fewer drug interactions** with **citalopram & venlafaxine**
- ♦ ↓ Sexual dysfunction with **bupropion & moclobemide**
- ♦ Discourage combinations of antidepressants & antipsychotics

### ANTIPSYCHOTICS:

- ♦ Caution: Antipsychotics with high anticholinergic effects (i.e. chlorpromazine at doses >30mg/day)
- ♦ Low-dose antipsychotics such as **risperidone 0.25-2mg/day**, **quetiapine 12.5-150mg/day**, **olanzapine 1.25-10mg/day** & **haloperidol 0.25-2mg/day**, may be reasonable choices for those elderly in whom an antipsychotic is indicated. (Most weight gain, ↑ glucose & ↑ lipid profile was with olanzapine <sup>CATIE 2005</sup>)

### BENZODIAZEPINES:

- ♦ Minimize long-acting benzodiazepines (clonazepam, diazepam, flurazepam, chlordiazepoxide) due to ↑ fall risk & accumulation, leading to over-sedation, cognitive impairment & confusion
- ♦ Avoid triazolam (Halcion) due to amesic effects
- ♦ Minimize use of short-acting benzodiazepines for longer than 2-4 weeks (**temazepam, lorazepam & oxazepam**)
- ♦ Consider **mirtazapine, SSRI & venlafaxine** rather than chronic benzodiazepines in treating elderly patients with anxiety
- ♦ When discontinuing, convert to a long-acting benzodiazepine dose (i.e. diazepam <sup>or clonazepam (consider if benzo for anxiety)</sup> in equivalent doses), and then gradually taper <sup>10-25%/wk, esp. slow last 25%</sup> over weeks or over several months

### OTHER TREATMENTS FOR INSOMNIA:

- ♦ Promote **non-pharmacological sleep hygiene measures & rule out other contributing factors** <sup>depression, pain; medications- steroids, acetylcholinesterase inhibitors, SSRI etc.</sup>
- ♦ Avoid antihistamine sedatives (i.e. diphenhydramine & doxylamine), and barbiturates for treating insomnia
- ♦ Some low-dose TCA's useful for sleep but tolerance in weeks
- ♦ May consider low-dose **trazodone 25-50mg HS** for elderly patients with chronic "sundowning" or night-time agitated dementia, to avoid anticholinergic side effects/dependence; **zopiclone 3.75-5mg HS** may be an additional option <sup>↓ tolerance & withdrawal</sup> however dependency still a concern
- ♦ Limited duration of sedative therapy recommended <sup>no more than 3-4wks</sup>

### ANALGESICS:

- ♦ **Avoid** certain NSAIDs (indomethacin, ketorolac, mefenamic acid, piroxicam), <sup>mepredine, propoxyphene & pentazocine</sup> which are more likely to cause CNS related adverse effects

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

**Diagnosis:** (Evaluate behaviour  $\rightarrow$  ABC's Antecedents (causes: Physical Intellectual Emotional Cultural Environmental Social), Behaviours & Consequences),

$\Rightarrow$  Assess history unique factors like Down's Sx, physical exam, cognitive tests Feldman CMAJ08 & nurse observations; collateral family info essential!

**Lab Tests:** Recommend CBC, electrolytes, calcium, B12, 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  $\blacklozenge$  Eliminate delirium source Young BMJ07— eg. **meds** eg. opiates, benzos,

anticholinergics /withdrawal rx's/DI's, dehydration & infections (if indicated: urinalysis/C&S, chest x-ray, lumbar puncture if suspicion of meningitis)

**Tx 1: Assess for and treat any comorbidities** (eg. infection, pain, constipation, depression, psychosis)

**Tx 2: Explore environmental, exercise & behavioural measures** *Cope trial!* Reserve drug therapy for situations where non-pharmacological interventions have been fully explored & implemented or in cases of **significant danger**. Specify problem behaviour (eg. "agitation" is less useful than "screaming", "hitting when bathed"). Identify what brings it on & what makes it go away. Identify whom the behaviour is bothering (pt, caregiver/staff or other pts). Human interactions eg. activity, adequate staff eg. nursing home & proper environment most critical.

**Tx 3: Drug Treatment:** 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

**Start Low, Go Slow!**

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

**MAJOR DEPRESSION**

$\downarrow$  mood, apathy, amotivation

Mild  $\rightarrow$  non pharmacologic

Moderate to severe  $\rightarrow$

**ANTIDEPRESSANT Tx**

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

CANMAT 09 suggests:

**SSRI's, venlafaxine, mirtazapine, duloxetine, moclobemide, bupropion.**

See also RxFiles Charts book pg 104-5.

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

Allow  $>6$  week for adequate trial at an adequate dose



**SSRIs: SE:** nausea, vomiting, restlessness, falls, insomnia,  $\downarrow$ weight, agitation initially & hyponatremia

**Citalopram** 10-30mg/d, **escitalopram** 10-20mg/d, **sertraline** 25-100mg/d, **fluvoxamine** 25-150mg/d, **paroxetine** 10-30mg/d etc.

**Venlafaxine:** 37.5-225mg XR od (Similar SE as SSRI, but high GI SE & may  $\uparrow$  BP); **XR cap:** can sprinkle on food.

**Bupropion**  $\approx$   $\varnothing$  100-150mg bid or 150-300mg XL  $\approx$   $\varnothing$  to activate pt with withdrawal or psychomotor retardation

**TCA's:** Avoid anticholinergics  $\rightarrow$  less with **nortriptyline** 10-75mg hs & desipramine 25-150mg/d;

**SE:** hypotension, blurred vision, urinary hesitancy, cardiac conduction changes

**Mirtazapine:** consider if anorexia/anxiety/sleep problem; **RD** rapid dissolve form if difficulty swallowing;  $\leq 7.5-45$ mg/d

**Moclobemide:** role in anxiety & mood dx but may  $\uparrow$  stimulation; 100mg od-300mg bid

**Trazodone:** low doses used for sedation & some anxiolytic effect;

monitor for hypotension, serotonin syndrome & rare priapism in  $\delta$

Consider ECT in management of treatment resistant or severe depression

**Start Low, Go Slow, But go!**

**PSYCHOSIS/AGITATION**

delusions, hallucinations; agitation, aggression

-use non-pharmacological intervention where 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 Tx**

-first designate target Sx (**not wandering or mild Sx**)

-try to minimize **sedation**,  $\uparrow$  confusion, hypotension & **EPS;** (titrate no more frequent than q1-2wks)

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

**risperidone** 0.25-2mg/day

**quetiapine** 12.5-200mg/day

**olanzapine**  $\blacktriangledown$  1.25-10mg/day

**haloperidol** 0.25-2mg/day (especially useful in delirium)

[aripiprazole  $\times$  & ziprasidone  $\varnothing$ : caution stimulating agents]

$\blacklozenge$  Newer agents as effective but generally better tolerated.

Monitor for **SE:** sedation, hypotension, falls  $?$ , EPS (drooling, rigidity & akinesia), anticholinergic SE dry mouth, delirium, constipation, ??ECG,  $\uparrow$  weight/lipids/diabetes,  $?$   $\uparrow$  stroke OR 2.5-3/ death OR 1.5-1.8 Class effect & tardive dyskinesia  $\Rightarrow$  this highlights need to **reevaluate ongoing use.**

$\blacklozenge$  Pts with **Lewy bodies** (often visual hallucination symptoms) have  $\uparrow$  sensitivity to neuroleptics (quetiapine low dose an option)

monitor for SE  
may attempt med tapering q3 month

**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

**ANTI-ANXIETY Medication**

- consider **short term as needed**

**lorazepam** 0.5-2mg/day

**oxazepam** 5-30mg/day

**clonazepam** 0.125-2mg/day (Caution long-acting!)

**Benzodiazepines-caution!**

**SE:** sedation, ataxia, altered sleep architecture, motor & **cognitive** impairment & propensity to cause withdrawal Sx when D/C. Paradoxical excitation, **disinhibition** & **falls** may occur. An intermediate acting such as temazepam/oxazepam/lorazepam can be best used for **short term**, if possible sleep/anxiety states or before planned anxiety provoking situations

**Trazodone** 12.5-100mg/day considered option by some 50-100mg po hs

**Bupirone:**  $\varnothing$  10-30mg/day

low sedation,  $\downarrow$ DI's,  $\downarrow$  withdrawal &  $\downarrow$  impairment of motor fx; option  $\rightarrow$  chronic anxiety but delayed **onset**  $\sim$  3wk

**APATHY**

Tx with **external activity & environmental** measures. Possible options with concerns: 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 1<sup>st</sup>** redirection, distraction, avoiding stimulants, limited data on drug tx antidepressants, antipsychotics, cholinesterase inhibitor (see also RxFiles Hypersexuality Chart).

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

**Pain:** consider trial of **acetaminophen**  $\leq 3.2$ g/day (e.g. 650mg po QID; or long-acting 1300mg BID AM & HS) to reduce **agitation & pain** Husebo'11; opiates if necessary in select individuals

**Cholinesterase Inhibitors** -modest cognitive, functional & behavioural benefit; may help apathy, hallucination & delusion? -post hoc analyses;

**unlikely to help agitation & aggression** - **not** better than placebo for agitation Howard'07, may help **Lewy Body dementia**  $\downarrow$  visual sx's

Consider **cholinesterase inhibitors** in Alzheimer's (donepezil, galantamine, rivastigmine)  $\approx$   $\varnothing$ ; but SE: nausea/vomiting, fatigue, anorexia,  $\downarrow$  heart rate, urinary incontinence

**Memantine**  $\times$  NMDA receptor antagonist, may help with agitation, aggression, irritability, disinhibition, & psychosis case reports, only post-hoc analysis of RCT

**Anticonvulsants:** some use short term ( $<6$ weeks) in agitation, aggression, hostility, sleep-wake disturbance cycle & mania

$\blacklozenge$  carbamazepine 100-600mg/day  $\leq 400$ mg/day in BPSD **SE:** sedation, ataxia, falls, rash, headache, leukopenia &  $\uparrow$  liver tests & **DIs.**  $\checkmark$  Good for impulsivity or if brain injury.

$\blacklozenge$  ? topiramate 25-50mg/day cognitive difficulties  $\blacklozenge$  valproate no longer recommended dose required associated with significant sedation, diarrhea, tremor, nausea, hair loss,  $\uparrow$  liver tests - useful if manic

$\blacklozenge$  other agents gabapentin, lamotrigine, levetiracetam benefit unknown - concerns re: worsening existing behaviour gabapentin-worsening agitation if Lewy Body dementia

**BETA BLOCKER:** propranolol 10-80mg/d; possible  $\downarrow$  aggression but diminishes over time; SE:  $\downarrow$  heart rate & hypotension Caution: asthma, PVD & possibly depression Hx

BP=blood pressure CI=contraindication DI=drug interaction Dx=disorder fx=function HR=heart rate Hx=history n/v=nausea/vomiting Pt=patient PVD=peripheral vascular disease SE=side effect Sx=symptom Tx=treatment  $\approx$ =Exception Drug Status Sask.  $\times$ =non-formulary in Sask.  $\otimes$ =not covered by NIHB  $\blacktriangledown$ =covered by NIHB  $\varnothing$ =prior approval NIHB

<sup>1</sup> Adapted from: Primary Care Management & Pharmacological Management of BPSD, International Psychogeriatric Association, Module 1-8 2002. <http://www.ipa-online.org/ipaonline3/ipaprograms/bpsdrev/6BPSDFinal.pdf>

<sup>2</sup> Hien le TT, Cumming RG, Cameron ID, et al. Atypical antipsychotic medications and risk of falls in residents of aged care facilities. *J Am Geriatr Soc.* 2005 Aug;53(8):1290-5.

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### Useful Web sites:

Alzheimer Society Canada [www.alzheimer.ca](http://www.alzheimer.ca)  
 Alzheimer Association USA [www.alz.org](http://www.alz.org)  
 Alzheimer Society UK [www.alzheimers.org.uk](http://www.alzheimers.org.uk)