Managing Challenging Behaviours in Dementia Care: The Rational use of Antipsychotics, Benzodiazepines, and More

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## Objectives

#### Learning objectives:

- 1. Review common challenging behaviours in dementia care and an approach to medication management when necessary
- 2. Describe the rational use of antipsychotics and benzodiazepines, and practical strategies for antipsychotic and benzodiazepine withdrawals.

# BPSD = "symptoms of disturbed perception, thought content, mood or behavior that frequently occur in patients with dementia"

International Psychogeriatric Association Consensus Conference Statement, 1996

Prevalence of neuropsychiatric symptoms:

- o 43% of patients with MCI
  - •depression (20%)
  - apathy (15%)
  - irritability (15%)
- o 75% of patients with dementia (2+ symptoms in 55%)
  - apathy (36%)
  - depression (32%)
  - agitation/aggression (30%)

Lyketsos CG et. Al. JAMA 2002

#### **BPSD**

- reported in 63% of dementia patients living in the community
- •"...afflict almost all patients with dementia over the course of their illness"
- ... may have a greater impact on health care resources and caregiver distress than cognitive abnormalities"
- those with behavioral disturbances will enter LTC 2 years earlier

Hogan DB, et al. Alzheimer's & Dementia 2007 Lyketsos CG et al. JAMA 2002 Mega MS et al. Arch Neurol 1999

#### P.I.E.C.E.S. framework

Look at the reasons behind the behavior (what's changed?), impact, and risk to individual and others:

- Consider role of Physical factors e.g., co-morbidities, meds, pain
- Assess "intrinsic factors" (Intellectual, Emotional, Capacities)
- Seek collateral info sources re situational precipitants (Environmental)
- Consider in relation to premorbid personality / Social circumstances

Ontario 's Strategy for Alzheimer Disease and Related Dementia: Initiative #2

Always consider behavioral interventions first

Agitation, Aggression, and Psychosis

## Agitation, Aggression, Psychosis

- Nonpharmacologic Strategies

- Assess for physical discomfort
- Avoid confrontation
- Plan structured daily activities (exercise, arts and crafts, gardening, simple housework)
- Assign household chores that can be easily accomplished
- Provide clocks and calendars in clear view
- Avoid interactions with strangers and unfamiliar environments
- Ignore behavior that is only annoying and not a threat
- Reward positive experiences
- [Play soft music; introduce aromatherapy]

Blaszczyk AT, Mathys M. Journal of Pharmacy Practice 2007

		ES of My Personh		
		PAST	PRESENT	
	Preferred name			
	Preferred language			
	I am most proud to be			
	known as/for			
	Spirituality/religion			
	Significant persons in			
	life/relationships			
	Significant dates and			
	meaning			
"DIE CE C C L	Pets/names			
"PIECES of M	Life role/previous occupation			
Personhood				
Personnood	Sources of comfort.		-	
	pleasure, favorite things			
	Dislikes/fears			
	Significant high point(s) in life (especially up to			
	age 30)			
	Significant low point(s)			
	in life/traumatic			
	experiences (especially			1
	up to age 30)			1
	Expressions of emotion			
	Coping mechanisms/			
	Validation phrases			1
	Mealtime preferences			
	Socialization preferences			
	Sleep/wake preferences			
	Other relevant information			

#### Agitation, Aggression, Psychosis

- Nonpharmacologic Strategies
- "Get into their world", age 3-30, and identify potential triggers
  - > PIECES of My Personhood
  - Artful distraction
    - o "Mountain top experiences" proud, positive moments
    - o Recognize traumatic experiences abuse, stressful times
    - Suggest a physical task/activity to help the person feel useful
  - Communicate feeling smile, sorry, calm
  - Don't confront the false belief; validate the feeling

Sources: Dr. Ken LeClair, NE LHIN Behavioural Supports Ontario

#### Agitation, Aggression, Psychosis

- Pharmacologic treatment
- AchEls
- Memantine
- Antidepressants
  - -Citalopram (10-20mg/d)
  - Trazadone (50-250mg/day; limited evidence; watch for sedation, orthostatic hypotension)

Porsteinsson AP, et al. JAMA 2014 Blaszczyk AT, Mathys M. Journal of Pharmacy Practice 2007 Ballard C, et al. Current Opinion in Psychiatry 2009 Ballard CG, et al. Nature Reviews/Neurology 2009 Okereke OJ, Harvard Dementia Review 2010 Lonergan E, Luxenberg J. Cochrane Database Syst Rev 2009 Täriot PN, et al. Arch Gen Psychiatry 2011

# Canadian Coalition for Senior's Mental Health www.ccsmh.ca/en/projects/ltc.cfm Tool on Pharmacological Treatment of Behavioral Symptoms of Dementia in Long Term Care Facilities for Older Adults Based on: Canadian Codition for Seniors' Mental Health (CCSMH) National Guidelines: The Assessment and Treatment of Mental Health Issues in Long Term Care Homes For more information or to order additional brochures, visit the Canadian Coalition for Seniors' Mental Health website: www.ccsmh.ca This pocket card was supported by a Canadian Institutes of Health Research Knowledge Synthesis Grant: KRS #103345: "Interventions for Neuropsychatric Symptoms of Dementia in Long-Term Care". USCLAMIR: This tool, propored in April 2012, is on all for healthcare provides. It is not a substitute for a physician diagnosis and treatment and is not mendal advice. The art of the proposal in the Coalities of the Coalitie

Table 1: Medi	cations for Agita	ition or Psychosis			
Medication	Initial Dose	Titration & Maximum Dose	Formulations	Adverse Events	Comments
Atypical Antipsychotics	;				$\overline{}$
Risperidone*	0.25mg BID or 0.5 mg OD	0.5mg every 3-7 days, 2mg max. total daily dose. May use 0.5 mg PO BID as prn	Tablet (0.25, 0.5, 1.0, 2.0 mg), oral dissolving, liquid, ointment, long- acting injection.	Most likely of atypicals to cause EPS	Best supported atypical antipsychotic for NPS
Olanzapine*	2.5mg QHS	2.5mg every 3-7 days, 10mg max. total daily dose. May use 2.5mg PO BID as prn	Tablet (2.5, 5.0, 7.5, 10.0 mg), oral dissolving, short-acting IM.	More sedating than risperidone or aripiprazole	Most likely to cause metabolic side-effects
Aripiprazole*	2mg PO OD	2-5mg every 3-7 days, max 10 mg total daily dose	Tablet (2.0, 5.0, 10 mg), short-acting IM.	Most likely to cause akathisia	
Quetiapine	12.5mg PO BID	12.5mg BID every 3-7 days to max. total daily dose of 200mg	Immediate & extended release formulations. (25,50, 100, 200mg, XR not available in 25 mg)	More sedating then a risperidone or aripiprazole	May be used for Parkinson's disease dementia or dementia with Lewy bodies at lower doses
Antidepressants					_
Citalopram**	10mg PO OD	10mg every 1-2 weeks, max 20mg	Tablet, liquid forms	May cause hyponatremia	Best supported SSRI for NPS
Escitalpram**	5mg PO OD	5mg every 1-2 weeks, max of 10mg	Tablet	Same as citalopram	
Sertraline**	25mg PO OD	25mg every 1-2 weeks, max of 100mg	Tablet	Same as citalopram	
Anticonvulsants					
Carbamazepine	50mg PO OD	50mg every 1-2 weeks, given BID-QID, max. 500 mg	Tablet, liquid forms	Sedation, gait disturbance, neutropenia, hyponatremia	High potential to cause drug interactions, therapeutic drug level monitoring required
Typical Antipsychotics					
Haloperidol	0.5mg PO BID	0.5mg BID every 3-7 days, max 1.5mg BID	Oral, short-acting intramuscular, long-acting depot formulations	Most likely to cause EPS	May be used in emergency treatment where other IM medications are not available

#### Risk of Death With Atypical Antipsychotic Drug Treatment for Dementia

Meta-analysis of Randomized Placebo-Controlled Trials

Lon S. Schneider, MD, MS Karen S. Dagerman, MS Philip Insel, MS

MAJORITY OF ELDERLY PAtients with dementia develop aggression, delusions, and other neuropsychiatric symptoms during their illness course. Antipsychotic medications are commonly used to treat these behaviors,

**Context** Atypical antipsychotic medications are widely used to treat delusions, aggression, and agitation in people with Alzheimer disease and other dementia; however, concerns have arisen about the increased risk for cerebrovascular adverse events, rapid cognitive decline, and mortality with their use.

**Objective** To assess the evidence for increased mortality from atypical antipsychotic drug treatment for people with dementia.

Data Sources MEDLINE (1966 to April 2005), the Cochrane Controlled Trials Register (2005, Issue 1), meetings presentations (1997-2004), and information from the sponsors were searched using the terms for atypical antipsychotic drugs (aripiprazole, clozapine, olanzapine, quetiapine, risperidone, and ziprasidone), dementia, Alzheimer disease, and clinical trial.

- JAMA 2005 meta-analysis of 15 trials
- Odds Ratio of death = 1.54
- ■over 10-12 weeks, "for every 9 to 25 persons helped in these trials there possibly will be 1 death"

Schneider LS, et al. JAMA 2005

# The dementia antipsychotic withdrawal trial (DART-AD): long-term follow-up of a randomised placebo-controlled trial

- 164 patients randomized to continue antipsychotic or switch to placebo at 12 months
- 24 m survival 46% vs 71%
- 36 m survival 30% vs 59%

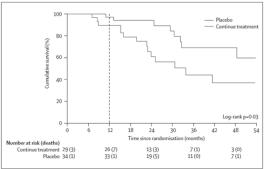


Figure 3: Kaplan-Meier survival estimates of participants who received at least one dose of treatment and

• "avoid protracted periods of treatment with antipsychotic drugs in people with dementia"

Ballard C, et al. Lancet Neurology 2009

# Antipsychotic Adverse Events in Persons with Dementia

#### **Serious Adverse Events**

- 1-2% increased risk of death associated with use of atypical antipsychotics over 6-12 months (odd ratio=1.6, number needed to harm = 50-100)
- Approximately 1% risk of stroke with short-term treatment (relative risk = 2.7)

#### **Other Adverse Effects**

- Sedation
- Worsening of cognitive impairment and functional decline
- Affect gait, increased risk of falls and fractures
- Extrapyramidal symptoms (risperidone > quetiapine)
- Metabolic changes blood glucose, dyslipidemia, weight gain

Seitz DP. Canadian Coalition for Senior's Mental Health. 2012

#### Agitation, Aggression, psychosis

- Pharmacologic treatment Antipsychotics
- 4<sup>th</sup> Canadian Consensus Conference on Dementia, 2012:

Risperidone, olanzapine and aripiprazole can be used for severe agitation, aggression and psychosis <u>where there is a risk of harm to the patient and/or others</u>. The potential benefit of all antipsychotics must be weighed against the <u>significant</u> risks such as cerebrovascular adverse events and mortality (Grade 2A).

- Discontinue antipsychotics drugs
  - o after 1 week for delirium
  - o after 6 months for psychotic major depression
  - o taper within 3 6 months for agitated dementia to determine lowest effective maintenance dose

Schwab W, et al. Cleveland Clinic Journal of Medicine 2009

## Agitation, Aggression, psychosis

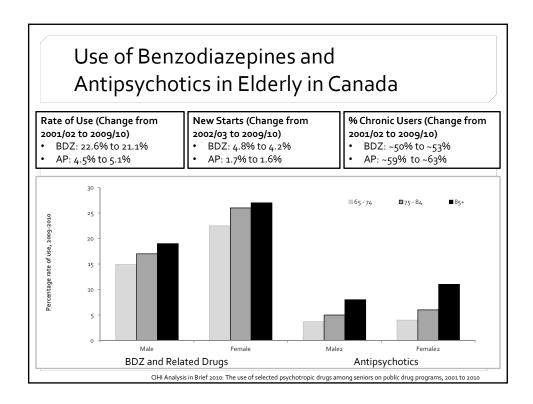
- Pharmacologic treatment Antipsychotics
- Use atypical antipsychotics short term (6-12 weeks) in cases of "severe physical aggression and severe psychosis causing tangible risk or extreme distress"

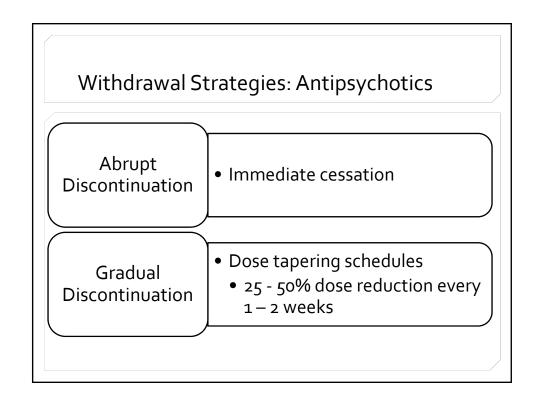
Ballard C, et al. Current Opinion in Psychiatry 2009

- Document use of behavioral /environmental interventions, and education of caregiver/family about benefits and risks
- Use lowest doses necessary for the shortest time period, and monitor for side effects
- "longer-term use of antipsychotics in people with AD is probably inadvisable, other than in exceptional clinical circumstances"

Gauthier S. et al. International Psychogeriatrics 2010

Withdrawal strategies for Antipsychotics in the Cognitively Impaired Elderly





# Antipsychotic Withdrawal in BPSD: Cochrane Review

Study	Antipsychotic	Withdrawal Strategy
Ballard 2004	Neuroleptic use	Abrupt D/C
Ballard The DART – AD Trial	Thioridazine, chlorpromazine, haloperidol, trifluoperazine, risperidone	Abrupt D/C
Bridges- Parlet 1997	NA	Abrupt D/C  • Equivalent doses of neuroleptics for chlorpromazine doses < 50mg Dose Taper  • Equivalent doses of neuroleptics > 50mg chlorpromazine: reduce 50% in week 1, then d/c week 2.
Cohen- Mansfield 1999	Haloperidol, thioridazine or lorazepam	3 week taper
Devanand 2011	Haloperidol	Abrupt D/C  • Doses of 0.5 – 1mg daily  Dose Taper  • Doses of 2 – 3 mg daily: reduce to 1mg x 2 weeks, then d/c  • Doses 4mg daily: reduce to 2mg x 1 week, 1mg x 1 week, then d/c
Devanand 2012	Risperidone	
Findlay 1989	Thioridazine	Dose Taper • Reduce 50% 1st week, then d/c the 2 <sup>nd</sup> week
Ruths The BEDNURS	Haloperidol, risperidone or olanzapine	Abrupt D/C
Van Reekum 2002	NA	Dose Taper  • Reduce 50% 1st week, 50% reduction in the 2std week, then d/c  Declercy 1, et al. Cochrane Collaboration 2013

## Results of Antipsychotic Withdrawal

- + Ballard 2004 (continuation vs. abrupt withdrawal)
  - + No significant difference in change in NPI score or key psychiatric behaviours (agitation, psychosis or mood)
  - $+ \qquad \text{NPI} \leq \textbf{14} : \text{abrupt d/c particularly good outcome; NPI} > \textbf{14} : \text{abrupt d/c led to marked behavioural problems}$
- Pooled: Ballard 2004 + Ballard DART-AD (continuation vs. abrupt withdrawal)
- + No significant difference in NPI scores at 3 months
- Bridges-Parlet (continuation vs. withdrawal)
  - + No significant difference in PAB
- + Cohen-Mansfield (continuation vs. withdrawal)
  - + No difference in CMAI or BPRS scores; Verbal fluency better in withdrawal group
- + Devanand 2012
  - + 60% relapse rate in d/c vs. 33% relapse rate in continuation group
- + Ruths BEDNURS (continuation vs. withdrawal)
  - + No significant changes in NPI Q scores between groups; Patients with behavioural deterioration had higher baseline doses
- + Van Reekum (continuation vs. withdrawal)
  - + No significant difference in BEHAVE-AD

Declercq T, et al. Cochrane Collaboration 2013

# Results of Antipsychotic Withdrawal: Adverse Effects

- + Ballard DART-AD
  - + Slight, non-significant advantage in withdrawal group in change parkinsonism severity
- + Cohen-Mansfield 1999
  - + No significant difference in adverse effects
- + Devanand 2012
  - + No significant differences in adverse effects
- Findlay 1989
  - + No significant differences but trend for greater reduction of adverse effects in withdrawal group
- + Van Reekum 2002
  - + No difference in EPS between two groups

Declercq T, et al. Cochrane Collaboration 2013

# Factors Associated with Severity of Withdrawal Symptoms

- + Abrupt discontinuation
  - + Discontinuation syndromes
    - + Nausea, vomitting, diarrhea, diaphoresis, cold sweats, muscle aches and pains, insomnia, anxiety and confusion
  - + Psychosis
    - + Exacerbation or precipitation of severe, rapid onset or supersensitivity psychosis
  - + Movement disorders
    - + Withdrawal dyskinesias, rebound dystonia, parkinsonism, akathisia
- + Receptor affinity
  - + Dopaminergic rebound (e.g. risperidone)
  - + Cholinergic rebound (e.g. olanzapine)
  - + Histaminergic rebound (e.g. clozapine)
  - + Seroternergic rebound (e.g.olanzapine)
- + Prolonged use
- + Half-life of antipsychotic
- + Baseline dose

Cerovecki A, et al. CNS Drugs 2013; Virani AS, et al. Clin Handbook Psych Drugs 2009

## Strategies for successful withdrawal\*

- + Trial after 3 months on treatment
- + No recent change in dose or frequency
- + Ensure problematic BPSD symptoms not demonstrated
- + Abrupt d/c reserve for significant drug interaction or severe adverse effect
- + Go Slow (esp short half-life, long duration of use, higher dose)
  - + 25 50% dose reduction every 1 2 weeks
- + Monitor for relapse, withdrawal effects

\* Expert opinion and personal experience

Osser D, et al. NaRCAD 2013

# **Sleep Disorders**

- 14-59% prevalence of sleep disorders in MCI
- 40% of AD patients suffer from sleep disturbances, spending 40% of their time in bed awake
- a major source of stress for caregivers, increasing likelihood of institutionalization
- ☐ Restless leg syndrome
- ☐ REM sleep behavior disorders
- ☐ Obstructive sleep apnea
- ☐ Circadian rhythm sleep disorders

Bombois S, et al. J Nutrition, Health & Aging 2010 McCurry SM, et al. Sleep Medicine Reviews 2000

### **Sleep Disorders**

#### ☐ Restless legs syndrome

- unpleasant leg sensations that disturb sleep
- prevalence 10% in population, increasing with age to 19% in persons >80
- > eliminate aggravating medications (TCA, SSRI, antipsychotics)
- ➤ Dopamine agonists (ropinirole or pramipexole) watch for orthostasis

Bombois S, et al. J Nutrition, Health & Aging 2010 Bloom HG, et al. JAGS 2009

#### ☐ REM sleep behavior disorders

- a parasomnia involving vigorous dream-enacting behavior and nightmares
- typically onsets age 60-70
- may be due to brainstem disorders or medications
- affects 50-83% of DLB patients
- > eliminate aggravating medications (TCA, SSRI, MAOI) and caffeine
- ➤ Clonazepam 0.5 -1mg qhs

Bombois S, et al. J Nutrition, Health & Aging 2010 Bloom HG, et al. JAGS 2009

## **Sleep Disorders**

#### ☐ Obstructive sleep apnea (OSA)

- Partial or complete cessations in respirations during sleep due to pharyngeal collapse
- at risk if neck collar size >17" in men and > 16" in woman
- prevalence in elderly 24-73%, increases with age even with normal BMI (decline in muscular strength, edentate patients)
- 50-80% prevalence in persons with dementia
- OSA → impairments in executive function, working memory, episodic memory, attention, early morning confusion

Cochen V, et al. J Nutrition, Health & Aging 2009 Bombois S, et al. J Nutrition, Health & Aging 2010 Bloom HG, et al. JAGS 2009 McCurry SM, et al. Sleep Medicine Reviews 2000

#### ☐ Obstructive sleep apnea

- **≻** CPAP
- > weight loss, avoid alcohol and sedatives
- > treatment in early dementia may slow disease progression

Bombois S, et al. J Nutrition, Health & Aging 2010 Bloom HG, et al. JAGS 2009

### **Sleep Disorders**

#### ☐ Circadian rhythm sleep disorders

- relatively normal sleep that occurs at abnormal times
- circadian timing is sensitive to environmental light and melatonin, controlled by SCN of hypothlamus
- o Advanced Sleep Phase Disorder
  - earlier bedtimes and early morning wakenings, frequent daytime sleepiness
  - prevalence of 1-7% in older adults

#### o Irregular Sleep-Wake Disorder

- time asleep broken into at least 3 different periods → erratic day time napping, fragmented shortened night time sleeping
- common in dementia

Bombois S, et al. J Nutrition, Health & Aging 2010 Bloom HG, et al. JAGS 2009

#### ☐ Circadian rhythm sleep disorders

- o Advanced Sleep Phase Disorder
  - > behavioral management

#### o Irregular Sleep-Wake Disorder

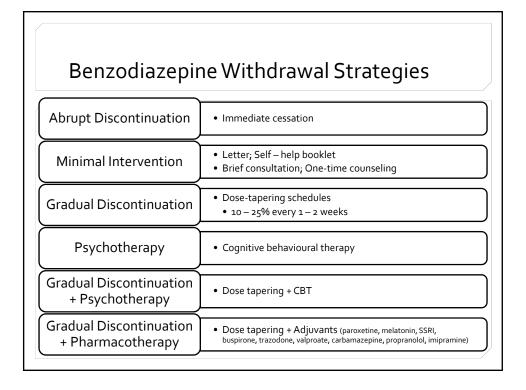
- > 30+ minutes sunlight exposure/day, increased social and physical activity during daytime, less night time light and noise
- > ?bright light therapy + melatonin < 2.5mg

Riemersma-van der Lek RF, et al. JAMA 2008 Bombois S, et al. J Nutrition, Health & Aging 2010 Bloom HG, et al. JAGS 2009

### **Sleep Disorders**

- ➤ Avoid benzodiazepines use associated with worsened cognition, disinhibited behavior, falls
- Consider Trazadone 25-50mg q evening
  - Mirtazapine 15-30mg

Withdrawal strategies for Benzodiazepines in the Cognitively Impaired Elderly



# BDZ Withdrawal: SR of Non-pharmacological Interventions in Elderly

Study	Author	Mean age	Women (%)	Minimum BDZ Use	Interventions				
Α	Bashir 1994	62	61	3x/wk x 1 yr	MI		RC	RC	
В	Cormack 1994	69	79	1 Rx Q2M x 6M	MI		RC	RC	
С	Gorgels 2005; de Gler 2010	63	72	Rxn x 3M + 6oD use	МІ		RC	RC	
D	Heather 2004	69	77	1 Rx Q2M x 6M	MI		RC	RC	
E	Salonja 2010	73	84	NA	MI		RC	RC	
F	Vicens 2006	59	82	5x/wk x 1y	MI + DT		RC	RC	
G	Baillargeon 2003	67	58	OD x 3M	CBT + DT		DT	DT	
Н	Morin 2004; Morin 2005	63	50	50% QHS x 3M	CBT + DT	DT	СВТ		
1	Oude Voshar 2003; Oude Voshar 2006	63	70	Rxn x 3M + 6oD use	CBT +DT		DT	RC	
J	Tannenbaum 2014	75	69	Mean 1.3mg LZP E/day	MI + DT		RC	RC	

Lee M, et al. CJHP 2014; Tannebaum C, et al. JAMA 2014

Benzodiazepine Cessation Rates

3 month FU
6 month FU
12 month FU
15, 21 and 24 month FU
12 month FU
15, 21 and 24 month FU
15, 21 and 24 month FU
16 month FU
17 month FU
18 month FU
19 month FU
19

# Benzodiazepines: Factors Associated with Severity of Withdrawal

- + Pharmacologic Variables
  - + Higher daily dose of benzodiazepines
  - + Potency of benzodiazepine dose
  - + Longer duration of benzodiazepine therapy
  - + More rapid rate of taper
- + Patient Variables
  - + Diagnosis of panic
  - + Higher pre-taper levels of anxiety/depression
  - + Higher levels of personality psychopathology
  - + Concomitant alcohol and/or substance dependence/abuse

Rickels K, et al. J Clin Psychopharm 1999

# Strategies for Benzodiazepine Withdrawal

- + Treat underlying disorder (anxiety, insomnia, seizures) adequately
- + Go slow (especially if elderly, long-term use)
- + If required, switch to diazepam (equivalent dose)
- → Decrease daily dose by 25 50% per week initially (may decrease by 10 25% for elderly, chronic use and prolonged time frame i.e. every 2 4 weeks)
- + Slow down taper further once titrated to 50% (taper by 10%, over q 2 4 weeks based on patient preference)
- + To improve rates of cessation, incorporate CBT

# Benzodiazepines: Discontinuation Syndromes

- + Withdrawal
  - ★ Short/intermediate-acting benzodiazepines (occurs within 1 2 days)
    - + Examples: triazolam, alprazolam, lorazepam, temazepam, oxazepam
  - + Long-acting benzodiazepines (occurs within 5 10 days)
    - + Examples: clobazam, clonazepam, diazepam, flurazepam
  - + Insomnia, agitation, anxiety, dysphoria, headache, muscle aches, tremors, twitches, loss of appetite, seizures (acute withdrawal)
- + Pseudo withdrawal
  - + Psychological withdrawal which results from patient's apprehension about discontinuing the drug

# Inappropriate Sexual Behavior

## **Inappropriate Sexual Behavior**

- 7-25% of demented patient exhibit inappropriate sexual behaviors
- involvement of frontal lobes, temporo-limbic system, striatum (basal ganglia), or hypothalamus

Black B, et al. Journal of Geriatric Psychiatry & Neurology, 2005

#### **Inappropriate Sexual Behavior**

- Behavioral treatment
- Education for spouse/family and patient
  - reframe sexual expression (desire for closeness, comfort)
- Behavioral modification for inappropriate behavior in public
  - do not ignore, but avoid confrontation
  - simple, repeated explanation of inappropriateness
  - distraction and redirection
  - single room
  - avoid overstimulating TV or radio programs
  - modified clothing (trousers that open at back or no zippers)
  - adequate social and physical activity

Black B, et al. Journal of Geriatric Psychiatry & Neurology 2005

## **Inappropriate Sexual Behavior**

- Pharmacologic treatment

- eliminate disinhibiting drugs (benzodiazapines), alcohol
- L-dopa can increase sexual behaviors in persons with Parkinson's disease

Black B, et al. Journal of Geriatric Psychiatry & Neurology, 2005

- no studies on women
- mainly case reports

### **Inappropriate Sexual Behavior**

- Pharmacologic treatment
- Paroxetine or Citalopram 2omg/d
- Clomipramine 150-200mg/d
- Quetiapine 25mg/d
- Trazadone 100-500mg/d (→priapism in 1/6000)
- Gabapentin 300mg TID
- Pindolol 4omg /d divided BID-TID
- Estrogen o.625mg/d
- Leuprolide acetate 7.5mg IM/month

Black B, et al. Journal of Geriatric Psychiatry & Neurology