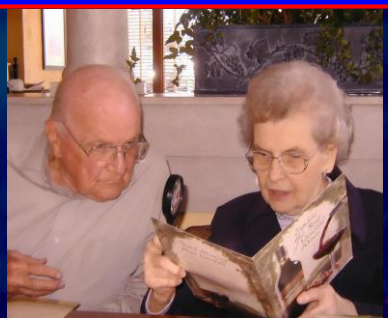
Behavioral & Psychological Symptoms of Dementia: Recognition & Management

Kiran Rabheru MD, CCFP, FRCP, ABPN
Professor
University of Ottawa
Geriatric Psychiatrist
The Ottawa Hospital

NO CONFLICTS

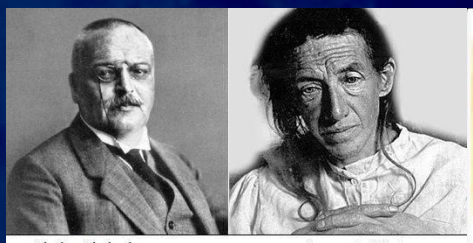


Objectives

Participants will be able to develop an approach to:

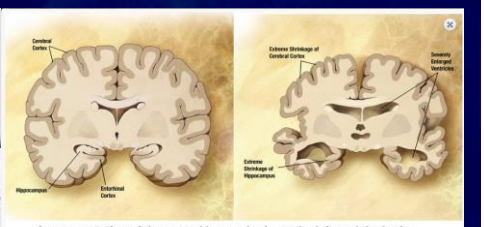
- Recognize and assess a person with BPSD
- Develop a better understanding for managing a person with BPSD
- Pharmacological strategies in appropriate use of psychotropic medication for BPSD

Auguste Deter *– taken in 1906 shortly before her death (April 8, 1906, during her stay at Frankfurt's City Mental Institution*

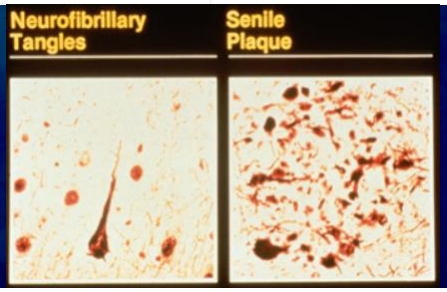


Alois Alzheimer

Auguste Deter



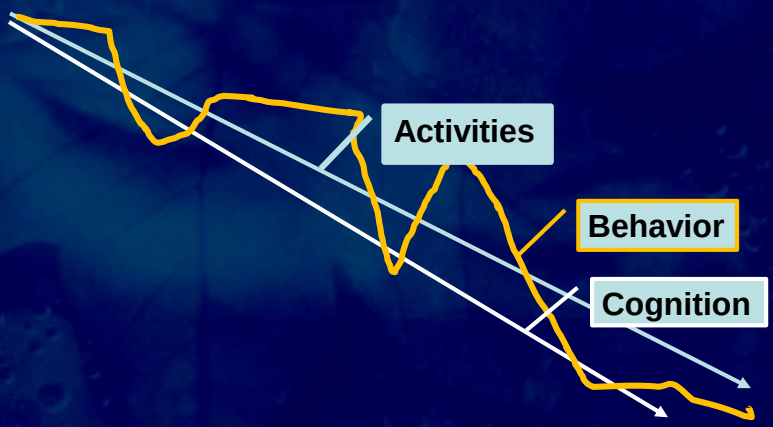
A representation of the normal human brain on the left, and the brain affected by Alzheimer's disease on the right.



What is "BPSD"?

- Occurs in all types of dementia
- Some types of dementias present with characteristic symptoms
  - e.g. Lewy Body - visual hallucinations
  - Frontotemporal dementia – disinhibition
- BPSD leads to earlier institutionalization, hospitalization, decreased quality of life

A-B-Cs of Dementia

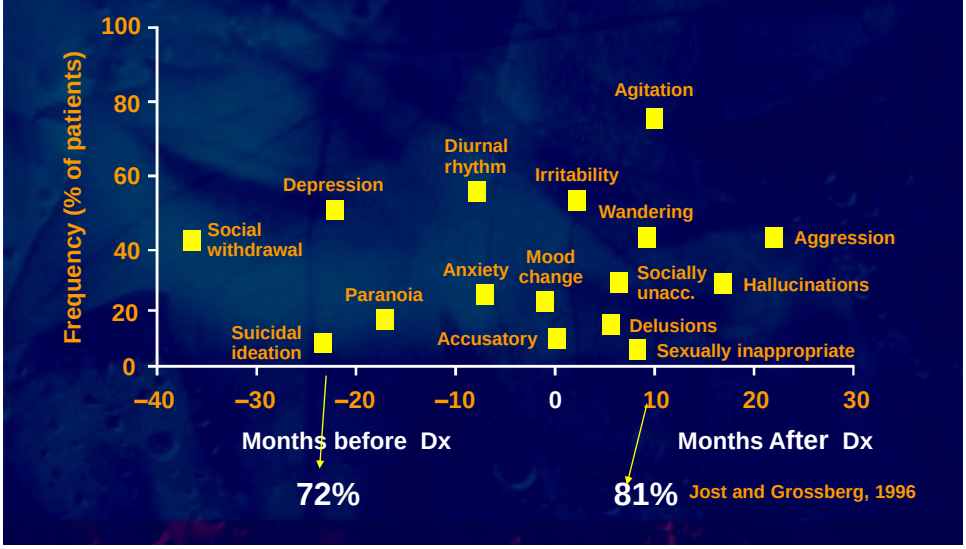


CONCEPT:

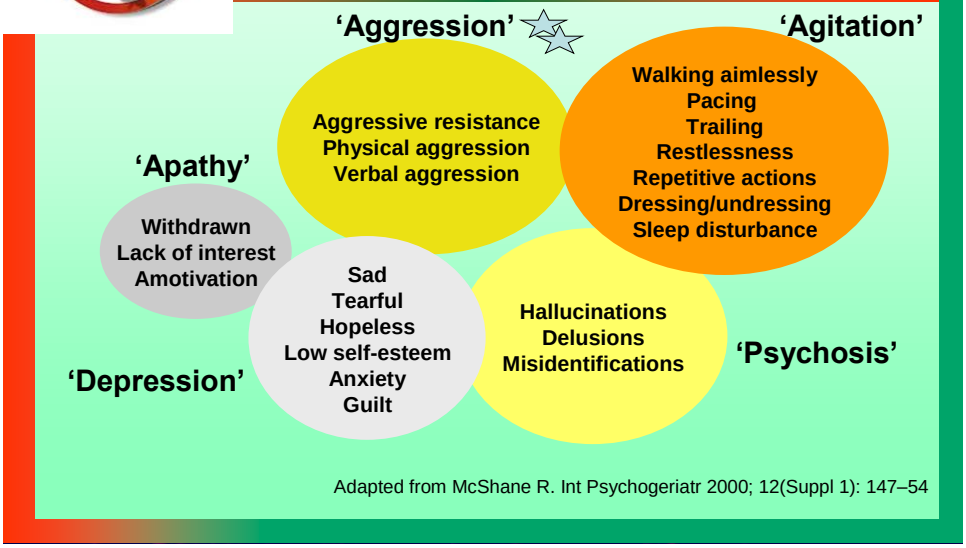
1. SYMPTOMS

2. CLUSTERS OF SYMPTOMS

Symptoms of BPSD



Clusters of BPSD



Adapted from McShane R. Int Psychogeriatr 2000; 12(Suppl 1): 147–54

Clusters

- Four clusters – that is, the affective, psychotic, hyperactive and apathetic clusters
- Apathy, depression, anxiety and agitation - most frequent

Aalten A, Verhey FR, Boziki M*, et al*. Consistency of neuropsychiatric syndromesacross dementias: results from the European Alzheimer Disease Consortium. Part II. *Dement Geriatr Cogn Disord* 2008; 25: 1–8.

Course of BPSD

- Cross-section: BPSD can occur at any time during the course of dementia
- Prevalence: Non-linear course with the highest prevalence seen in the intermediate stages of disease.
- Symptoms: may persist or be episodic over time, and this may differ between symptoms

Purandare N, Allen NHP, Burns A. Behavioural and psychological symptoms of dementia. Rev Clin Gerontol 2000; 10: 245–60.

Lovheim H, Sandman PO, Karlsson S, Gustafson Y. Behavioral and psychological symptoms of dementia in relation to level of cognitive. impairment. Int Psychogeriatr 2008; 20: 777–89.

Course of BPSD

- Hyperactivity & Apathy: high persistence and incidence
- Depression & Anxiety: low-moderate persistence, moderate incidence
- Psychotic symptoms low persistence with moderate-low incidence
- Apathy : only symptom with high baseline prevalence, persistence and incidence during the course of dementia

Longitudinal course of behavioural & psychological symptoms of dementia:systematic review. Rianne M. van der Linde, Tom Dening, Blossom C. M. Stephan, A. Matthew Prina, Elizabeth Evans and Carol Brayne . The British Journal of Psychiatry (2016) 209, 366–377. doi: 10.1192/bjp.bp.114.148403

Agitation, aggression, or psychosis is a symptom of:

- Delirium
- Schizophrenia
- Delusional Disorder
- Mood Disorder
- Dementia
- Substance Abuse
- Drug-induced Psychosis
- Medical / Neurological Conditions

Presentation & Diagnosis: Highly variable
Key Principle: Comorbidity

Agitation / Aggression / Psychosis
Phases of Treatment

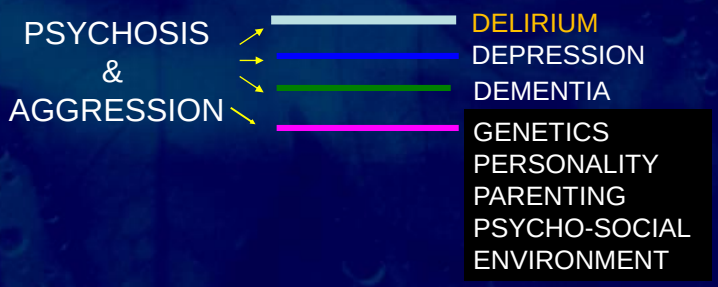
ACUTE → SAFETY → patient,staff,residents

MEDIUM → ASSESS → 1) rule out delirium
2) medicate or not?

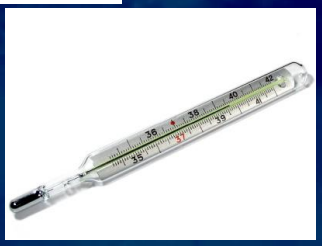
LONG-TERM → **MAINTENANCE** → 1) on what?
2) how long?

Comorbidity is The Rule

DELIRIUM OFTEN
PRESENTS WITH
VIOLENT / PSYCHOTIC / AGGRESSIVE BEHAVIOR



Measurement of vital signs

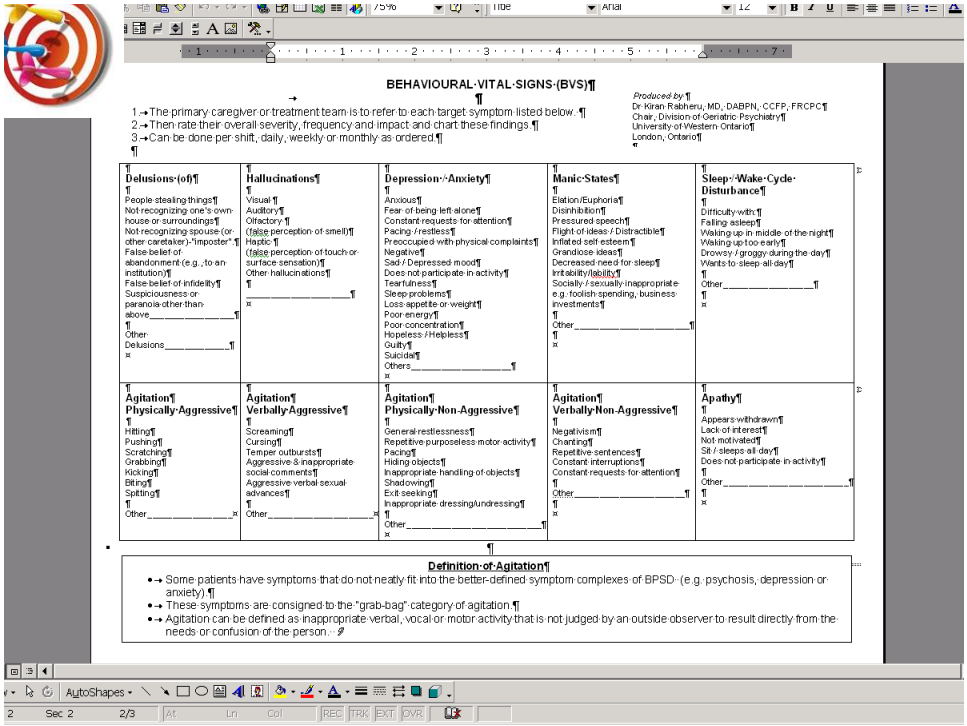


Identifying & Measuring BPSD

Google “Behavioral Vital Signs” or “BVS” Tool

Target
Symptoms & Clusters

- **Frequency**
- **Severity**
- **Impact**



BEHAVIOURAL·VITAL·SIGNS·(BVS)¶

→ ¶

1.→The primary caregiver or treatment team is to refer to each target symptom listed below. ¶
2.→Then rate their overall severity, frequency and impact and chart these findings.¶
3.→Can be done per shift, daily, weekly or monthly as ordered.¶
¶

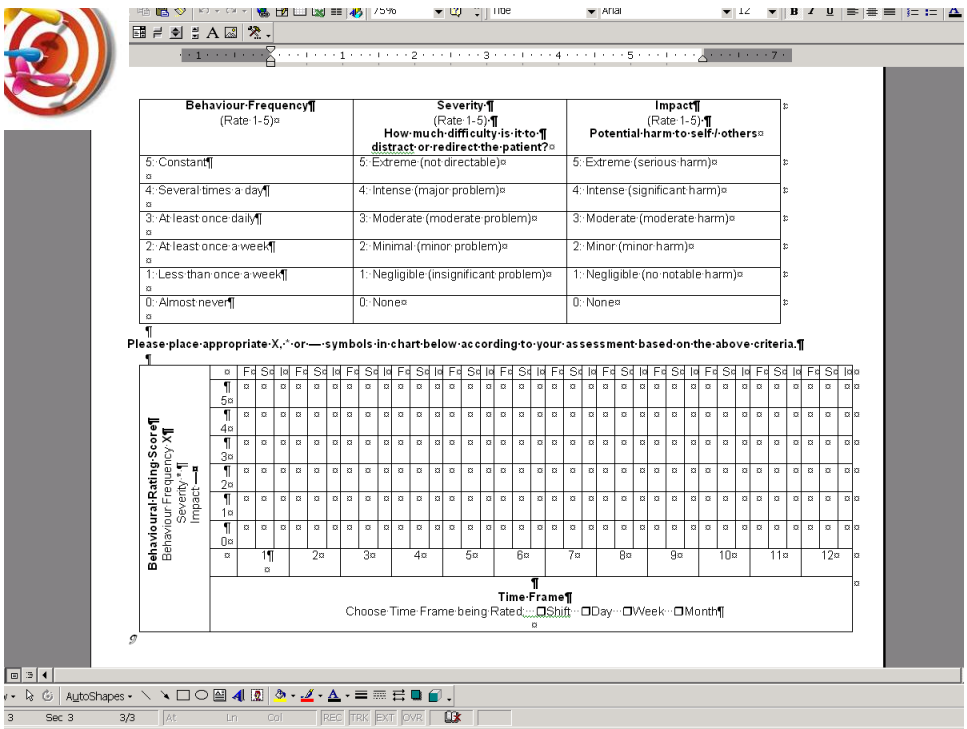
Produced by:¶
Dr Kiran Rabheru, MD, DABPN, CCFP, FRCPC¶
Chair, Division of Geriatric Psychiatry¶
University of Western Ontario¶
London, Ontario¶
¶

Delusions (of)¶ ¶ People stealing things¶ Not recognizing one's own house or surroundings¶ Not recognizing spouse (or other caretaker) "Imposter"¶ False belief of abandonment (e.g., to an institution)¶ False belief of infidelity¶ Suspiciousness or paranoia other than above_____¶ ¶ Other Delusions_____¶ ¤	**Hallucinations**¶ ¶ Visual ¶ Auditory¶ Olfactory ¶ (false perception of smell)¶ Haptic ¶ (false perception of touch or surface sensation)¶ Other hallucinations¶ ¶ _____¶ ¤	**Depression / Anxiety**¶ ¶ Anxious¶ Fear of being left alone¶ Constant requests for attention¶ Pacing / restless¶ Preoccupied with physical complaints¶ Negative¶ Sad / Depressed mood¶ Does not participate in activity¶ Tearfulness¶ Sleep problems¶ Loss appetite or weight¶ Poor energy¶ Poor concentration¶ Hopeless / Helpless¶ Guilty¶ Suicidal¶ Others_____¶ ¤	**Manic States**¶ ¶ Elation/Euphoria¶ Disinhibition¶ Pressured speech¶ Flight of ideas / Distractible¶ Inflated self esteem¶ Grandiose ideas¶ Decreased need for sleep¶ Irritability/lability¶ Sociably / sexually inappropriate e.g. foolish spending, business investments¶ ¶ Other_____¶ ¶ ¤	**Sleep / Wake Cycle Disturbance**¶ ¶ Difficulty with:¶ Falling asleep¶ Waking up in middle of the night¶ Waking up too early¶ Drowsy / groggy during the day¶ Wants to sleep all day¶ ¶ Other_____¶ ¤
Agitation Physically Aggressive¶ ¶ Hitting¶ Pushing¶ Scratching¶ Grabbing¶ Kicking¶ Biting¶ Spitting¶ ¶ Other_____¤	**Agitation Verbally Aggressive**¶ ¶ Screaming¶ Cursing¶ Temper outbursts¶ Aggressive & inappropriate social comments¶ Aggressive verbal sexual advances¶ ¶ Other_____¤	**Agitation Physically Non-Aggressive**¶ ¶ General restlessness¶ Repetitive purposeless motor activity¶ Pacing¶ Hiding objects¶ Inappropriate handling of objects¶ Shadowing¶ Exit seeking¶ Inappropriate dressing/undressing¶ ¶ Other_____¤	**Agitation Verbally Non-Aggressive**¶ ¶ Negativism¶ Chanting¶ Repetitive sentences¶ Constant interruptions¶ Constant requests for attention¶ ¶ Other_____¤	**Apathy**¶ ¶ Appears withdrawn¶ Lack of interest¶ Not motivated¶ Sit / sleeps all day¶ Does not participate in activity¶ ¶ Other_____¤

¶

Definition of Agitation¶

- →Some patients have symptoms that do not neatly fit into the better-defined symptom complexes of BPSD (e.g. psychosis, depression or anxiety).¶
- →These symptoms are consigned to the "grab-bag" category of agitation.¶
- →Agitation can 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.



Behaviour Frequency¶ (Rate 1-5)¤	**Severity**¶ (Rate 1-5)¶ **How much difficulty is it to distract or redirect the patient?**¤	**Impact**¶ (Rate 1-5)¶ **Potential harm to self / others**¤
5: Constant¶ ¤	5: Extreme (not directable)¤	5: Extreme (serious harm)¤
4: Several times a day¶ ¤	4: Intense (major problem)¤	4: Intense (significant harm)¤
3: At least once daily¶ ¤	3: Moderate (moderate problem)¤	3: Moderate (moderate harm)¤
2: At least once a week¶ ¤	2: Minimal (minor problem)¤	2: Minor (minor harm)¤
1: Less than once a week¶ ¤	1: Negligible (insignificant problem)¤	1: Negligible (no notable harm)¤
0: Almost never¶ ¤	0: None¤	0: None¤

¶

Please place appropriate X, ·, or — symbols in chart below according to your assessment based on the above criteria.¶

¶

Behavioural Rating Score¶
Behaviour Frequency X¶
Severity · ¶
Impact —¶

¤	Fr	Sv	Id	Fr	Sv	Id	Fr	Sv	Id	Fr	Sv	Id	Fr	Sv	Id	Fr	Sv	Id	Fr	Sv	Id	Fr	Sv	Id	Fr	Sv	Id	Fr	Sv	Id	Fr	Sv	Id	Fr	Sv	Id
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¤	1¶ ¤			2¤			3¤			4¤			5¤			6¤			7¤			8¤			9¤			10¤			11¤			12¤		

¶

Time Frame¶
Choose Time Frame being Rated: ☐Shift ☐Day ☐Week ☐Month¶

Approach to BPSD:

The *SMART* Approach:

- Safety: remove patient to safe environment
- Medical: organic workup to treat reversible causes; reduce medication load
- Assess Competency: personal care decisions, financial, driving; protect assets
- Rest, sleep, nutrition, hydration; pain, ambulation, dental, vision, hearing, constipation, urinary, skin, feet, mobility
- Trial of medication: cholinesterase inhibitor / antipsychotic / antidepressant/ mood stabilizer

Rabheru K. Can Family Physician Vol 49 March 2003 pg. 389

The Problem & Impact

- Serious issue: residents & staff
- Up to 2/3 NH staff assaulted (1-9 x / month)
- Resident-resident violence
- Co-mingling of residents with and without dementia
- Deficits in the quality of care due to understaffing and undertraining
- Up to 40% require medical treatment
- Falls, #, lacerations, depression, anxiety, poor QoL
- Promotion of culture of safety

What actually happens?

- When patients are hurried
- During Transfers / Turning 33%
- During ADLs (Bathing, Toileting) 40%
  - Grabbing, pinching, hair pulling 40%
  - Scratching, biting (4-28%)
  - Hitting, punching (12-51%)
  - Pushing/shoving (8-8.2%)
  - Hitting with object, throwing objects at staff (3-9%)
  - Kicking (2-27%)
  - Spitting (1-11%)
  - Verbal aggression includes verbal insults (18.1%), verbal threats (10.7%), and sexual advances (0.7%)

Barriers

- Resident
  (e.g., health status)
- Environmental
  (e.g., lack of space for physical activity)
- Organizational
  (e.g., staffing and funding constraints)
- These barriers intersect to adversely affect the physical activity of older people living in LTC

Predisposed resident

- Multi-morbidity
- Polypharmacy
- Functional impairment
- Diminished everyday competence
- Impaired Communication

Use of Psychotropic Meds

- 50-60% of residents were taking some form of psychotropic medication
- 15-22% - anxiolytics/hypnotics
- Up to 25% - neuroleptics
- Use of atypical antipsychotics for dementia has increased by > 20%
- Public concern is very high!

The Effect of Regulatory-Agency Safety Warnings on Antipsychotic Drug Use in the Elderly: A Population-based Time Series Analysis (CMAJ 2008)

Restraints may worsen delirium!

- Physical Restraints
- Geri-chair, Posey vest
- Physical injuries

Chemical Restraints
Antipsychotics
Side Effects

- May make a resident with delirium or confusion experience more agitation
- Adjusted odds ratio (OR) for risk of physically attacking staff than those who did not get restrained:
- Treated with antipsychotics = 1.74 (95% confidence interval [CI] of 1.38-2.19).
- Treated with physical restraints = 1.79 (95% CI of 1.37-2.33)

Voyer et al. 2003

Nursing Aides

- > 90% of resident interactions are with nursing aides
- Behavioral management skills training
  - Only ½ to 2/3 receive this
  - Reduces violence by ~ 50%
  - Less physical and chemical restraint
  - Non-pharmacologic approaches to address disruptive behaviors
  - Decreases the number of aggressive incidents

Patient Risk Factors

- Cognitive Impairment: 90% +

	Verbal	Physical
– Mild-Moderate:	2	2-3
– Severe:	1.5	8

- Male
- Younger (age 65 to 84 years)
- Psychiatric history
  - Mood, psychosis, socially withdrawn

Staff Risk factors

- High resident-to-staff ratio
- High staff workload
- High staff anger scores
- Feeling untrained / not competent
  - to deal with dementia / aggression
- Younger-aged staff member

Protective Factors

- Higher staff-to-resident ratio
- Choose to work on the higher-risk units
- Better designed physical spaces for dementia
- Better specialized education
- Better application
- Greater level of overall satisfaction with work and colleagues

Environment & Family

- Environmental Interventions
  - Reduced levels of environmental stimulation
  - Crowding
  - Look for environmental solutions to meet unmet needs
- Family interactions & visits
  - calm fears of abandonment & isolation in residents
  - maintains communication with NH staff
  - reduces risk of being dehumanized by staff

Staff's Communication with Family

- To reduce apprehension & agitation for family and the resident:
  - Update family on resident's status
  - Trusted staff member to accompany the family during part of a visit

Restraints

- Hierarchy of restraints:
- Posey vest
- Reclining chair with or without a lockable tray (e.g., geri-chair)
- Two-point restraint (e.g., both wrists)
- Restraining in a seated position may be dangerous
- Syncope or stroke with low or unstable blood pressure
- Since the 1980s →great effort to reduce reliance on these techniques as the first line of intervention

DICE Clinical approach

- Define behavior (or cluster)
- Investigate - contributing factors
- Create a plan – improve communication
- Evaluate – Effective teaching de-escalation skills and methods

Kales HC, Gitlin LN, Lyketsos CG. Assessment and management of behavioral and psychological symptoms of dementia. *BMJ* 2015; **350:** h369

Non-pharmacological Rx

Approach A kind, unrushed, non-confrontational, face-to-face approach may work better

Schedules Patient-centred care schedules

Demands Reduce demands on patient

Communication Communicate more effectively

Personal Care Meticulous attention to good personal care is essential

Activity and Environment Appropriate daytime activity and environment

Non-pharmacological Rx

- Appropriate eye contact
- Providing positive statements
- Using simple one-step commands
- Allowing residents to
  - respond to statements before offering physical assistance
  - perform independent tasks where appropriate.

Non-pharmacological Rx

- Discourage:
- Negative communication skills
- Giving multiple commands
- Announcing multiple activities
- Arguing with residents
- Encourage behavioral modification e.g. distraction
- Staff “timeouts” → reduce frustration and anger

Psychological Therapy

- People with dementia are individuals deserving care and respect, to be treated kindly and with dignity'. Shifting the concept from behaviors, to communication of individual wants and needs, would not only be less demeaning, but also more conducive to working collaboratively with people with dementia.

Innovative Practice

The use of cognitive behaviour therapy in the management of BPSD in dementia (Innovative practice)

Deborah Koder
Specialist Mental Health Service for Older People, Sydney Local Health District, NSW, Australia

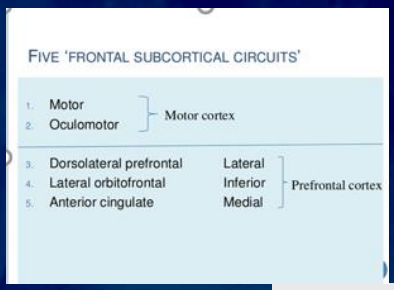
Dementia
2018, Vol. 17(2) 227–233

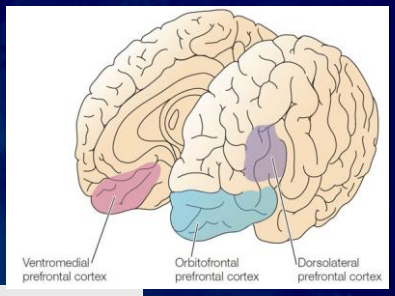
DOI: 10.1177/1471301216636261
journals.sagepub.com/home/dem
SAGE

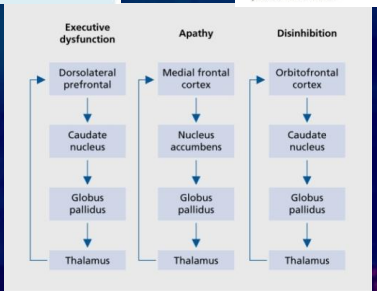
Neurobiology

- 3 major neurobiological circuits relevant to NPS in AD:
  - Frontal-subcortical circuits
  - ✓ Dorsolateral circuit: planning, organization, & executive function
  - ✓ Apathy circuit: motivated behavior
  - ✓ Orbitofrontal circuit: inhibitory control and conformity with social norms
  - Cortico-cortical networks
  - Monoaminergic system

Frontal- subcortical circuits







MCI→AD Risk Factors

- DM, Pre-DM, metabolic syndrome, lower serum folate levels, and NPS *increase risk*
- Lower education *does not*
- A Mediterranean diet *decreases risk* MCI →dementia vs. other diets

Mild Behavioral Impairment (MBI) in MCI

- Apathy, Affect s/s, Impulse control problems, Social inappropriateness are Prodromal dementia symptoms
- 1/3 to ¾ of MCI have some s/s
- Most common: depression, anxiety, apathy, and irritability
- May be causative

Modifiable Risk Factors MCI→Dementia

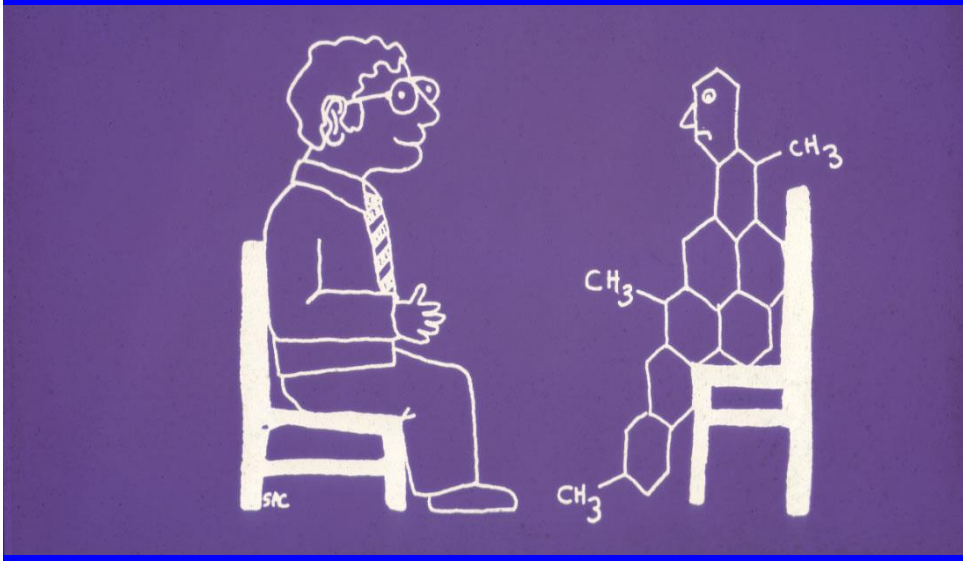
	Relative risk for dementia (95% CI)	Prevalence	Communality	PAF	Weighted PAF*
Diabetes	1·65 (1·12–2·43)	6·4%	7·6%	4·0%	1·5%
Neuropsychiatric symptoms	2·52 (1·18–5·37)	29·0%	61·1%	30·6%	11·5%
Diet	1·92 (1·10–3·33)	32·5%	66·7%	23·0%	8·7%

Data are relative risk (95% CI) or %. Total weighted PAF adjusted for communality=21·7%. We used population prevalence of obesity as a proxy for diet and depression as a proxy for neuropsychiatric symptoms. PAF=population attributable fraction. *Weighted PAF is the relative contribution of each risk factor to the overall PAF when adjusted for communality.

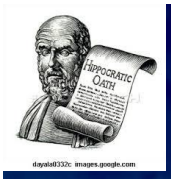
Table 2: Potentially modifiable risk factors for progression to dementia from mild cognitive impairment

Lancet 2017; 390: 2673–734

DRUGS: NECESSARY BUT NEVER SUFFICIENT ALONE!!



JAMA 2002 Apr 10;287(14):1840-7
Placebo response in studies of major depression: variable, substantial, and growing.
Walsh BT, Seidman SN, Sysko R, Gould M.



Goals

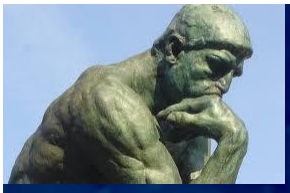
- 1. First, do no harm
- 2. Second, to work to improve patients' quality of life
- 3. Must assess:
  - Risks vs. Benefits of treatment options
  - Examine all therapeutic modalities

Mandatory:

- Individualized Care for each patient
- Careful documentation
- Targeted behavior
- Side effects
- Dosing adjustment to the lowest effective dose possible

“Necessary Drug “

- Supporting diagnosis
- Reason listed in the medical record
- Adequately monitored
- Age-appropriate dose
- Appropriate duration
- Not be duplicative therapy
- Monitor for significant side effects or adverse consequences
- Must document the benefits of continuing the medication outweighs the risk



Who are we really treating?

- The caregivers—professionals and family members
- Often the driver of overutilization
- Not properly trained in non-drug methods of managing unwanted behaviors
- Prescribers, caregivers, and team must work together to optimize care of BPSD in dementia

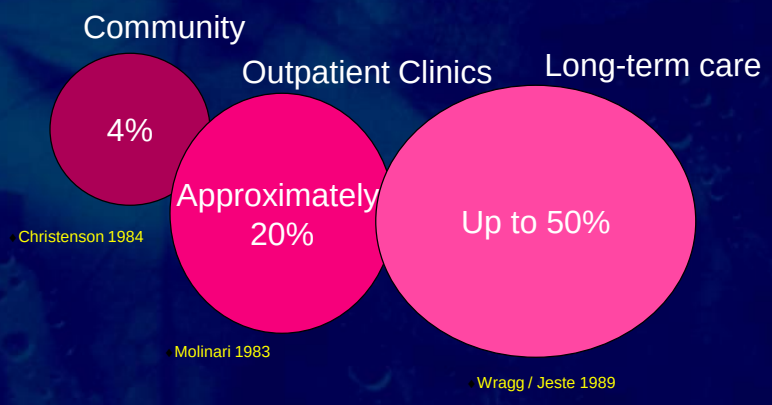
Drugs for BPSD

- If drugs are bad……..
- Why do we still use them?
- If we have to use them, how do we use them safely?
- Goal is to:
  - Maximize benefit
  - Minimize risk
  - Explain these to patient & family
  - Consent

Psychosis

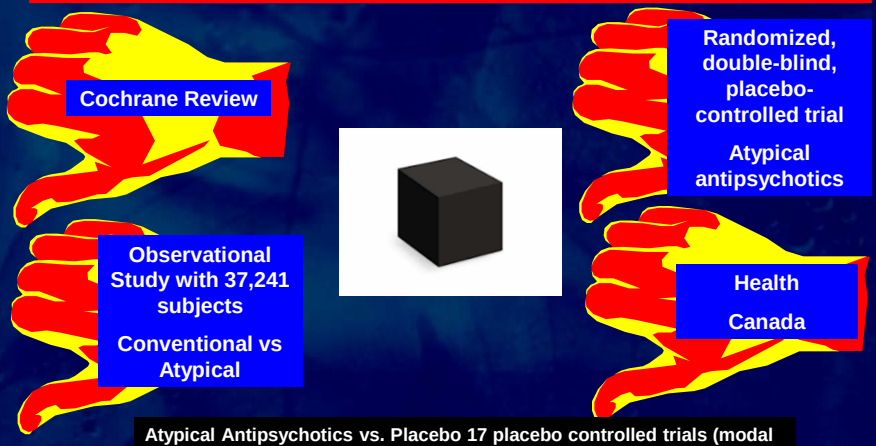
- 18% at any given time and persists
- Delusions – common & simple
- Hallucinations – less common
- Treat if distress – patient / caregiver

Psychotic symptoms in Late Life
Prevalence by Setting



WARNING:

Use of Antipsychotics in Elderly Dementia Patients:
Benefits out-weighed by adverse events



Atypical Antipsychotics vs. Placebo 17 placebo controlled trials (modal duration of 10 weeks) - 1.6 to 1.7 times risk of death vs. placebo-treated patients; Drug = 4.5% vs. 2.6% in the Placebo
Causes of death varied- Most : Cardiovascular
(e.g., heart failure, sudden death) Infectious (e.g., pneumonia)

Mortality: Atypicals vs. placebo

- Odds ratio of death all drugs pooled = 1.54 (1.06-2.23) vs PBO
- Black box warnings of death on atypicals: 4.5% vs 2.6% on PBO
- Causes: “cardiovascular, infection”.

Antipsychotics vs. other psychotropics

- People taking antipsychotics have higher mortality (22.6 – 29.1%) than those taking other psychotropic medications (14・6%), except for anticonvulsants

Kales HC, Valenstein M, Kim HM, et al. Mortality risk in patients with dementia treated with antipsychotics versus other psychiatric medications. *Am J Psychiatry* 2007; **164:** 1568–76

Mortality with typical APs

- Higher risk of cognitive impairment
- Mortality on typical antipsychotics, including haloperidol, up to twice that of risperidone, with greater risk at higher doses. Patients who have been recently started on antipsychotics seem to be particularly at risk, especially in the first 30 days.

Maust DT, Kim HM, Seyfried LS, et al. Antipsychotics, other psychotropics, and the risk of death in patients with dementia: number needed to harm. JAMA Psychiatry 2015; 72: 438–45

Wang PS, Schneeweiss S, Avorn J, et al. Risk of death in elderly users of conventional vs. atypical antipsychotic medications. N Engl J Med 2005; 353: 2335–41.

Huybrechts KF, Gerhard T, Crystal S, et al. Differential risk of death in older residents in nursing homes prescribed specific antipsychotic drugs: population based cohort study. BMJ 2012; 344: e977.

Kales HC, Kim HM, Zivin K, et al. Risk of mortality among individual antipsychotics in patients with dementia. Am J Psychiatry 2012; 169: 71–79.

Arai H, Nakamura Y, Taguchi M, Kobayashi H, Yamauchi K, Schneider LS. Mortality risk in current and new antipsychotic Alzheimer's disease users: large scale Japanese study. Alzheimers Dement 2016; 12: 823–30.

Mortality: Typicals vs. Atypicals

- Typicals: higher mortality RR = 1.37
  - For every 100 patients treated with typicals….7 additional deaths….no black box warning for typicals
- Other medications have less evidence for efficacy or safety.
- Absence of evidence ≠ Evidence of absence

Risk of Stroke-NNH

Calculation of CVAE NNH

- – 6.3 for 1 year of exposure
- – 37 for 8-12 weeks of exposure

UK Committee on Safety of Medicines March 2004)

Consent: must remember…

- Risks of not providing pharmacologic treatments for residents experiencing aggression despite environmental and behavioral attempts to calm them have failed
- Can hurt themselves and others
- Increased risk for falls, malnourishment, not having their ADLs as needed, isolation and other complications from the refusal of medication

Antipsychotics: Other Safety Concerns

• EPS – especially in PD, DLB	1.5
• Tardive Dyskinesia	>60% / 3 years
• Gait Disturbance	3.4
• Hip #	1.37
• Worsens cognition	most studies
• Diabetes mellitus	1.5
• Weight	most
• Hyperlipidemia	no Δ
• QTc & Ventricular arrhythmias	1.8-2.3

Agitation

- Common: 50%-20% significant
- Range of behaviors
- Restlessness, pacing, repetitive vocalizations,
- Often accompanied by a feeling of inner tension,
- Difficult to detect in people with more severe dementia

- Communication of physical or psychological distress, a misinterpretation of threat, or result from delusions or hallucinations
- Reduced ability to communicate, satisfy, or even know their needs and makes it more likely that they will repeat a behavior

- Trigger / unmet need

Agitation

- Person Centered Care & Activities
  - Goal oriented → not
  - Multi step→ single step
- Music
- Dementia Care Mapping
- Risperidone & Citalopram

Depression

- Heterogenous
- psychological therapies, including cognitive behavioural therapies, interpersonal therapy, or counselling
- Meds:
  - Not for mild – moderate
  - OK for moderate to severe & prior history

Depression in Dementia

- No clear established & validated criteria
- citalopram, sertraline, venlafaxine, mirtazapine, & bupropion
- Treatment may help other neuropsychiatric symptoms eg. aggression or psychosis
- Rule out: alcohol, sedative-hypnotics, other drug dependence, CNS pathology, and medical problems eg hypothyroidism

Sleep

- No large + trials
- Maybe trazodone
- No benzos or Z drugs
- REM behavior disorder→ 20% of DLB / PDD
- Clonazepam

Apathy

- Common & persistent
- Increase activity or methylphenidate might be helpful.

Cholinesterase Inhibitors for BPSD

- Treatment with cholinesterase inhibitors (ChEIs) has been reported to show behavioural benefits for AD patients in:
  - Mild-to-moderate AD[1-3]
  - Moderate-to-severe AD[4,5]
  - AD patients in nursing homes[6]
- Unlike most psychotropics[7], ChEIs appear to treat multiple behavioural symptoms (eg, affective and psychotic)[1-6]

[1]Holmes C et al. *Neurology.* 2004;63:214-9; [2]Cummings et al. *Am J Psychiatry*. 2004;161:532-8; [3]Finkel et al. *Int J Geriatr Psychiatr*. 2004;19:9-18; [4]Feldman H et al. *Neurology*. 2001;57:613-21; [5]Gauthier S et al. *Int J Psychogeriatr*. 2002;14:389-404; [6]Hatoum et al. *J Am Med Dir Assoc*. 2005;6:238-45; [7]Lee et al. *BMJ*. 2004;329:75; [8]Pratt et al. *Int J Clin Prac*. 2002;56:710-7.

DOMINO Trial

Well done, double-blind, discontinuation study, found that donepezil cessation (replaced by a placebo) in patients with moderate-to severe Alzheimer's disease (MMSE <12):

- cognitive (MMSE mean difference 1.9)
- functional decline
- increase in neuropsychiatric symptoms
- doubling of risk of care home admission

in the year after discontinuation.

Suggest cholinesterase inhibitors should be continued for people whose dementia has become severe.

Howard R, McShane R, Lindesay J, et al. Donepezil and memantine for moderate-to-severe Alzheimer's disease. *N Engl J Med* 2012; **366:** 893–903.
Howard R, McShane R, Lindesay J, et al. Nursing home placement in the Donepezil and Memantine in Moderate to Severe Alzheimer's Disease (DOMINO-AD) trial: secondary and post-hoc analyses. *Lancet Neurol* 2015; **14:** 1171–81.

DLB / PDD & ChEIs

- Rivastigmine (6–12 mg) and donepezil (5 mg and 10 mg)
- Double-blind, placebo-controlled trials
  - Safe and well tolerated
  - Cognitive effect
  - Reduction in visual hallucinations
- Meta-analyses: ChEIs improve cognition and global function in DLB & PDD

Memantine

- Memantine is a non-competitive modulator of the N-methyl-D-aspartate receptor and normalizes glutamatergic neurotransmission.
- It prevents excitatory amino acid neurotoxicity

MEMANTINE:

Mild to moderate: very small advantage over placebo. Individuals may consider….little risk.

In moderate to severe: evidence & indication given upto 6 months (APA) with or without a ChEI

Memantine in moderate to severe Alzheimer's disease
Barry Reisberg, M.D., *et al.*
The New England Journal of Medicine April 2003

Memantine treatment in patients with moderate to severe AD already receiving donepezil
Pierre Tariot, M.D., *et al.*
JAMA, January 2004

Memantine in severe dementia:
Results of the M-BEST study
(Benefit and Efficacy in Severely Demented Patients During Treatment with Memantine)
Bengt Winblad, M.D., Ph.D., *et al.*
International Journal of Geriatric Psychiatry, 1999

Benzodiazepines

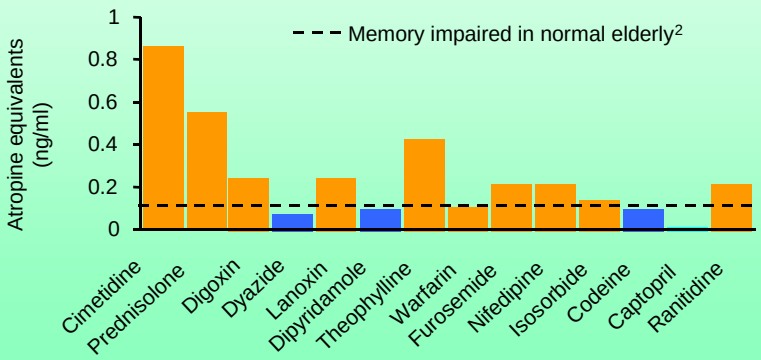
- Better vs. PBO
- Equal IM olanzapine at 2 hours but inferior at 24 hours. No data beyond 8 weeks
- Sedation, ataxia, amnesia, confusion , delirium, paradoxical anxiety→ falls, respiratory suppression.
- All are dose related
- With alcohol: may cause disinhibition or withdrawal

Benzodiazepines

- Useful if anxiety is prominent, occasional PRN s, procedures
- Use low dose, short t1/2,
- Clonazepam has longer t1/2…use with caution as ….falls …increase
- Start SLOWLY…monitor…..taper very slowly.

Common Medical drugs with Anticholinergic Effects

- 14/25: detectable anticholinergic activity[1]
- 10/25: activity with the potential to impair memory[2]



1. Tune L *et al.* Am J Psychiatry 1992; 149: 1393–4
2. Miller PS *et al.* Am J Psychiatry 1988; 145: 342–5

JAMA Review

❑ **No first-line** recommended drug treatment for agitation without delusions

- **Typical antipsychotics**:
  - No clear evidence that typical AP are useful.
  - Haloperidol with aggression: too many adverse effects.
- **Serotonergics**: recommended only for depression.
- **Anticonvulsants**: Carbamazepine, Valproate: **Not recommended**
- **Cholinergic medications**:
  - Statistical significance of small magnitude & questionable clinical significance.
  - Only mild BPSD symptoms in all trials except two.

Concerns re: drug usage

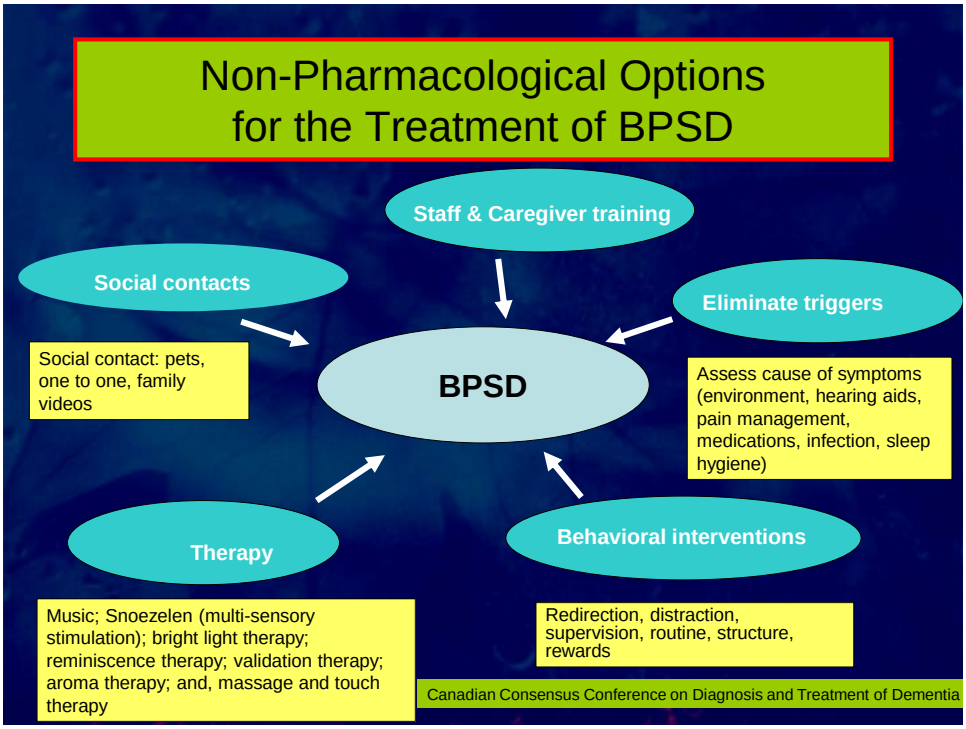
- CONCERN→ decreased use
- Education and support of staff or multicomponent interventions
- Reduced short-term inappropriate prescribing of antipsychotic drugs in care homes
- BUT evidence of long-term effectiveness and sustainability is still needed

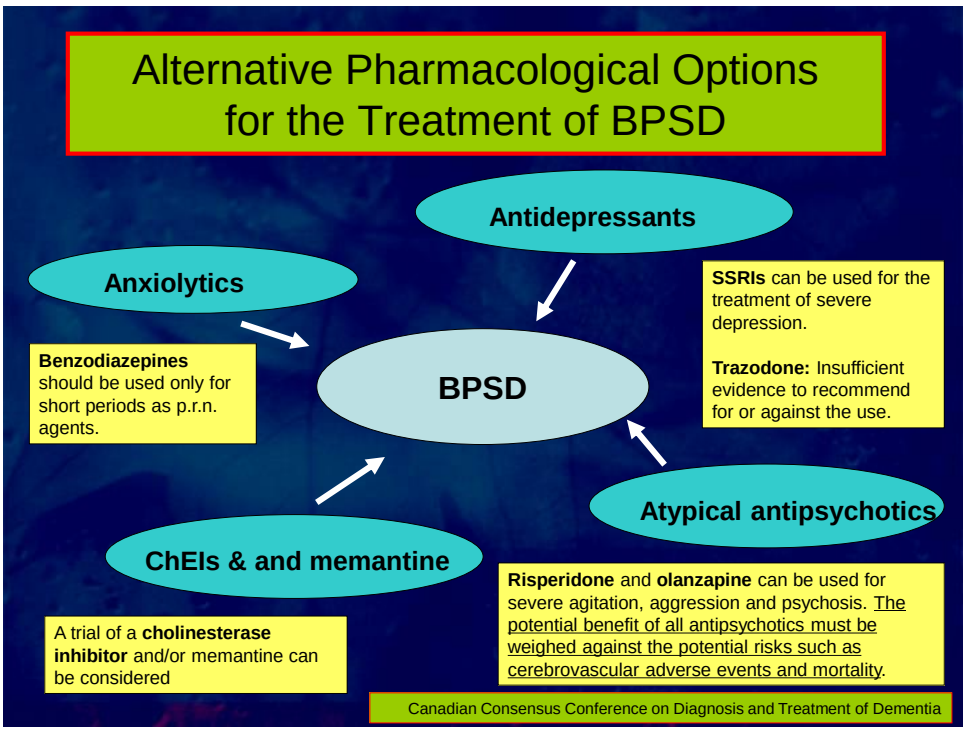
Concerns re: drug usage

- A care home with low antipsychotic use found that reducing antipsychotics, without adding other interventions for NPS symptoms is not helpful because NPS increased
- Implementation of effective interventions requires substantial training and longer term supervision or working alongside care home staff for a prolonged period

Transitions

- Care transitions from acute care → care homes require better communication between hospitals and nursing homes and between families and care home staff in order to improve outcomes for patients by lowering incidence of both transfer and transfer-related harm, such as mistakes in medication


Non-Pharmacological Options for the Treatment of BPSD
Staff & Caregiver training
Social contacts
Eliminate triggers
Social contact: pets, one to one, family videos
BPSD
Assess cause of symptoms (environment, hearing aids, pain management, medications, infection, sleep hygiene)
Therapy
Behavioral interventions
Music; Snoezelen (multi-sensory stimulation); bright light therapy; reminiscence therapy; validation therapy; aroma therapy; and, massage and touch therapy
Redirection, distraction, supervision, routine, structure, rewards
Canadian Consensus Conference on Diagnosis and Treatment of Dementia


Alternative Pharmacological Options for the Treatment of BPSD
Antidepressants
Anxiolytics
SSRIs can be used for the treatment of severe depression.
Trazodone: Insufficient evidence to recommend for or against the use.
Benzodiazepines should be used only for short periods as p.r.n. agents.
BPSD
Atypical antipsychotics
ChEIs & and memantine
Risperidone and olanzapine can be used for severe agitation, aggression and psychosis. The potential benefit of all antipsychotics must be weighed against the potential risks such as cerebrovascular adverse events and mortality.
A trial of a cholinesterase inhibitor and/or memantine can be considered
Canadian Consensus Conference on Diagnosis and Treatment of Dementia

Pharmacokinetics & Clinical Potency of Atypical Antipsychotic Agents

	Clozapine	Risperidone	Olanzapine	Quetiapine	Ziprasidone
Drug class	Dibenzo-diazepine	Benzio-xazol	Thienoben-zodiazepine	Dibenzo-thiazepine	Benziso-thiazolyl piperazine
Potency	50	1	4.0	80	20
Time to peak plasma conc. (hrs)	3	1.5	5	1.5	4
Protein binding (%)	92 - 95	90	93	83	98 - 99
Active metabolites	No	Yes	No	No	No
Metabolism	CYP1A2, CYP3A4	CYP2D6	CYP1A2, CYP2D6	CYP3A4	CYP3A4
Elimination half-life (hrs)	10 - 100	6 - 24	20 - 70	4 - 10	3 - 10[1]

MD Jibson. J Psychiatric Research 32 (1998) 215-228

Pharmacologic Options in Dementia

Possibly Prevent Emergence of BPSD

✓ Consider Cholinergic medication early in AD & Mixed AD /CVD

Mild/Moderate Agitation

✓ Consider Trazodone & Consider SSRI

Aggressive / Psychotic

✓ Consider Atypical antipsychotics

CAUTION: AVOID LONG-TERM USE OF BENZODIAZEPINES