

Grandma did what?? When dementia and acute care meet

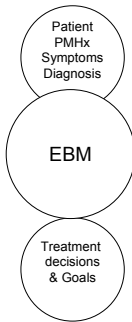
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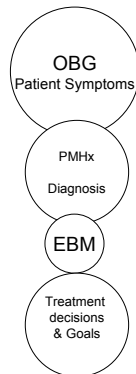
Goals/Objectives

- To identify behavioural symptoms in elderly dementia patients in the acute care setting
- To review predisposing factors and precipitating causes of behaviours
- To discuss the pharmacist's role in the identification of causes and potential treatment suggestions
- To review the role of antipsychotics & acetylcholinesterase inhibitors in the hospitalized dementia patient

ACUTE CARE



ELDER CARE



Grandma's Acute Care Adventure

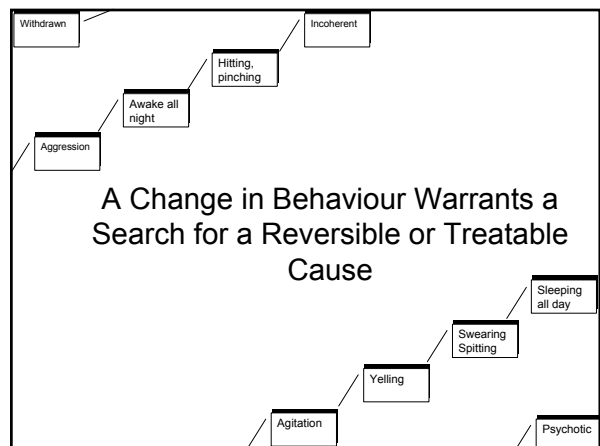


Behaviour Changes: *A New Form of Communication*

- In order to interpret--you need to know baseline
- Acute care healthcare professionals at a disadvantage.
- Gathering needed information can be labour intensive
- Family & other Caregivers know best



A Change in Behaviour Warrants a Search for a Reversible or Treatable Cause



Behaviours

- Recognize & describe
- Acuity of change
- Frequency or timing of occurrence
- Change in cognition?
- Prior history
- Document

Acute Change

Acute exacerbation: chronic medical condition(s)

⇒ CHF, COPD, Arthritis, GERD....

New medical illness in concert with multiple comorbidities

⇒ Infection, GI bleed, cancer, MI, CVA..

New psychiatric illness

⇒ Delirium

Acute exacerbation: chronic psychiatric condition

⇒ Dementia, bipolar, depression, schiz.

Poorly controlled chronic condition

Behavioural and Psychiatric Changes in the Elderly

- Persistent psychotic features in the elderly-->dementia
- Acute onset of behaviours or psychosis --> delirium, depression
- Main focus: delirium & presentation in patients with dementia
- BPSD in dementia

Karim S. Byrne EJ Adv Psychiatr/Treat. 2005;11:286-296

Table 1. Clinical Features of Dementia, Depression and Delirium*

FEATURE	DEMENZA	DELIRIUM	DEPRESSION
Onset	• Insidious	• Acute	• Gradual, may coincide with life change
Duration	• Months to years	• Hours to less than one month, seldom longer	• At least two weeks, but can be several months to years
Course	• Stable and progressive • "Wax" usually improve	• Fluctuates: worse at night • Lucid periods	• Diurnal, usually worse mornings improves as day goes on
Apathy	• Generally normal	• Fluctuates lethargic or hyper-vigilant	• Normal
Orientation	• May be normal but often impaired for location in the disease place	• Always impaired, time/place/person	• Usually normal
Memory	• Impaired recent and sometimes remote memory	• Global memory failure	• Recent may be impaired • Long-term memory intact
Thoughts	• Slowest, reduced interests • Makes poor judgments • Words difficult to find • Perseverative	• Disorganized, distorted, fragmented • Extreme ideas and topics such as paranoid grandiose	• Usually slowest, preoccupied by sad and hopeless thoughts • Anxious, pessimistic • Mood congruent delusions
Perception	• Normal • Hallucinations often visual	• Distorted: Visual and auditory • Hallucinations common	• Intact • Hallucinations absent except in postnatal depression
Emotions	• Shallow, apathetic, labile • Irritable	• Irritable, aggressive, fearful	• Flat, unresponsive or sad and fearful • May be irritable
Sleep	• Often disturbed, nocturnal awakening common • Nocturnal confusion	• Nocturnal confusion	• Early morning awakening
Other features	• Poor insight into deficits • Careless	• Other physical disease may not be obvious • Inattentive	• Past history of mood disorder • Poor effort on cognitive testing; opens up readily
Standard Tests	• Comprehensive assessment (history, physical, lab, SIBIRS)	• Confusion Assessment Method (CAM) see Appendix A	• Geriatric Depression Scale (GDS) see Appendix B

*Reprinted from the Guide for Health Professionals and Health Professionals Education (copyright University College London, Dementia: Patient Diagnosis and Management)

Delirium: The Diagnosis

Core Features:

- Disturbance of consciousness with reduced ability to focus, sustain or shift attention
- A change in cognition (memory, disorientation, language) or
- Development of perceptual disturbance not accounted for by pre-existing condition
- Disturbance develops over a short period of time and fluctuates during the course of the day

DSM-IV

Etiology of Delirium

- Cholinergic deficiency
- Serotonin excess or deficiency
- Cytokines (interleukin-2, TNF)
- Other neurotransmitters: GABA & dopamine)

Delirium: Clinical Tools Confusion Assessment Method (CAM)

CAM Diagnostic Algorithm:

1. Acute Onset & Fluctuating Course
and
2. Inattention
Plus
3. Disorganized thinking
or
4. Altered Level of Consciousness

Types of Delirium

Hypervigilant Hyperactive

- ~ 25%
- More likely to be identified due to behaviours

Hypovigilant Hypoactive

- > 50%
- Least likely to be identified--not causing any problems!
- Rx may identify as oversedation

Mixed

Types of Delirium & Effect of Dementia

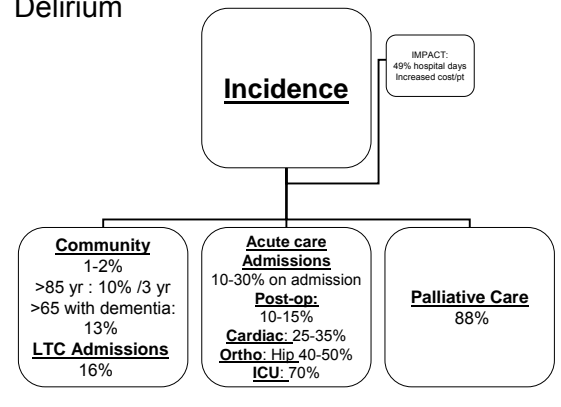
Table 2. Differences Between Delirious Participants With and Without Dementia—Type of Delirium and Clinical Variables

	Statistical Parameters		P Value
	With Delirium (n = 279)	Without Delirium (n = 209)	
Hypervigilant delirium (n = 156/179)	24 (14.8)	27 (12.8)	.405
Hypovigilant delirium (n = 120/131)	39 (32.4)	47 (35.9)	.692
Mixed delirium (n = 103/110)	66 (64.8)	66 (60.3)	.052
Unaffected delirium (n = 170/171)	9 (5.3)	20 (11.7)	.014
Ever had delirium (n = 120/131)	112 (93.4)	107 (81.7)	.007
Psychotic delirium (n = 120/131)	69 (57.2)	76 (57.7)	.983
Thoughts, hallucinations, delirious day (n = 120/131)	69 (57.2)	69 (52.7)	.237
Thoughts, delirious day (n = 120/131)	69 (57.2)	69 (52.7)	.692
Thoughts, delirious day (n = 120/131)	69 (57.2)	69 (52.7)	.281
Thoughts, delirious day (n = 120/131)	69 (57.2)	69 (52.7)	.280
Thoughts, delirious day (n = 120/131)	69 (57.2)	69 (52.7)	.285

2007

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Delirium



Consequences of Delirium in the Elderly

Increased: ► Length of Stay ► Morbidity ► Mortality

Delirium vs none in hospital—**○**mortality post D/C

- 1 yr 35% vs 22 (p=.006)
- 2 yr 58% vs 42 (p=.005)

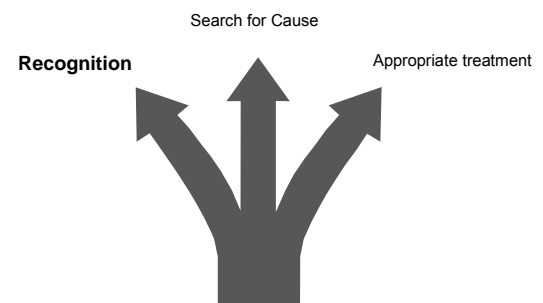
Home-dwelling at baseline:

- 2 yr post D/C 54% in LTC vs 28% (p=.001)

Delirium independent predictor for mortality:

- @ 1 yr (OR 1.86 95% CI 1.1-3.1)
 - @ 2 yrs OR 1.76 CI 1.1-2.8,
 - & for Institutionalization (OR 2.45, CI 1.2-4.9)
- (Pitkala 2005)

DELIRIUM: A Complex System Failure



Delirium at Discharge:

Medical: 3-16% discharged with delirium:

- **Risk Factors:** Dementia; poor vision; functional impairment; high comorbidity & physical restraint use
- Persistent delirium: worse cognitive & functional outcomes
- Discharged from acute care: 2.6 x mortality or nursing home placement.
- Discharge from ER: (37%); 7x increased mortality

Inouye 2007; Husley 2001

"The under recognition of delirium is a daily reminder that what we are now teaching is not working...."

*Dr. Ken Rockwood
4th Canadian Colloquium on Dementia
Vancouver. October 2007*

Recognition of Delirium

What's the problem?

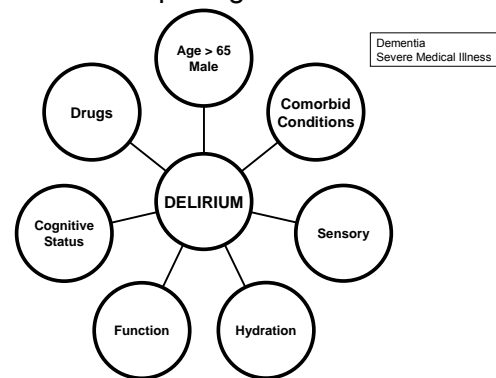
Fluctuating nature
Overlap with dementia,
Lack of formal cognitive assessment,
Under appreciation of clinical consequences
Failure to consider diagnosis important.

Assessment of RN knowledge:

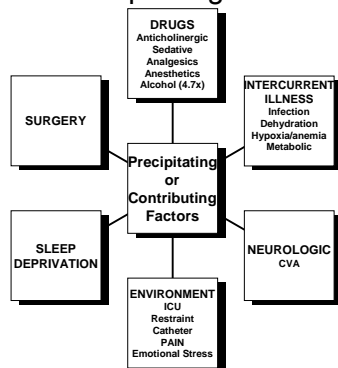
- 21% identify hypoactive delirium in patients with dementia; 41% in non demented

Fick 2007

Predisposing Factors:



Precipitating Factors:



Inouye 2006

Evaluation

- Gather information: Family
- Optimize communication first
Non verbal ≠ not comprehending
- Routine screening:
Instruments— DRS R-98; CAM; NEECHAM
- ALL health disciplines: Report, **record** any change in behaviour or cognition
- Describe "target" symptoms

EVALUATION: History & Physical

History

- Time course of cognitive changes
- Medication review, including OTC drugs, alcohol

Physical examination

- Vital signs/O2 sats/PAIN
- General medical evaluation
- Neurologic and mental status examination

Interdisciplinary Approach:

- MDs, RN, Rx, family...

Treatment: Non-Pharmacologic Multidisciplinary approach

- Optimal Stimulation
- Environment more familiar
- Cues for orientation
- Optimize sensory input
- Social Restraints :Family Communication@ poor attention
- Face to face
- Clear, slow, short, simple & repetitive
- Avoid abstract language
- 1 stimulation at a time
- Anticipate needs may prevent behaviours
- Same Faces

Treatment with Antipsychotics

Antipsychotics:

Drugs of first choice

Best available evidence: haloperidol

Symptoms requiring treatment:

- Agitated/severe psychiatric symptoms
- Prevent self-injury or injury to others
- Carry out essential investigation; initiate treatment
- NOT for hypoactive delirium ?

REGULARLY dosed monotherapy, lowest dose, shortest time

Haloperidol 0.25-0.5mg daily or bid

Risperidone 0.25-0.5mg po daily/bid.

Olanzapine 2.5-5 mg po daily

Additional PRN's: orders need Max. dose/d

Caution: Lewy Body Dementia, Parkinson's Disease

Table 4. Pharmacologic Treatment of Delirium.

Class and Drug	Dose	Adverse Effects	Comments
Antipsychotic Haloperidol	0.5-1.0 mg twice daily orally, with additional doses every 4 hr as needed (peak effect, 4-6 hr) 0.5-1.0 mg intramuscularly, observe after 30-60 min and repeat if needed (peak effect, 20-40 min)	Extrapyramidal symptoms, especially if dose is >3 mg per day Prolonged corrected QT interval on electrocardiogram Avoid in patients with withdrawal syndrome, hepatic insufficiency, neuroleptic malignant syndrome	Usually agent of choice Effectiveness demonstrated in randomized, controlled trials ^{11,12} Avoid intravenous use because of short duration of action
Atypical antipsychotic Risperidone Olanzapine Quetiapine	0.5 mg twice daily 2.5-5.0 mg once daily 2.5-3.0 mg once daily 12.5-50 mg bid or daily	Extrapyramidal effects equivalent to or slightly less than those with haloperidol Prolonged corrected QT interval on electrocardiogram	Tested only in small uncontrolled studies Associated with increased mortality rate among older patients with dementia
Benzodiazepine Lorazepam ^a	0.5-1.0 mg orally, with additional doses every 4 hr as needed ^a	Paradoxical excitation, respiratory depression, oversedation	Second-line agent Associated with prolongation and worsening of delirium symptoms, demonstrated in clinical trial ¹³ Reserve for use in patients undergoing sedative and alcohol withdrawal, those with Parkinson's disease, and those with neuroleptic malignant syndrome
Antidepressant Trazodone	25-150 mg orally at bedtime	Oversedation, BP	Tested only in uncontrolled studies

^a Intravenous use of lorazepam should be reserved for emergencies.

Keys to Medical Management

Treat the underlying disease

Avoid complications

- Remove indwelling devices ASAP/ restraints
- Hydration
- Anemia/lytes/O2

Optimize medications

- Remove medication contributors
- Ensure prior medications for behaviours have not been stopped inadvertently
- Provide adequate analgesia
- Prevent or treat constipation and urinary retention
- Encourage proper sleep hygiene, avoid sedatives

Antipsychotics: SIDE EFFECTS

SEDATION

HYPOTENSION

ANTICHOLINERGIC EFFECTS

Peripheral vs Central

FALLS

MOVEMENT DISORDERS: EPS, TD

NMS

Endocrine: Wt gain, diabetes

Morbidity & Mortality: Data in delirium?

Cause: ? BP, ?Sedation, decreased mobility-->chest infections, diuretics...

Prevention: Modify Risk Factors

Inouye 1999

Targeted risk factors :

Cognitive impairment, sleep deprivation, immobility,
Visual & hearing impairment, dehydration
Medical inpatients N=850 Age >70yr
Prospective, matched.

Delirium 9.9% in intervention group vs 15% in usual
care.(OR 0.60 95%CI 0.39-0.92%)

Total # days & # episodes also decreased.

► Severity & recurrence..no change

Bogardus 2003:

Follow-up study: no benefit evident @ 6 months

Prevention: Modify Risk Factors

Marcantonio, 2001

Hip Fractures: Geriatric consults N=126

Targeted risk factors:

O2 delivery,fluid/lytes balance, pain, eliminate unnec.
drugs, bowel/bladder, nutrition,mobilization,environment
Prevention, early detection and treatment of post-op
complications.

Delirium rates: 32% vs 50% NNT 6

Decreased severity of delirium

No change in LOS or discharge destination.

↻↻ No effect on dementia subgroup (N=50)

Caplan 2005

Early home rehab:

- New onset delirium: in home 0.6% vs 2.6% (p=0.003)

Prophylaxis: Haloperidol/ AChEI

Kalisvaart 2005

N=430 Age>70 Hip Surgery

Treatment group: Haloperidol 1.5 mg/d pre-op & 3d post

Delirium risk factors:

Visual impairment;severity of illnesses;cognitive impairment,
dehydration

No effect on preventing delirium

Decrease in severity, duration & LOS

Geriatric consultation in both groups

Moretti 2004

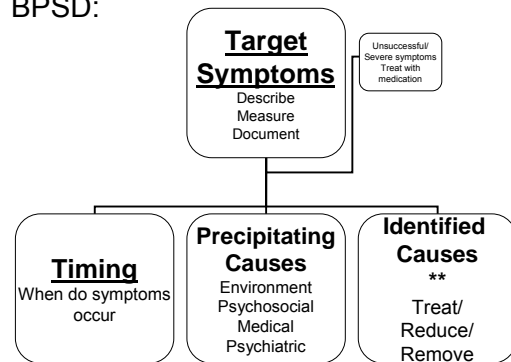
Rivastigmine N=246 Not well controlled

Fewer episodes of delirium,shorter duration,less use of
antipsychotics and BDZ

Chronic Refractory delirium

Donepezil: Case reports

BPSD:



Behavioural Psychological Symptoms of Dementia (BPSD)

- 85% of Dementia patients will exhibit clinically significant behavioural problems at some point in their illness
- BPSD adversely affects QOL, caregiver burden, daily functioning, cost of care, increases LTC admissions

Use medications when:

- Behaviour is frequent & may be amenable to drug treatment
- Behaviour/social/environmental changes are not effective
- Resident at risk of harm to themselves or others
- Basic personal care cannot be done

Symptoms & Response to Medications

Poor Response to medications

- Wandering, pacing, hoarding, ..
- Constant calling out..

Symptoms which may respond to antipsychotic medications

- Delusions/hallucinations/suspiciousness
- Aggressive behaviours
- Irritability
- Sleep disturbances

Efficacy of Medications

- No longterm (> 6mo.) efficacy for agitation documented

Other Options:

Carbamazepine

Antidepressants: Citalopram

Other Treatment Options for BPSD

Cholinesterase Inhibitors:

Some evidence that they may be effective for BPSD
 ?Do they delay onset of BPSD

Carbamazepine:

Better than placebo in several small placebo controlled studies
 Problem: Side effects and drug interactions
 CVAE not documented

Antidepressants: (Agitation/sexual inappropriate behaviour)

Citalopram:
 Multiple small studies for BPSD
 Small study (Nov 2007) comparing with risperidone for agitation & psychosis
 NO statistical difference: Trend citalopram better for agitation, risperidone for psychosis.

Antipsychotics: Morbidity & Mortality in Patients with Dementia

- Re-analysis of multiple trials with the use of antipsychotics for BPSD (duration of most ≤ 12 wks)
- Outcomes: CVA, TIA, death

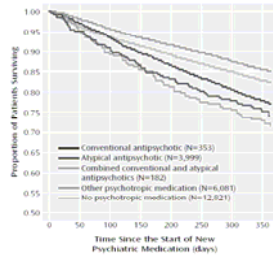
As of this week:

Typical & Atypical antipsychotics = risk?

- Shown for risperidone & olanzapine. OR 1.5-1.7 mortality risk. AR: 1.9% incr NNH 52
- Recent study (<12 weeks): CVA events with aripiprazole (7 events vs 0 in placebo)
- 8 deaths vs 3 OR 2.7
- Longterm therapy?? Similar risk or not

Ballard 2007 Mintzer 2007

FIGURE 1. Association Between Type of Psychiatric Medication and 12-Month Survival Among Outpatients With Dementia*



*Kaplan-Meier survival curves.

Non antipsychotic medications:
 Mortality significantly different from antipsychotic group
 Except: Anticonvulsant group?
 Combining antipsychotics \rightarrow increased risk
 Comorbidity, severity of dementia, males

Kales 2007

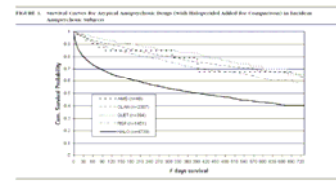


FIGURE 2. Individual Characteristics of Conventional Medication for Older Outpatients and the Patients Who Were the Subject Focus of an Antipsychotic Study, with Data on 12-Month Survival

	Conventional Drug (N)	Atypical Drug (N)	Combined Subtotal (N)	Other Psychotropic Drug (N)	No Psychotropic Drug (N)
Age (Mean)	81	81	81	81	81
Female (%)	47	47	47	47	47
AD (%)	47	47	47	47	47
AD with Vascular (%)	14	14	14	14	14
AD with Lewy Bodies (%)	14	14	14	14	14
AD with Mixed (%)	14	14	14	14	14
AD with Other (%)	14	14	14	14	14
AD with Unknown (%)	14	14	14	14	14
AD with No AD (%)	14	14	14	14	14
AD with Other (%)	14	14	14	14	14
AD with Unknown (%)	14	14	14	14	14
AD with No AD (%)	14	14	14	14	14
AD with Other (%)	14	14	14	14	14
AD with Unknown (%)	14	14	14	14	14
AD with No AD (%)	14	14	14	14	14

Hollis 2007

Cholinesterase Inhibitors: Just a few things....That's all I can remember



Alzheimer's Drug Therapy Initiative

October 2007: AchEI coverage commenced

For coverage, diagnosis must be Alzheimer's Disease (AD), AD with a vascular component, and AD with Lewy bodies or mixed dementia with predominant AD.

Acetyl Cholinesterase inhibitors (AChEIs)

Goals:

- Prolong stay in the community vs LTC
- Decrease or delay BPSD
- Maintain or slow functional loss
- Reduce Caregiver burden
- Cognitive stabilization

AChEIs: Side effects

- **GI:** Nausea/vomiting. Most common side effect and most common reason for discontinuing.
- Less common: diarrhea, muscle cramps, bad dreams (donepezil only). Syncope, dizziness.
- Possible contraindications: bradycardia or AV block, active peptic ulcers, asthma, seizure disorder (lowers threshold).
- Drug interactions may result from CYP P450 inhibitors or inducers. Anticholinergic drugs may limit efficacy of ChEIs.

Summary of the most common adverse events by AChEI type

AChEI	Common adverse effects	NNH
Donepezil	Diarrhea	8
	Nausea	20
Rivastigmine	Nausea	6
	Vomiting	7
Galantamine	Nausea at 24mg/d	5

Dosing AChEI

Drug	Starting dose	Titration period	Dose increase per titration	Usual effective to maximal dose
Donepezil	5 mg q.d.	4-6 weeks	5 mg q.d.	10 mg q.d.
Rivastigmine	1.5 mg b.i.d.	2-4 weeks	1.5 mg b.i.d.	3-6 mg b.i.d.
Galantamine	ER 8 mg q.d.	4-6 weeks	ER 8 mg q.d.	ER 16-24 mg q.d.

Drug	Starting Dose	Titration Period	Dose Increase Per titration	Usual effective max dose
Memantine	5mg	4 wks	5mg	10mg b.i.d.

Potential drug Interactions

Major drug interactions associated with Memantine include drugs which increase the pH in urine (for example, carbonic anhydrase inhibitors). Exercise caution when prescribing Memantine with other drugs which undergo renal tubular secretion. Doletide is considered a very severe risk, due to the potential for causing arrhythmias. The effects of dopamine agents will be increased when co-administrated with Memantine.

BC Guidelines

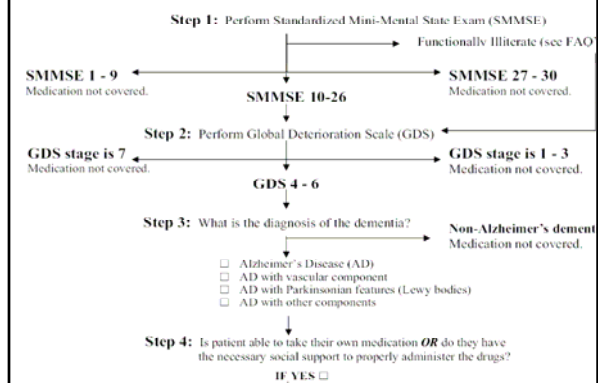
Switching ChEIs

- Lack of tolerability
- Tolerability can be improved by slower, more cautious titration.
- There are limited data on switching for lack of efficacy (especially since stabilization is the primary goal rather than symptomatic improvement).

Discontinuing AChEIs

- Stopping AChEIs in mild-moderate Alzheimer's disease for more than a few weeks may result in irreversible loss of accrued efficacy
- Consider stopping AChEIs when:
 - Alzheimer's disease is advanced and most ADLs lost
 - Patient is unlikely to realize AChEI benefits because of severe comorbid illnesses
- When stopping AChEIs in late disease, watch for emergence of BPSD and consider restarting if indicated

ALGORITHM FOR INITIAL COVERAGE FOR CHOLINESTERASE INHIBITOR FOR MILD TO MODERATE ALZHEIMER'S DISEASE



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