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.[1]

♦ See also additional ***RxFiles Psychotropic Comparison Charts***!

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

*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 [CATIE 2005])

BENZODIAZEPINES:

- Minimize long-acting benzodiazepines (clorazepate, diazepam, flurazepam, chlordiazepoxide) due to ↑ fall risk & accumulation, leading to over-sedation, cognitive impairment & confusion
- Avoid triazolam (Halcion) due to amnesic 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 [or clonazepam (consider if benzo for anxiety)] in equivalent doses), and then gradually taper [10-25%/wk, esp. slow last 25%] over weeks or over several months

OTHER TREATMENTS FOR INSOMNIA:

- Promote **non-pharmacological sleep hygiene measures & rule out other contributing factors** [depression, pain; medications- steroids, acetylcholinesterase inhibitors, SSRI etc.]
- 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 [↓ tolerance & withdrawal] however dependency still a concern
- Limited duration of sedative therapy recommended [no more than 3-4wks]

ANALGESICS:

- Avoid certain NSAIDs (indomethacin, ketorolac, mefenamic acid, piroxicam), [meperidine, propoxyphene & pentazocine] which are more likely to cause CNS related adverse effects

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Management of Behavioural & Psychological Symptoms of DEMENTIA (BPSD)[1] Sep/11

Background: very common ≤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→**ABC's** **A**ntecedents (causes: Physical Intellectual Emotional Cultural Environmental Social), **B**ehaviours & **C**onsequences),
⇨ Assess history unique factors like Down's Sx, physical exam, cognitive tests Feldman CMAJ'08 & 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 ◆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)

Tx 1: **Assess for and treat any comorbitities** (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. activiy, 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

↓ mood, apathy, amotivation

Mild→ non pharmacologic

Moderate to *severe*→
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 →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, ↓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 ↑ 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 →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; ≤7.5-45mg/d
Moclobemide: role in anxiety & mood dx but may ↑ stimulation; 100mg od-300mg bid
Trazodone: low doses used for sedation & some anxiolytic effect;
monitor for hypotension, serotonin syndrome & rare priapism in ♂
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**,↑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/day
quetiapine 12.5-200mg/day
olanzapine ☎ ▼1.25-10mg/day
} monitor for SE may attempt med tapering q**3** month
haloperidol 0.25-2mg/day (especially useful in delirium)
[**aripiprazole** ✗⊗ & **ziprasidone** ✆: caution stimulating agents]

◆Newer agents as effective but generally better tolerated. Monitor for **SE**: sedation, hypotension, falls [2], EPS (drooling, rigidity & akinesia), anticholinergic SE dry mouth, delirium, constipation, ??ECG, ↑weight/lipids/diabetes, ? ↑stroke OR 2.5-3/death OR 1.5-1.8 Class effect & tardive dyskinesia ⇒ this highlights need to **reevaluate ongoing use**.
◆Pts with **Lewy bodies** (often visual hallucination symptoms) have ↑sensitivity to neuroleptics (quetiapine low dose an option)

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/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

Buspirone: ✆ 10-30mg/day
low sedation, ↓DI's, ↓ withdrawal & ↓ impairment of motor fx; option→ chronic anxiety but delayed onset ~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 1st** 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** ✗⊗ 3.75-5mg HS, **Limit to 3-4wk**

Pain: consider trial of **acetaminophen ≤ 3.2g/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** ↓ visual sx's
Consider **cholinesterase inhibitors** in Alzheimer's (**donepezil**, **galantamine**, **rivastigmine**) ☎ ✆; but SE: nausea/vomiting, fatigue, anorexia, ↓ heart rate, urinary incontinence

Memantine ✗⊗ NMDA receptor antagonist, may help with agitation, aggression, irritability, disinhibition, & psychosis case reports, only post-hoc analysis of RCT

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

BETA BLOCKER: propranolol 10-80mg/d; possible ↓ aggression but diminishes over time; SE:↓ 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 ☎=Exception Drug Status Sask. ✗ =non-formulary in Sask. ⊗=not covered by NIHB ▼=covered by NIHB ✆=prior approval NIHB

[1]Adapted from: Primary Care Management & Pharmacological Management of BPSD, International Psychogeriatric Association, Module 1-8 2002. http://www.ipa-online.org/ipaonlinev3/ipaprograms/bpsdrev/6BPSDfinal.pdf

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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