Welcome to the Medication Safety Community of Practice Webinar Series

Hosted by ISMP Canada

March 21, 2012

Opportunities for Quality Improvement:

Contemporary Issues in the Use of Psychotropic Medications in the Management of Behavioural and Psychological Symptoms of Dementia in Long-Term Care

Medication Safety CoP Aim

- To improve Medication Safety within Long Term Care homes. It is a collaboration of three organizations HQO, QHN and ISMP Canada with support from SHRTN

Medication Safety CoP Team

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Opportunities for Quality Improvement:

Contemporary Issues in the Use of Psychotropic Medications in the Management of Behavioural and Psychological Symptoms of Dementia in Long-Term Care

Presenter

- **Carlos Rojas–Fernandez,** BSc (Pharm), PharmD
- Schlegel Research Chair in Geriatric Pharmacotherapy
- Schlegel-UW Research Institute on Ageing & School of Pharmacy, University of Waterloo

Objectives

- Increase awareness of medication use issues in the management of behavioural and psychological symptoms (BPSD) in long-term care (LTC) residents.
- Increase knowledge of improvement opportunities in LTC medication management system that affects physicians, nurses, pharmacists, and ultimately residents.
- Highlight actions that each profession can take to enhance the safety and care of residents with BPSD.

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Schlegel-UW RIA RESEARCH INSTITUTE *for* AGING

The Centre for Family Medicine

Opportunities for Quality Improvement: Contemporary issues in the use of psychotropic medications in the management of Behavioural and Psychological Symptoms of Dementia (BPSD) for residents in long term care.

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pharmacy.uwaterloo.ca

Carlos Rojas-Fernandez, BSc(Pharm), PharmD
Schlegel Research Chair in Geriatric Pharmacotherapy
March 20th, 2012

Disclosures

- Current funding:
  - UW-RBJ Schlegel RIA
  - CIHR
  - Pfizer
  - Purdue
  - AstraZeneca

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Roles

- **Research**
  - Long term care and primary care
    - Alzheimer's disease and related disorders, falls
    - Various other diseases
- **Clinical Geriatric Pharmacotherapy**
  - CFFM Memory Clinic
- **Teaching**
  - UW School of Pharmacy
  - AHS Health Studies & Gerontology
  - MacMaster Family Medicine

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Questions

- >50%-90% of patients with dementia will be affected by BPSD.
  - True or false?
- BPSD are best treated with medications
  - True or false?
- When medications are necessary for BPSD, any of the antipsychotics may be used interchangeably.
  - True or false?

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Questions

- In many cases, BPSD may be the result of reversible causes.
  - True or false?
- When drugs are used to manage BPSD, what is the optimal duration of therapy?
  - 6 months
  - 3 months
  - 9 months
  - 12 months
  - 24 months

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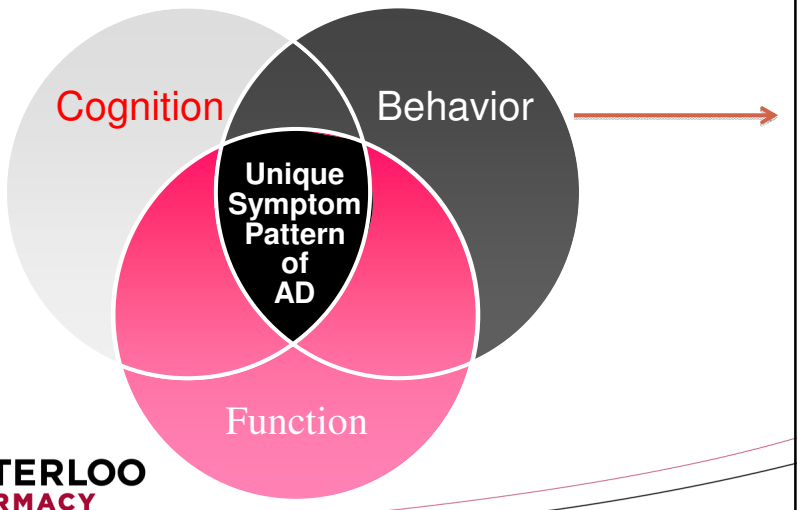
Symptomatic expression of dementia



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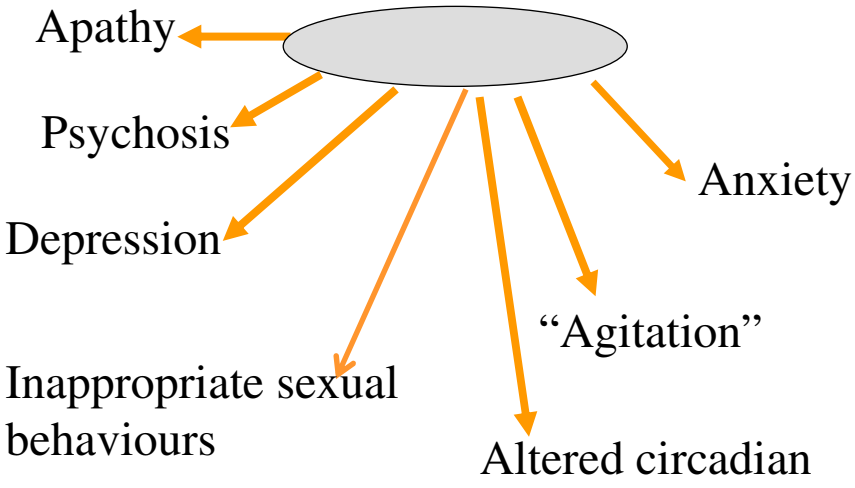
Symptom Complexes of BPSD



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Relevance of BPSD

- >50%-90% of patients are affected
- Reduced ADL function (incl. incontinence)
- Compromised nutrition and hydration
- Falls, aspiration, injuries
- Suffering, excess disability

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Relevance of BPSD

- Caregiver time, stress, depression.
- Increased hospitalizations.
- Premature institutionalization.
- Overall ↑ in health care use (e.g., ER visits, ALC time).
- Interference with medical and nursing care

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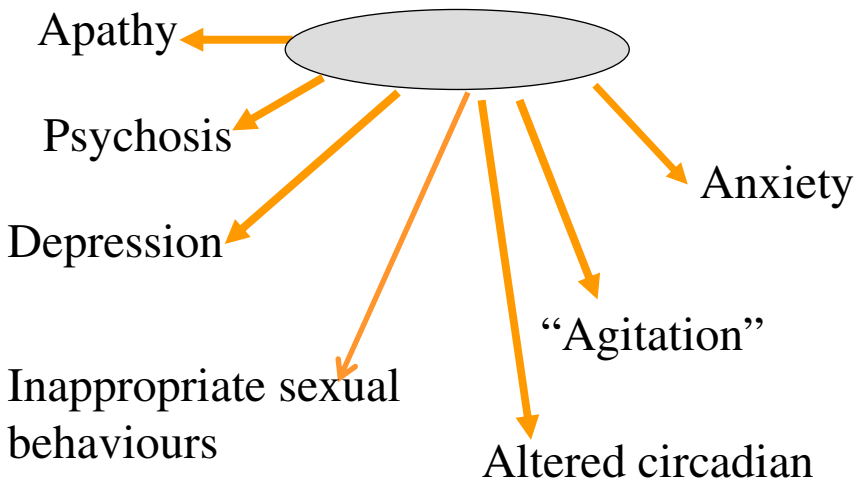
Symptom Complexes of BPSD



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Apathy

- Is a behavioural sign of executive dysfunction.
- May be characterised by loss of motivation:
  - Reduced initiative
  - Poor persistence
  - Lack of interest
  - Indifference
  - Blunted emotional response, lack of concern
  - Low social engagement

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Apathy

- Compare w depression:
  - Negative thoughts, dysphoria, pessimism, self criticism
- One of the most commonly occurring BPSD (up to 92% of AD patients).
- Increases care demands, CG burden and stress.

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Landes AM. J Am Geriatr Soc 2001

Psychosis: AD Vs Schizophrenia.

	Psychosis of AD	Schizophrenia
Bizarre or complex delusions	Rare	Frequent
Misidentifications of caregivers	Frequent	Rare
Common form of hallucinations	Visual	Auditory
Active suicidal ideation	Rare	Frequent
Past history of psychosis	Rare	Frequent

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Delusions

- Theft
- House is not one's home
- CG or spouse is impostor
- Abandonment
- Infidelity

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Depression in AD.

- Depressive symptoms often fluctuate.
- Depressed patients with AD exhibit more self-pity, rejection sensitivity, anhedonia and psychomotor disturbance than depressed older patients without dementia.
- Major depression in AD is associated with an increased mortality rate, but no acceleration of cognitive decline.

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Inappropriate sexual behaviours

- Up to 25% of patients with dementia exhibit these behaviours
- Non-pharmacological approaches very important:
  - Education
  - Avoid confrontation
  - distraction,
  - Modified clothing, etc

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Tucker I. Int Psychogeriatr 2010;22:5:683-92.

Circadian Rhythm Disturbances

- Functional and anatomic changes occur in the suprachiasmatic nucleus in dementia.
- Alterations of the daily rhythm of serum melatonin have been correlated to some cases of sleep disturbances in Alzheimer's disease.

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Stopa, Volicer, et al. 1999, Uchida, Okamoto, et al. 1996

Circadian Rhythm Disturbances

- Disturbances of sleep and day-night reversals are common.
- Sleep disturbances may be more common in VaD, DLB & PSP, compared to those found in AD.

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Agitation

- Some symptoms don't fit well into defined symptom complexes of BPSD such as psychosis, depression or anxiety.
- They are consigned to the "grab-bag" category of "agitation", which is a sensitive, but non-specific term.
- Agitation
  - May be defined as inappropriate verbal, vocal or motor activity that is not judged by an outside observer to result directly from the needs or confusion of the person.

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Physically Non-Aggressive

- General Restlessness
- Repetitive mannerisms
- Pacing
- Hiding Objects
- Inappropriate Handling
- Shadowing
- Escaping protected environment
- Inappropriate Dressing/Undressing

Verbal Non-Aggressive

- Negativism
- Chanting
- Repetitive Sentences
- Constant Interruptions
- Constant Requests for Attention

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Physically aggressive

- Hitting
- Pushing
- Scratching
- Grabbing
- Kicking
- Biting
- Spitting

Verbally aggressive

- Screaming
- Cursing
- Temper Outbursts

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Aggression symptom complexes include:

- Reactive aggression associated with personal care, discomfort.
- Aggression associated with delirium
- Aggression associated with depression
- Aggression associated with psychosis
- Spontaneous disinhibited aggression

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Anxiety Symptoms in BPSD

- No specific definition of anxiety in BPSD is available;
  - Generalized anxiety disorder type symptoms
  - Godot syndrome (repeatedly asking questions on a forthcoming event)
  - Fear of being left alone
  - Pacing
  - Wringing of hands, fidgeting
  - Chanting

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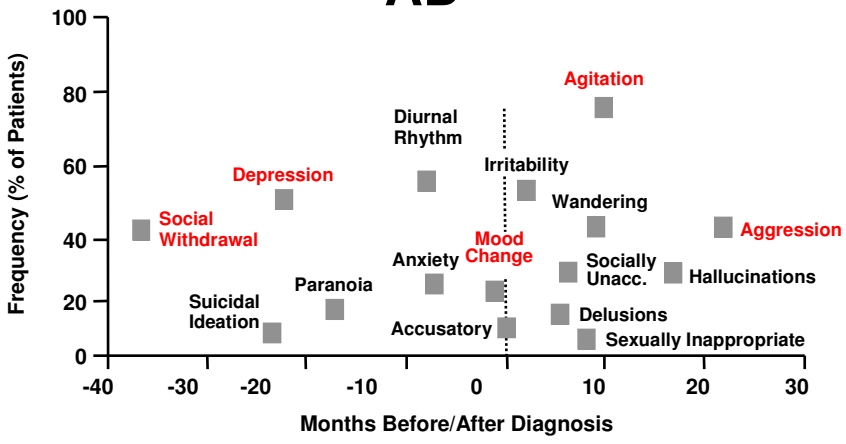
Peak Frequency of Behavioral Symptoms with Progression of AD



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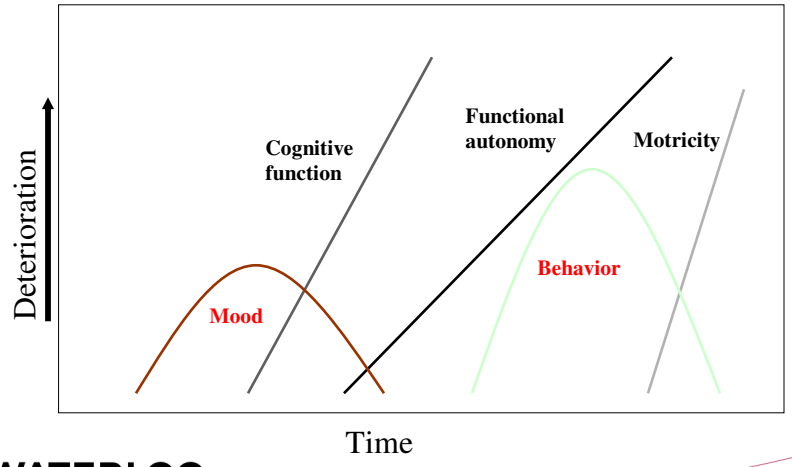
Jost BC, Grossberg GT. J Am Geriatr Soc. 1996;44:1078-1081

Symptomatic domains over time



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Gauthier, et al. 1996; Gelinas and Auer. 1996; Eastwood and Reisberg. 1996; Barclay, et al. 1985.

Most common/ most distressing symptoms.

- Psychological
  - Delusions
  - Hallucinations
  - Depressed mood
  - Sleeplessness
  - Anxiety
- Behavioural
  - Pacing
  - Physical aggression
  - Wandering
  - Restlessness

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Most persistent symptoms

- Wandering
- "Agitation" (restlessness, increased motor activity)
  - –i.e., physical or verbal aggression

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Devanand, et al. Arch Gen Psych 1997;54:257-63 & Alz Dis Rel Disord 1999;13(Suppl 2):S3-S8.

Symptoms that may respond to Rx

- Anxiety, restlessness, depressive symptoms.
- Withdrawal, apathy
- Elation, pressured speech and hyperactivity
- Delusions or auditory hallucinations
- Physical or verbal aggression
- Sexually inappropriate behaviour

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Symptoms that do not tend to respond to Rx

- Simple wandering
- Inappropriate voiding
- Inappropriate dressing/undressing
- Perseveration
- Hiding, hoarding
- Eating inedibles

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Therapy

- First think of the obvious:
  - Responsive behaviours:
    - i.e., Reversible causes
      - E.g., infection, cold, hot, hunger, recent change in routine &/or medications, etc
      - Appropriate pain management may be effective in reducing BPSD.
        - » Husebo BS. BMJ 2011;343:1-10.

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Nonpharmacologic Therapy

- Environmental modifications such as music, white noise, plants, animals
- Speak slowly, keep commands simple and positive, use gestures, gentle touch
- Behavioral management techniques
- Structured activities and use of schedules
- Massage, exercise

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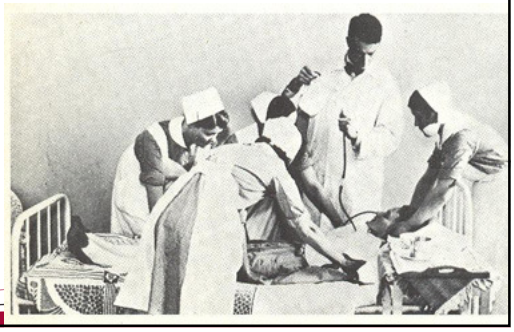
Rowe, Alfred 1999
Gerdner, Swanson 1993

When to treat with medications?

- Personal biases, thresholds..
- Perceived CG stress
- Regulations
- Etc…



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Pharmacotherapeutic principles for BPSD:

- Look for symptom complexes to help guide initial choice of agent.
  - E.g., depression, depression/anxiety, psychosis.
- Medications should be given in lower doses than recommended adults (50% less) and follow guidance from appropriate study data.
- Ideally, use agents with **demonstrable efficacy** as first line agents.
  - NB: Demonstrable does not = Health Canada or FDA approval….
- Carefully consider **side effects**……

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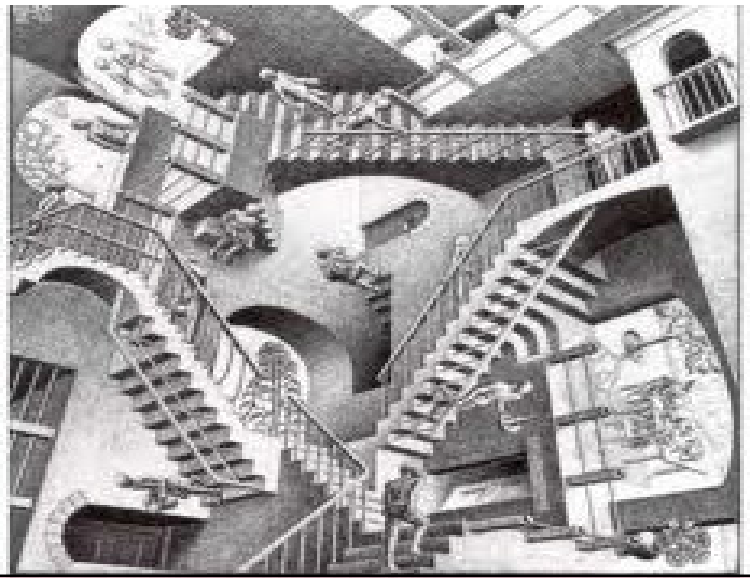
Associations between antipsychotics and adverse outcomes: The tale of safety.



CVAE warnings for atypical antipsychotics

- Risperidone 2002-03
- Olanzapine 9/04
- Aripiprazole 1/05

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"Black Box" warnings

- April 2005, FDA
- June 2005, Health Canada
- June 2008, FDA for typical APs

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Bottom line?

- They are all potentially risky with a 1.5 to 1.8X greater risk of mortality.

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Safety Considerations of particular importance in older people

- ↑ risk for antipsychotic-related AEs
  - EPS
  - Tardive dyskinesia (TD)
- Orthostatic hypotension
- Sedation
- Anticholinergic effects
- **Cognitive impairment**
- Cardiac conduction abnormalities
- **↑ fall risk due to any/all of above**

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ANTIPSYCHOTIC SIDE EFFECTS

	HAL	RIS	OLZ	QUET	ZIP	CLZ	ARIP
Anticholinergic	-	-	++	-/+	-	+++	-
Weight gain	+	+	+++	+	-	+++	-
Prolactin	+++	++	-/+	-	-	-	-
EPS/TD	+++	+/++	+	-/+	-/+	-	-
Sedation	-	+	+/++	+/++	-/+	+++	-/+
Cardiac	-	-	-	-	-/+	+	-

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Evidence for the Efficacy of Antipsychotics and current use

- The best of a bad bunch…..

Current evidence supports use of risperidone or aripiprazole, at least for up to 12 weeks for agression or psychosis

Efficacy and Adverse Effects of Atypical Antipsychotics for Dementia: Meta-analysis of Randomized, Placebo-Controlled Trials

Lon S. Schneider, M.D., M.S., Karen Dagerman, M.S., Philip S. Insel, M.S.

risperidone; increased risk for death overall was reported elsewhere. **Conclusions:** *Small statistical effect sizes on symptom rating scales support the evidence for the efficacy of aripiprazole and risperidone. Incomplete reporting restricts estimates of response rates and clinical significance. Dropouts and adverse events further limit effectiveness. Atypicals should be considered within the context of medical need and the efficacy and safety of alternatives. Individual patient meta-analyses are needed to better assess clinical significance and effectiveness.* (Am J Geriatr Psychiatry 2006; 14:191–210)

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The reality

- Risperidone or aripiprazole are not always effective (**nothing is**) nor always tolerated.
- Above factors (& others) lead to use of various drugs.
- Must therefore **carefully consider evidence & be knowledgeable regarding alternatives and their safety profile in this vulnerable population….**

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Additional considerations

- Effect size for BPSD vs other diagnoses.
- Effect size for NH vs community subjects.
- Waxing and waning of BPSD/reassessment and discontinuation (to be covered later).

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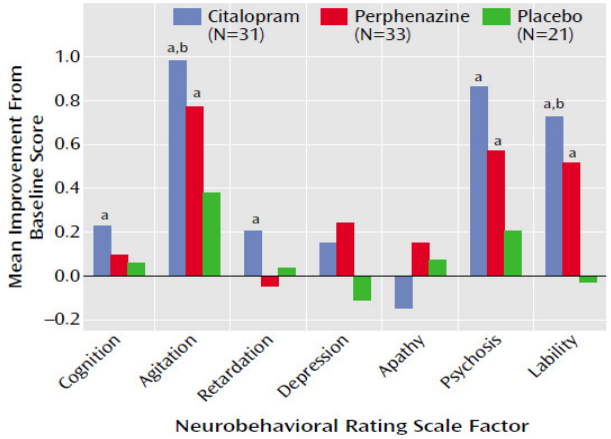
Are antidepressants helpful?

FIGURE 1. Change in Neurobehavioral Factor Scores From Baseline to Study Termination (≤17 Days) in Patients With Dementia in a Randomized, Double-Blind, Placebo-Controlled Trial of Citalopram and Perphenazine



[a] Significant difference within group between baseline and termination scores (Wilcoxon signed-rank test, $p<0.05$).
[b] Significant difference between the citalopram and placebo groups (Kruskal-Wallis test, $p<0.05$).

Am J Psychiatry 159:3, March 2002

Are antidepressants helpful?

Lancet 2011; 378:403-11.

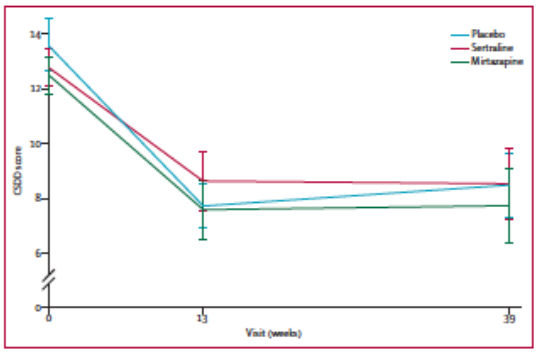


Figure 2: Unadjusted mean CSDD scores by treatment group
Lowest score is best. Error bars show 95% CIs. CSDD=Cornell scale for depression in dementia.

Before you say no, consider:

1.Study setting
2.Other benefits
3.Power
4.Severity of depression
5.50% overall failure of antidepressant studies, and not many have been done in AD
6.Lack of response to on SSRI does not predict it to the other

These drugs are used empirically for depression & aggression.

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5-HT drugs

- Fluoxetine: t ½ can be a problem.
- Fluvoxamine: Nausea can be a problem.
- Paroxetine: Anticholinergic properties.
- **Citalopram/escitalopram: Very well tolerated.**
  - Citalopram: 5-10mg/day, can increase to 20mg/day
  - Escitalopram:5-10mg/day, may increase to 20mg/day

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5-HT drugs

- **Sertraline: Well tolerated, good second choice.**
  - 25mg daily, may increase if needed.
- **Trazodone: Very well suited for sleep and aggression.**
  - Start with 25-50mg and titrate as needed

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Mood stabilisers??

- VPA (Depakote and others)
  - Data from case reports & small case series.
  - Cochrane review concluded no benefit.
  - Dose to response/side effects.
  - Would you draw levels?
- Gabapentin
  - From case reports
  - Dose to response/side effects.
  - Drowsiness may be problematic
  - 100% renally excreted…
  - Best avoided

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Mood stabilisers

- Carbamazepine
  - Evidence for efficacy better than w other mood stabilisers.
  - Can be difficult to use.
  - Would you draw levels?
  - Dosing?

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Apathy Pharmacotherapy

- Evidence to guide us is scant…
  - AChEIs (donepezil)
  - Bupropion
  - Methylphenidate
  - ? Memantine

Mega MS. Arch Neurol 1999, Landes AM. JAGS 2001, Dolder CR. Ann Pharmacother 2010.

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Inappropriate sexual behaviours

- Pharmacological approaches:
  - **Eliminate drugs that are disinhibiting (etoh, BZPs**)
  - Perhaps AChEIs
  - Most data are **case reports**
    - Citalopram, trazodone, quetiapine
    - Gabapentin
    - Estrogens
    - Leuprolide, cyproterone

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Tucker I. Int Psychogeriatrics 2010:22:683-92.

Circadian Rhythm Disturbances

- **Nonpharmacologic therapies include:**
  - **keeping patients awake during the day with various external stimuli**
  - sometimes structuring short nap after lunch to avoid sundowning
  - **early evening activities**
  - **stimulus control at night**
  - "**white noise**"
  - bright light exposure

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Circadian Rhythm Disturbances

- Pharmacologic interventions include melatonin, nonbenzodiazepine hypnotics (e.g. zopiclone, ***trazodone***).
- Caregiver interventions include: educational programs, respite, and assistance with their own sleep needs.

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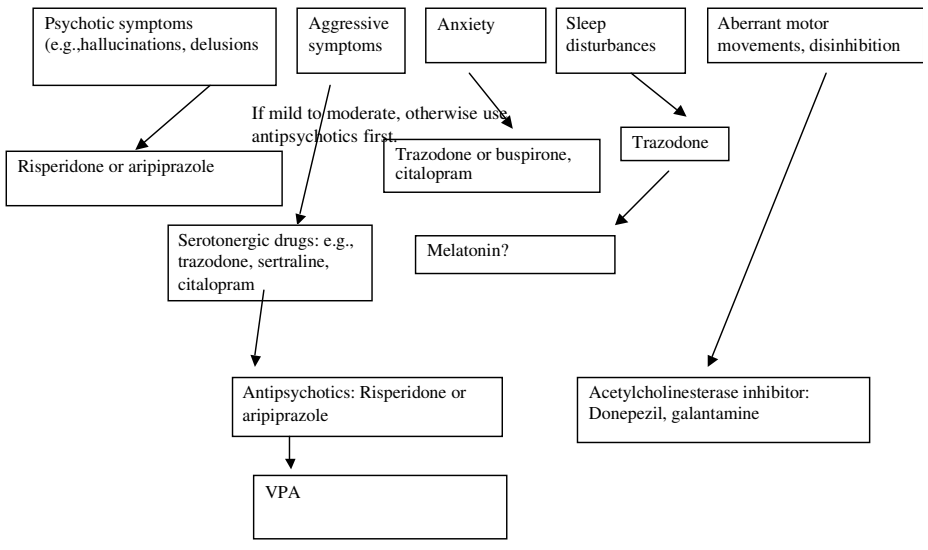
Figure 1. Putative approach to BPSD



Alternatively, acetylcholinesterase inhibitors may be used as first line

Measuring effectiveness

- Keep it simple & look at/measure:
  - Frequency
  - Severity
  - XS work due to symptom
- Alternatively:
  - Goal setting?

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How long to treat?

- Guidelines suggest attempt at lowering dose and stopping the medication **after 3 months of stability.**
  - E.g., Paranoid delusions or hallucinations occurred at ¾ consecutive visits over 2 years of f/u in only 10-15% of patients. (Devanand 1997)

Herrmann N. Alzheimer's and Dementia 2007;3:385-97.

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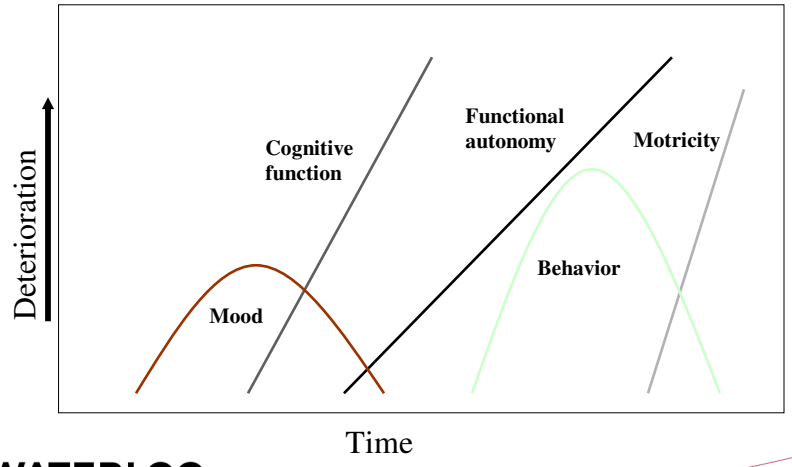
Symptomatic domains over time



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Gauthier, et al. 1996; Gelinas and Auer. 1996; Eastwood and Reisberg. 1996; Barclay, et al. 1985.

Discontinuing antipsychotics is NOT a new concept!

SPECIAL ARTICLE

A RANDOMIZED TRIAL OF A PROGRAM TO REDUCE THE USE OF PSYCHOACTIVE DRUGS IN NURSING HOMES

JERRY AVORN, M.D., STEPHEN B. SOUMERAI, SC.D., DANIEL E. EVERITT, M.D., DENNIS ROSS-DEGNAN, SC.D., MARK H. BEERS, M.D., DAVID SHERMAN, R.PH., SUSANNE R. SALEM-SCHATZ, SC.D., AND DAVID FIELDS, M.D.

Conclusions. An educational program targeted to physicians, nurses, and aides can reduce the use of psychoactive drugs in nursing homes without adversely affecting the overall behavior and level of functioning of the residents. (N Engl J Med 1992;327:168-73.)

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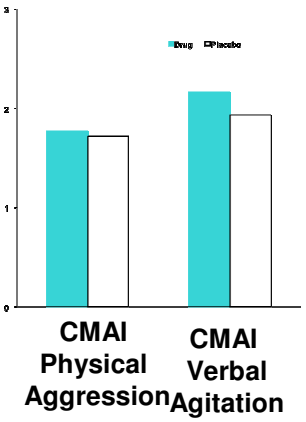
Withdrawal of haloperidol, thioridazine & lorazepam in NH Residents



- DB controlled crossover trial: 60% completed
- Mean duration of therapy: 16.5 months
- **No behavioral or functional differences detected after placebo crossover**

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Cohen-Mansfield J, Lipson S, Werner P et al. Arch Intern Med. 1999;159:1733-174

Ballard C, et al. A randomised, blinded, placebo-controlled trial in dementia patients continuing or stopping neuroleptics. PLoS Med 2008;5(4):e76.

Conclusions

For most patients with AD, withdrawal of neuroleptics had no overall detrimental effect on functional and cognitive status. Neuroleptics may have some value in the maintenance treatment of more severe neuropsychiatric symptoms, but this benefit must be weighed against the side effects of therapy.

Trial registration: Cochrane Central Registry of Controlled Trials/National Research Register (#ISRCTN33368770).

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INTERNATIONAL JOURNAL OF GERIATRIC PSYCHIATRY
Int J Geriatr Psychiatry 2008; **23**: 889–895.
Published online 27 February 2008 in Wiley InterScience
(www.interscience.wiley.com) **DOI**: 10.1002/gps.1998

Stopping antipsychotic drug therapy in demented nursing home patients: a randomized, placebo-controlled study—The Bergen District Nursing Home Study (BEDNURS)

Results By study completion, 23 of the 27 intervention group patients were still off antipsychotics. Symptom scores (NPI remained stable or even improved in 42 patients (intervention group, 18 out of 27; reference group, 24 out of 28; $p = 0.18$). As compared to patients with stable or improved symptom scores, patients with behavioural deterioration after antipsychotic cessation used higher daily drug doses at baseline ($p = 0.42$).
Conclusion A large share of elderly nursing home patients on long-term treatment with antipsychotics for BPSD, do well without this treatment. Standardized symptom evaluations and drug cessation attempts should therefore be undertaken at regular intervals.

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Summary

- Pharmacologic treatment is often indicated for BPSD.
- Use a structured approach (vs. using antipsychotics for all BPSDs).
- Revisit in a few months with a goal of stopping medications.

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Web resources

- www.ipa-online.org
- http://livingwithdementia.uwaterloo.ca/
- www.alzforum.org
- http://www.alzheimer.ca/

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Case 1

- 85 year old female with AD has recently been telling her CG that she enjoys having a doorman at their house everyday.
- CG tells you no such person exists and wonders what he should do.
- Standard workup is unremarkable.
- No new medications added or deleted.
- No other consequences noted.

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Case 1

Which is the best treatment option?

A: Cholinesterase inhibitor

B: Trazodone

C: No drug therapy

D: Risperidone

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Case 2

- 80 year old female with multiple diseases and medications
- Dx: AF, hypothyroid, OA, OP, HTN, atonic bladder
- Rx: include warfarin, APAP, thyroxine, etc
- Recent INR: 1.1; TSH: 18; BP: 175/86

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Case 2

- CG reports patient only takes ~ 50% of her doses & has hit him and their daughter when they try and help with her medicines.
- She is also very angry, and believes her husband is having an affair.
- Also believes that he and their daughter are plotting to poison her with all these drugs.

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Case 2

Which is the best treatment option?

A: Cholinesterase inhibitor

B:Trazodone

C: Risperidone or aripiprazole

D: Olanzapine

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PHARMACY

Case 3

- 82 year old male with AD living in NH has been resisting care (i.e., bathing and grooming) & constantly gets up at night and wanders.
- The patient states he doesn't care to be bathed four times a week and doesn't like his new caregiver, Mike who works 3 days/week.
- Staff are able to provide care but they state that it takes longer on the days that Mike works.

WATERLOO
PHARMACY

Case 3

Which is best treatment option?

A: Cholinesterase inhibitor

B: Trazodone

C: Valproic acid

D: No drug therapy

WATERLOO
PHARMACY

Questions?

We encourage you to report medication incidents

Reporting and Prevention Systems
Medication Incident and Near Miss Reporting Programs

REPORT a Medication Incident

Practitioners
Healthcare Professional - (e.g., nurse, pharmacist, physician)

SafeMedicationUse.ca
Supported by Health Canada

General Public
Preventing harm from medication incidents is not just a responsibility for health professionals - **consumers like you** can also play a vital role.

Community Pharmacy Incident Reporting

CPhIR - Community Pharmacy Incident Reporting Program
For participating community pharmacies.

ANALYZE-ERR®

Analyze-Err®
For participating healthcare facilities.

Post-session Questionaires:

- Post-session attendance statistics survey
- An Evaluation link will be sent to you
  - Please complete

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Thank You