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!

<table>
<thead>
<tr>
<th>Common Reactions</th>
<th>Agents &amp; Comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticholinergics</td>
<td>Benztpine, chlorpheniramine, dicyclomine, diphenhydramine, hyosine, oxybutynin, propantheline, scopolamine, solifenacin, tolterodine, trihexyphenidyl, tropisium</td>
</tr>
<tr>
<td>Mood Stabilizers</td>
<td>↓ Cognition possible; ↑ drug interactions; (in general, aim for lower levels in elderly); Lithium poorly tolerated in some elderly; divalproex reasonably well tolerated</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>1. Anticholinergic highest activity with chlorpromazine &amp; clozapine; lowest with risperidone &amp; quetiapine 2. Sedation highest with clozapine*; olanzapine, chlorpromazine &amp; methotreximeprazine; lowest with haloperidol &amp; risperidone 3. EPS side effects highest with haloperidol; lowest with clozapine* &amp; quetiapine 4. Hypotension highest with chlorpromazine &amp; clozapine*; lowest with haloperidol &amp; olanzapine</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Long-acting Clonazepam, Diazepam &amp; high doses increase risk of toxicity 2. Short-acting Lorazepam, Oxazepam increase risk of withdrawal but less accumulation in the elderly Ultra short acting Triazolam can ↑ amnesia &amp; behavioural disturbances</td>
</tr>
<tr>
<td>SSRI antidepressants &amp; venlafaxine</td>
<td>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)</td>
</tr>
<tr>
<td>TCA antidepressants</td>
<td>1. Anticholinergic &amp; Sedation: most with amitriptyline, doxepin, imipramine; least with desipramine, norppritline 2. Hypotension with antidepressants: most with trazodone; least with norppritline</td>
</tr>
</tbody>
</table>

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

ANTIDEPRESSANTS:
- Caution: TCA's with high anticholinergic, sedative & hypotensive effects (i.e. amitriptyline, imipramine, doxepin, trimipramine); if low doses of these TCA's 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/migain 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)2

BENZODIAZEPINES:
- Minimize long-acting benzodiazepines (clorazepate, diazepam, flurazepam, chlorzepoxide) 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 benzodiazapine dose (i.e. diazepam or clozapine) in equivalent doses, and then gradually taper

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

OTHER TREATMENTS:
- Avoid certain NSAIDs (indomethacin, ketorolac, mefenamic acid, piroxicam), meperidine, propoxyphene & pentazocine which are more likely to cause CNS related adverse effects
MAJOR DEPRESSION
↓ mood, apathy, amotivation

Moderate to severe → ANTIDEPRESSANT Tx

Anxiety often coexists thus use antidepressants with anxiolytic properties 

e.g. citalopram, sertraline, venlafaxine

CANMAT 09 suggests: SSRIs, 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 (discharge) 
(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 incelty & hypoanesthesia
Citalopram 10-30mg/d, escitalopram® 10-20mg/d, sertraline 25-100mg/d
Venlafaxine: 37.5-225mg XR od (Similar SE as SSRIs, but high GI SE & may ↑ BP); XR cap: can sprinkle on food.
Bupropion: ≥ 100-150mg bid or 150-300mg XL w/ 2-3yr to activate pt with withdrawal or psychomotor retardation
TCAs: 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/insomniaVsleep problems; RR sedation is common; 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 elderly
Consider ECT in management of resistant or severe depression

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

ANTIPSYCHOTIC Tx
- first designate target Sx (not wandering or mild Sx)
- try to minimize sedation ↑ confusion, hypotension & EPS: (titrate no more frequent than q3-6wk)

○target Sx (hallucinations, delusions, hostility, aggression, severe agitation, & violent/ high risk behaviour)
risperidone 0.25-2mg/day quetiapine 12.5-200mg/day olanzapine 1.25-20mg/day haloperidol 0.25-2mg/day (especially useful in delirium)
[ariprazole x 2 & ziprasidone]: caution stimulating agents

-Neuger agents as effective but generally better tolerated. 
Monitor for SE: sedation, hypotension, falls ?, EPS (drooling, rigidity & akinesia), anticholinergic SE (dry mouth, urinary, constipation, ?ECCG, ↑ weight/lipids/diabetes, ↑ troclear <2.5-8> death OR 1.5-1.8 Class effect & tardy dyskinesia ⇒ this highlights need to reevaluate ongoing use.

-Pts with Lewy bodies (often visual hallucination symptoms)

have ↑ sensitivity to neuroleptics (quetiapine use dose ↓ an option)

AntiANXIETY Medication
- consider short term as needed lorazepam 0.5-2mg/day oxazepam 3-50mg/day clonazepam 0.125-2mg/day (Caution long-acting!)

Benzodiazepines-caution!
SE: sedation, ataxia, altered sleep architecture & cognitive & impairment & propensity to cause withdrawal Sx when D/C. Paradoxical excitation, sedation & falls may occur.

An intermediate acting such as temazepam/oxazepam/clonazepam can be best used for short term, if possible sleep/ anxiety states or before planned anxiety provoking situations

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

Buspirone: ↑ 10-30mg/d 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:

mentholphenidate, dopamine agonists or cholinesterase inhibitors.

SEXUALLY INAPPROPRIATE BEHAVIOUR
Assess for medical reason → UTI & any drug causes → benzodiazepine, dopamine agonists

Behavioural interventions ↑redirection, distraction, avoiding stimuli, limited data on drug tx antipsychotics, antipsychotics, cholinesterase inhibitor

Sleep Disturbances assess for medical reason → heart failure, sleep apnea drug cause → stimulants, Options: behavioural, trazodone 25-30mg HS, zopiclone 3-7.5mg HS, limit to 3-4wk

Pain: consider trial of acetaminophen ≤ 3.2g/day (eg. 650mg po QID; or long-acting 1300mg BD MWL) to reduce agitation & pain 

Buspirone: ↑ 10-30mg/d low sedation, ↓DI’s, ↓ withdrawal & ↓ impairment of motor fx; option → chronic anxiety but delayed onset →3wk

CHOLINERGIC INHIBITORS
modest cognitive, functional & behavioural benefit; may help apathy, unlikelihood to help agitation & aggression - not better than placebo for agitation 

Consider cholinesterase inhibitors in Alzheimer’s dementia, galantamine, rivastigmine, donepezil & memantine as appropriate as secondary to depression or very chronic in nature

MEMENTANU IMECA nNMDA receptor antagonist: may help with agitation, aggression, irritability, disinhibition, & psychosis

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

• carbamazepine 100-600mg/d ↓400mg/d in BPSD; SE: sedation, ataxia, falls, rash, headache, leukopenia & ↑ liver tests & DI; Good for impulsivity or if brain injury.

• gabapentin 3-5mg/kg/day cognitive difficulties & valproate no longer recommended: dose required associated with significant sedation, drowsiness, tremor, nausea, hair loss, ↑ but useful if mania & gabapentin-worsening agitation if Lewy Body dementia

BETA BLOCKERS
propranolol 10-80mg/d, possible ↓ aggression

Caution: asthma, PVD & possibly depression

Additional references:


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Malouf R, Grimley Evans J. Placebo foe with or without vitamin B12 for the prevention & treatment of mild cognitive & dementia. Cochrane Database Syst Rev 2008 Oct 8 (4):CD004514. The small number of studies which have been done prove the efficacy of vitamin B12, on vitamin B12, with or without placebo, on cognitive performance. There was significant heterogeneity in the number of patients who chose to follow-up and the number of data points available for analysis using individual patient data.


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Wong Camilla L.; Holroyd-Leduc Jayna; Simel DL.; Straus SE. Does This Patient Have Delirium?. Value of bedside instruments. JAMA. 2010;304(7):779-786. The Confusion Assessment Method is the most accurate tool for diagnosing delirium in adults that can be performed in less than 5 minutes. The Mini-Mental State Examination (MMSE) was the least useful diagnostic tool for delirium. (LOE = 3a)

Wood D, Craven RF, Whitney J. The effect of therapeutic touch on behavioral symptoms of persons with dementia. Altern Ther Health Med 2005; 11:66-74. (InfoPOEMs: Short-duration therapeutic touch, a specific treatment modality often practiced by nurses, decreases behavioral problems in patients with dementia, especially vocalizing and manual manipulation of hands or objects. This simple intervention was administered twice daily for 5 minutes to 7 minutes by a trained practitioner. (LOE = 1b))


Men will live a median 4.1 years and women a median of 4.6 years beyond a diagnosis of dementia.


Zhong KX, Tariot PN, Mintzer J, et al. Quetiapine to treat agitation in dementia: a randomized, double-blind, placebo-controlled study. Curr Alzheimer Res. 2007 Feb-April;4(1):81-91. ar-333. The results of this study suggest that quetiapine 200mg/day was effective and well-tolerated for treating agitation associated with dementia. However, caution should be exercised given the concerns regarding increased mortality with antipsychotics in this vulnerable patient population.

Useful Web sites:
Alzheimer Society Canada www.alzheimer.ca
Alzheimer Association USA www.alz.org
Alzheimer Society UK www.alzheimers.org.uk