Assessment and Management of Depression in Later-life

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Agenda

- Review of epidemiology of Late-life Depression (LLD)
- Review of diagnosis of LLD
  - Phenomenology
  - Time of onset
  - Complications
- Screening tools
- Treatment options

Epidemiology of Late-life Depression I

- A major public health problem
  - 2nd only to heart disease in disability
- Remains under-diagnosed and under-treated in the elderly
  - Most will receive treatment in 1° care settings
  - However, rates of treatment are very low

Wells 1989; NIH Consensus 1992; Unutzer 1999; Jeste 1999; Steffens 2000

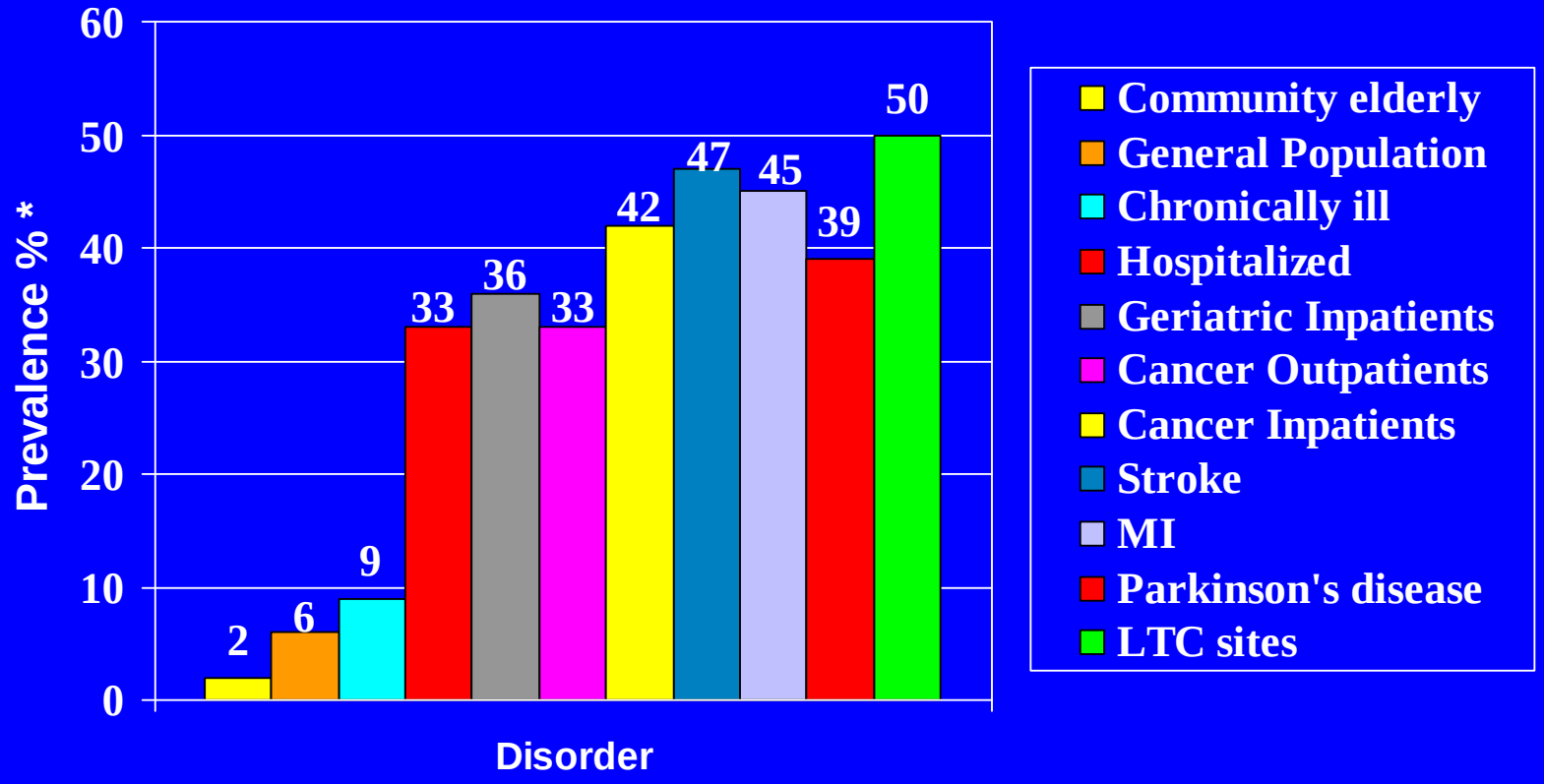
Epidemiology of Late-life Depression II

- Consequences
  - Amplifies disability and lessens Quality of Life
  - Increases morbidity and mortality
    - Medical: pain, heart disease
    - Psychiatric: suicide
  - Increases rates of healthcare utilization
  - Increases drug use and costs
  - Increases cost of care

NIH Consensus 1992; Frasure-Smith 1993, 1995; Unutzer 1999; Beekman 1999; Charney 2003

Epidemiology of Late-life Depression III

Prevalence rates vary across different sites and with different conditions.



* Range depends on the study

Phenomenology of Late-life Depression

- There are different types of depressive disorders.
  - Major Depression (and subtypes)
  - Subsyndromal depression (and subtypes)
- Not all require or respond to pharmacotherapy:
  - Know which type of clinical depression is being diagnosed as treatment selection may vary.
  - Some types and some patients may preferentially respond to psychotherapy (individual, group, family, or day program)
- Most types contribute to functional impairment and increased healthcare utilization.
- All types place patients at risk of complications or poorer outcomes.

NIH Consensus 1992; Consensus Update 1997; Jeste 1999

Phenomenology of Late-life Depression

- **Subsyndromal Depression**: patient has clinically significant depressive symptoms but does not meet either time duration, quantity or severity criteria for DSM-IV Major Depression
  - Minor depression
  - Brief, recurrent depression
  - Non-dysphoric depression
  - Dysthymia (depressed mood for ≥ 2 years)
- Except for Dysthymia, criteria are not well-delineated.
- However, these types may be more prevalent in older populations and difficult to detect.
- Pharmacological treatments may not be needed initially and adjunctive use of psychotherapies may lead to better outcomes.

Hermens 2004; Kumar and Lavretsky 2002

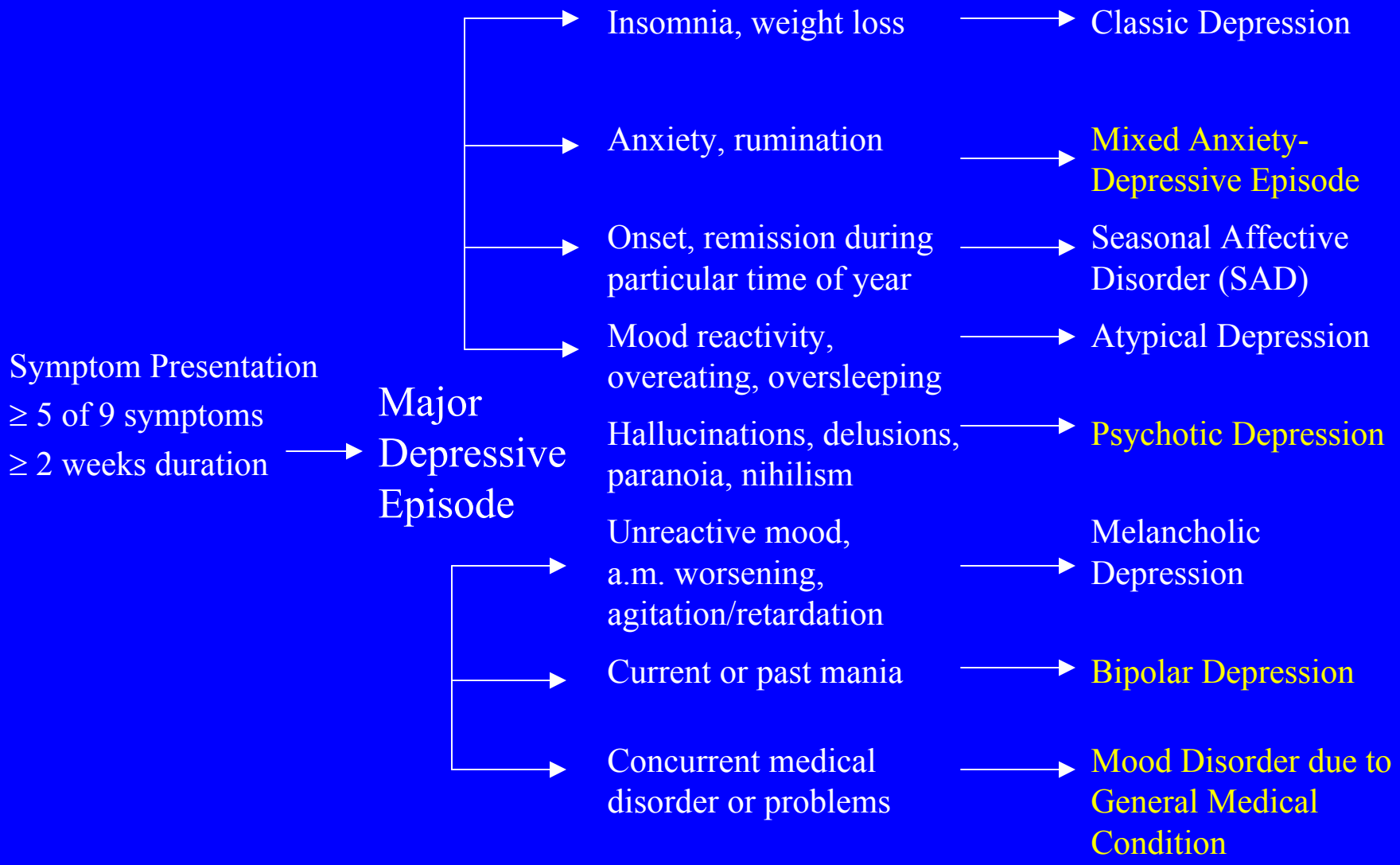
DSM-IV criteria for Major Depression

- Diagnosis requires 5 of 9 symptoms present for at least 2 weeks, nearly every day or more days than not
- To use the mnemonic - one symptom must be
  - depressed mood **OR**
  - decrease in interest/pleasure

- **S**: suicidal thoughts
- **I**: interest decrease
- **G**: guilt; worthlessness
- **E**: energy decrease
- **C**: cognitive problems
- **A**: appetite / weight change
- **P**: psychomotor changes
- **S**: sleep disturbance

American Psychiatric Association 1994

Major Depression: Symptom Clusters and Possible Sub-typing



Subtypes of particular relevance in Late-life Depression

- Cerebrovascular disease
  - Post-stroke depression: location and time effects
  - Vascular depression
    - DWM ischemic changes
    - Disruption of frontal-subcortical circuitry
    - Differing presentation: apathy, slowing, executive dysfunction, less insight; later age of onset; less psychosis?
- Post-MI depression
- Dementia complicated by depression
  - Alzheimer's disease
  - Parkinson's disease

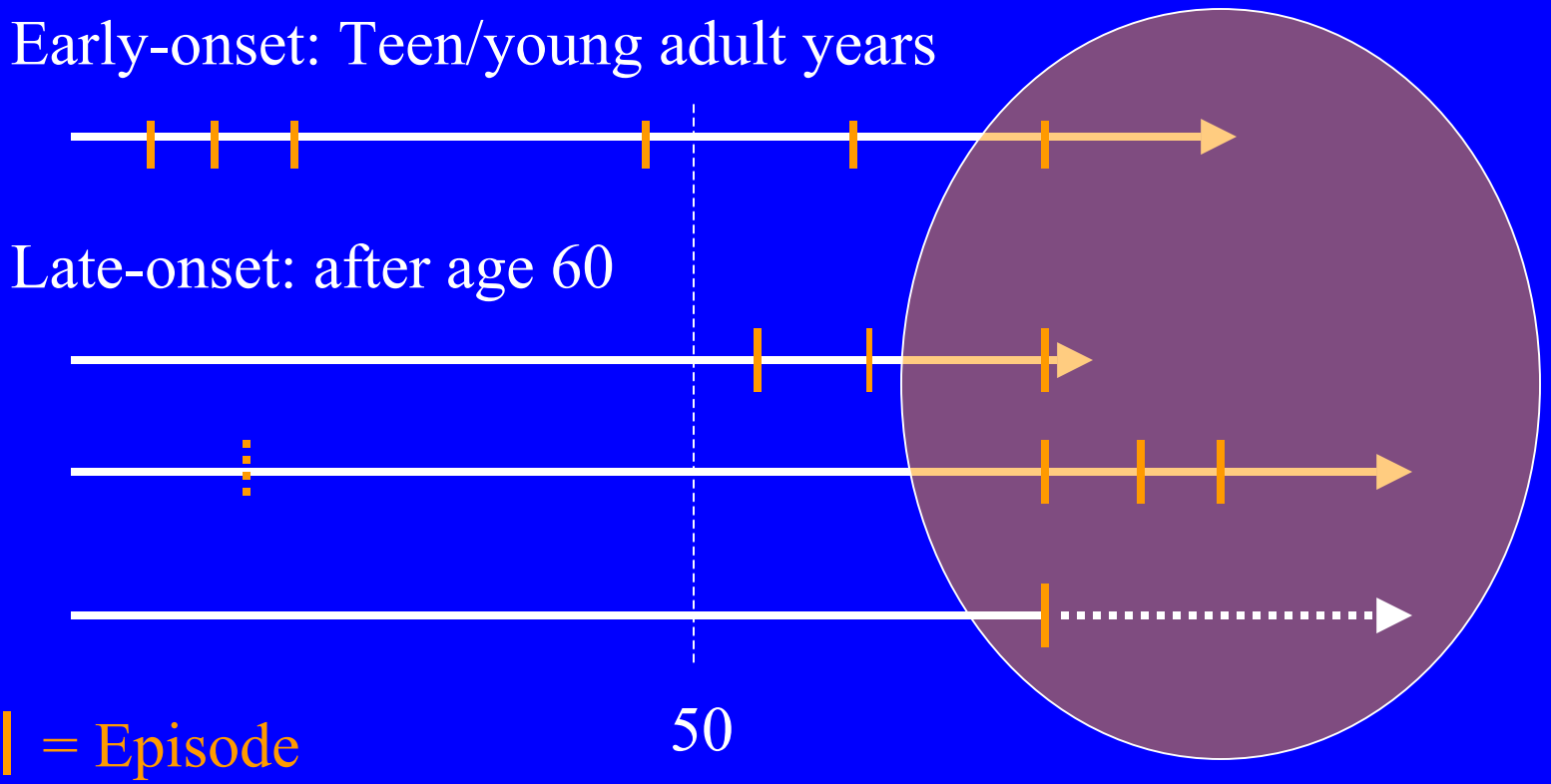
Alexopoulos 1997, 2003; Frasure-Smith 1999; Green 2003; Gournellis 2001; Krishnan 1997, 2004; Olin 2002; Wilson 2002

Complications of relevance in Late-life Depression

- Dementia of depression or "pseudodementia"
  - Subcortical neuropsychological impairment is typical
  - Frontal executive dysfunction may also be seen
  - Higher cortical dysfunction may predict AD conversion
- Psychotic depression
  - psychosis may be subtle, not endorsed. Must ask.
  - more lethal, usually requires hospitalization
  - combined pharmacotherapy
  - ECT
    - Indicated sooner
    - May be treatment of choice

Birkenhager 2003; Karim 2003; Kessing 2003; Petrides 2001; Schwartz 2004

Late-life Depression: Time of Onset Variable



Epidemiology of Late-life Depression IV
Early-onset Depression (EOD)

- Early onset
  - Develops earlier in life: teens or twenties
  - Higher biological or familial risk
    - Mood disorders
    - Substance abuse
    - Suicide
- Clinical history
  - How many episodes? Duration? Symptoms?
  - What treatments worked?
  - If family history, what worked for them?

Lebowitz 1997; Reynolds 2001; Alexopoulos 2003

Epidemiology of Late-life Depression V Late-onset cases

- Late-onset: 1st episode vs. recurrent
  - 1st episode: no prior history, no family history, may have higher suicide risk, more medical comorbidity
  - Remission rates similar to EOD but . . .
  - Recurrence rates higher: prior episodes, positive family history, degree of residual symptoms
  - Cognitive deterioration: may reflect patient at higher risk of subsequently developing dementia (AD, VaD, or Mixed dementia) or may be prodrome of dementia

Lebowitz 1997; Reynolds 2001; Alexopoulos 2003; Mitchell 2005

Complications in Late-life Depression: Suicide

- In geriatrics: 10th leading cause of death
  - More specifically related to late-onset, 1st episode depression
  - Higher or acute risk if suicidal ideation is present with
    - hopelessness
    - restlessness
    - comorbid anxiety or psychosis
    - insomnia
    - chronically, seriously ill or suffering condition
    - social isolation: recently bereaved or widowed
    - concurrent of alcoholism or substance abuse
  - Attempts in later-life decrease BUT successful completion of suicide increases

Mosciki 1997; Fawcett 1993; Rich 1986; Gliatto 1999

Challenges in Assessing Depression in Late-life

- Gender differences
  - Males: anger, apathy, anhedonia but not sadness
  - Females: somatic symptoms, dysphoria
- Over-expression of somatic complaints
- Minimization of psychological problems
- Presence of medical comorbidity
  - Symptoms: fatigue, anorexia, insomnia, psychomotor slowing, pain
  - Cognitive impairment: detection and expression
  - Medication side-effects
  - Competing time demands
- Presence of psychiatric comorbidity
- Rationalization: by patient, family and/or provider
  - "reasons to be depressed . . ."
  - Nihilism

Differential Diagnosis of Depression in Late-life

- Medical
  - Endocrinopathies
  - Metabolic derangement
  - Infections
  - Cardiopulmonary disease
  - GI disturbances / cancer
  - Inflammatory processes
  - Hematological conditions
  - Musculoskeletal problems
  - Delirium
- Neurological
  - Cerebrovascular disease
  - Primary or metastatic tumor
  - Basal ganglia disease
  - Dementia
- Medications
  - Antihypertensives
  - Analgesics (opiates)
  - CNS depressants
  - Others
- Psychiatric
  - Adjustment disorder
  - Anxiety disorder
  - Substance-induced disorder (Alcoholism)
- Life circumstances
  - Grief and bereavement
  - Social isolation / loneliness
  - Poverty

Diagnosis of Depression in Physically Ill Elderly

- Features of Physical illness
  - recent onset
  - greater severity
  - functional disability
  - poorly treated pain
  - higher number of illnesses
- Functional impairment, not physical illness per se, appears to be the greater risk factor for depression in the elderly:
  - Abrupt change
  - Lower level of function
- Variation with caregiver stress level

Other Risk Factors for Depression in Physically Ill Elderly

- Past history of depression
- Cognitive impairment
- Age over 75 years
- Impaired social support
- Alcohol abuse
- Poor education

Exclusion of Depression in Physically Ill Elderly

Look for “positive” or joining behaviors.
Unlikely to be depressed if:

- Appreciates humour (laughs and smiles broadly)
- Responds warmly to affection
- Shows an interest in life, pleasurable activities
- Looks forward to family visits
- Accepts help
- Participates in treatment (PT, OT, etc)
- Points to reasonable causes for physical symptoms

Diagnosing Major Depression In Physically Ill Elderly

- Depression criteria should emphasize:
  - change of mood or interest with at least 2 weeks duration
  - non-physical symptoms
  - social regression or incapacity
- Anorexia, sleep disturbances, fatigue and motor retardation:
  - These should only be considered if they accompany the above depressive symptoms and cannot be explained by physical illness or its treatment
  - If present at the outset, these symptoms get worse with mood and are out of proportion to symptoms expected from medical illness

Screening for Late-life Depression

- Two-question screen
- Geriatric Depression Scale
- Cornell Scale for Depression in Dementia
- PHQ-9

- Caveat on screening: should not be sole basis for diagnosis.
- Gold standard: clinical interview

Screening Tools for Assessment of Late-life Depression I

- Two-question screen
  - during the past month have you often been bothered by feeling down, depressed, or hopeless? And,
  - during the past month have you often been bothered by little interest or pleasure in doing things?
- Validated in primary outpatient care settings and in older patients
- Not validated in cognitively impaired patients or in inpatient or LTC settings
- Cannot be used to follow response to treatment

Screening Tools for Assessment of Late-life Depression II

- Geriatric Depression Scale
  - 30-item, 15-item, 10-item, and 5-item
  - Validated across outpatient and inpatient settings; available in several languages
  - Emphasizes psychological components of depression
  - May be limited in greater than mildly cognitively impaired individuals (MMSE < 17)
  - May not be sensitive to change

Brink and Yesavage 1982, 1987; Montorio 1996; Rinaldi 2003

Screening Tools for Assessment of Late-life Depression III

- Cornell Scale for Depression in Dementia
  - Observational and informant based
    - 19-item scale
    - 38 maximum; ≥ 12 indicates depression
  - Validated in mild to moderately impaired groups, but
  - Not yet validated across all cultural or ethnic groups
  - Can be used to follow change to treatment

Alexopoulos 1988

Screening Tools for Depression in Late-life IV: PHQ - 9

Spitzer, Williams, Kroenke, et al. 1999

Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at All	Several days	More than half the days	Nearly every day
a. Little interest or pleasure in doing things	0	1	2	3
b. Feeling down, depressed, or hopeless	0	1	2	3
c. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
d. Feeling tired or having little energy	0	1	2	3
e. Poor appetite or overeating	0	1	2	3
f. Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	1	2	3
g. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
h. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
i. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

Scores:

5-9 = mild

10-14 = moderate

≥10: likely major depression

15-19 = moderately severe

≥20 = severe

If you checked off any problems, how difficult have these made it for you to do your work, take care of things at home, or get along with others?

- not difficult
- somewhat difficult
- very difficult
- extremely difficult

Screening Instruments for Late-life Depression for Use in Primary Care

	Sensitivity	Specificity	Inpatient	Outpatient	Physically ill	Cognitively impaired
2-Question Screen	97%	67%	No	Yes	Unknown	No
GDS 5-item	94%	81%	Yes	Yes	Yes	Unknown
CSDD (19-item)	90%	75%	Yes	Yes	Unknown	Yes
CES-D (20-item)	93%	73%	No	Yes	Unknown	No
PHQ-9	88%	88%	No	Yes	Yes	Unknown

Treatment Strategies for Depression in Late-life

- Psychotherapy
- Somatic therapy
  - Medications
  - Brain Stimulation: ECT and VNS (rTMS?)
- Decision on which to pursue is predicated upon
  - severity
  - persistence
  - degree of associated suffering
  - extent of related disability
  - values expressed by patient and family

Treatment Strategies for Depression in Late-life

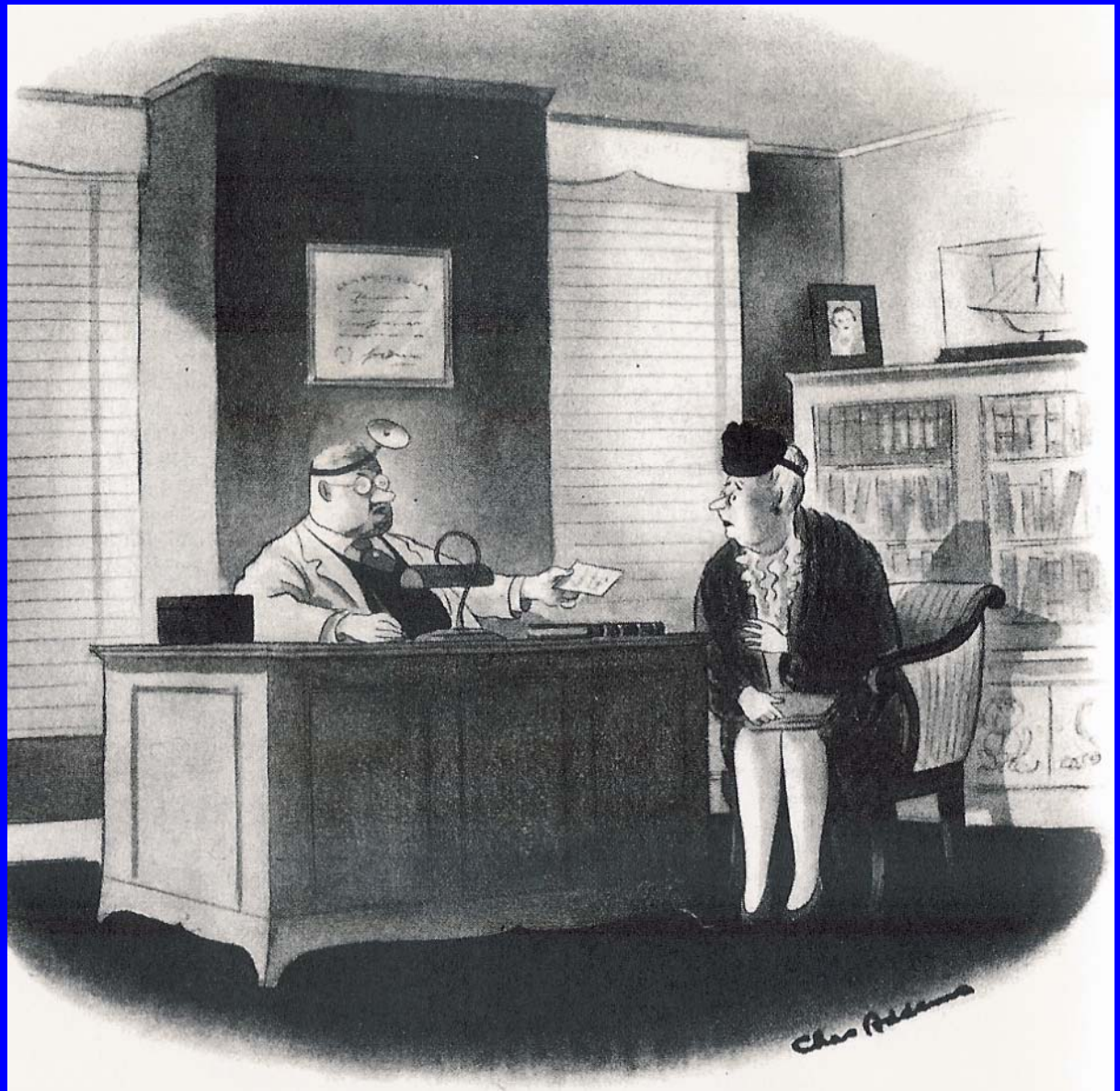
- Psychotherapy
  - Type: supportive psychotherapy, problem-solving therapy, cognitive-behavioral therapy, interpersonal psychotherapy
  - Modality: individual, couples, family, group
  - Location: office; partial hospital or day treatment; IOP; senior community centers; assisted living, residential or LTC sites
  - Practitioners: psychiatrists, psychologists, social workers, nurse therapists, MFTs

Arean 2002; Garner 2003; Unutzer 2003

Treatment Strategies for Depression in Late-life

- Indications for Psychotherapy
  - Patient or family preference
  - Sensitivity to medication(s) or reluctance to try
  - Polypharmacy
  - Minor depressive states: 1st choice?
- Adjunctive use
  - Collaborative care models: Project IMPACT (Unutzer 2002)
  - Stepped care models (Katon 1999)
- Obstacles
  - Limited coverage
  - Limited providers
  - Patient resistance / stigma
  - Therapist ageism

The New Yorker Magazine Collection



"Now have this prescription filled and take as directed. Then two nights after the first full moon, procure the left hind leg of a he-frog and a root of St. John's-wort . . ."

Treatment Strategies for Depression in Late-life

- Pharmacotherapy is indicated when:
  - psychotherapy has failed, ie, symptoms persist
  - serious depressive symptoms interfere with daily functioning or impair health or safety
  - after discussion, patient prefers
- Choice of antidepressant depends on:
  - Efficacy
  - Adverse events (safety)
    - Tolerability
    - Interruption
  - Compliance
  - Cost

Mittman 1999; Solai 2001; Sommer 2003; Williams 2000

Defining an Adequate Medication Trial

- Right medication, ie, accurate diagnosis
- Right dosage
  - Underdosing is very common in primary care and among elderly patients
  - Start low, go slow, but go.
- Right duration
  - 4 to 6 weeks for *maximal* effect, but
  - May be able to see some initial improvement after 2 weeks
  - For elderly, some may take as long as 8 to 12 weeks
- In the beginning, more frequent follow-up, encouragement, checking for compliance and providing reassurance will improve effectiveness of treatment.

Common SRI's

	Starting Dose/day	Therapeutic Range/day*	Generic	CYP 450 effects	Side-effects
Fluoxetine (Prozac®)	5-10mg Qam	10-20mg	Y	+++	+/++
Sertraline (Zoloft®)	12.5-25 Qam	50-150	Y	++	++
Paroxetine (Paxil®)	10 Qhs	20-30	Y	++	++
Citalopram (Celexa®)	10 Qhs	20-40	Y	+	+
Escitalopram (Lexapro®)	5-10 Qam	10-20	N	±	±

* Dosage for Major Depression

Mittman 1999; Solai 2001; Sommer 2003; Williams 2000

Adverse Effect Profiles of SRIs

SRIs: proserotonergic; variably anticholinergic, antihistaminergic or antidopaminergic

- Common
  - nausea
  - loose stools
  - restlessness
  - akathisia
  - insomnia
  - headache
  - sexual dysfunction
- Uncommon (?)
  - weight loss / gain
  - hyponatremia (SIADH)
  - sinus bradycardia
  - bleeding (anti-platelet effect)
  - Parkinsonism
  - Serotonin Syndrome

“Dual Action” and Atypical Antidepressants

	Starting Dosage (mg)	Range (mg)	Treatment Resistance	Drug Interactions
Venlafaxine (IR / SR)	18.75-37.5 BID	75-150	Yes 150-225mg	Minimal
Mirtazapine	15-30 Qhs	30-45	Yes 60-90mg	Minimal
Duloxetine	20mg Qam	20-90	Unknown	Minimal
Nefazodone	50-100 BID or TID	300-600	Unknown	Probable
Trazodone	25-50 Qhs	300-600	Unknown	Minimal
Bupropion (IR / SR / XL)	50-75 BID	100-450	Possible	Minimal

Other Options for LLD

- Tricyclic antidepressants
  - Secondary amines: nortriptyline, desipramine
  - Closer monitoring: EKG, BP, drug levels
  - Side effects; lethality in OD
- MAOIs
  - Isocarboxazid, phenelzine, tranylcypromine, selegiline (transdermal patch)
  - Safer cardiac profile
  - Side effects
- Combination strategies
  - Adjunctive: antidepressant + antidepressant
  - Augmentative: antidepressant + (lithium, thyroid, psychostimulant, atypical antipsychotic, anticonvulsant, D3 agonists, other drugs and supplements (fatty 3-omega acids, SAM-E)
  - Limited data in the elderly; no DBRCTs

Brain Stimulation Therapies

- ECT
- VNS
- rTMS
- Others: DBS, MST

Electroconvulsive Therapy in Late-life Depression

- Advantages of ECT
  - Superior efficacy (80 - 90%) in severe depression compared to antidepressant medication (when used as 1st line)
  - good efficacy (50 - 60%) in medication resistant depression
  - more rapid onset of action
  - good safety profile: very low mortality and low morbidity
  - absence of medication side effects

2001 APA Task Force on ECT; Espinoza 2003

Electroconvulsive Therapy in Late-life Depression

- Disadvantages of ECT
  - Repeated general anesthesia
  - Cognitive and memory effects: acute vs. chronic
  - Minor treatment side-effects: headache, muscle ache, falls (especially in the elderly)
  - Acute relapse if a maintenance plan is not instituted
  - Cost of series

2001 APA Task Force on ECT; Espinoza 2003

Electroconvulsive Therapy in Late-life Depression

- Indications
  - Serious, life-threatening mood disorders
  - Treatment failures
  - Chronic depression with significant psychosocial, functional, cognitive impairment
  - Psychotic depression: probably treatment of choice
  - Some dementia syndromes
    - Mood or psychotic features
    - Behavioral dyscontrol
  - Possibly cases of delirium

2001 APA Task Force on ECT; Espinoza 2003

Electroconvulsive Therapy in Late-life Depression

- Treatments can be inpatient or outpatient depending on severity of illness
- If patient shows a positive acute response, a maintenance plan must be instituted:
  - Meds: probably combination (TCA + lithium); others?
  - ECT
  - ECT + meds

2001 APA Task Force on ECT; Sackeim (2001); Espinoza (2003; 2006(abstract)); Kellner et al., in press (2006)

Vagus Nerve Stimulation

- Approved by the FDA in July 2005
  - Adjunctive use only in Treatment-Resistant Depression (TRD)
  - Failed at least 4 adequate antidepressant trials
- Not an acute treatment, may take 6 – 12 months for effect
- Does not replace medications, ECT or psychotherapy
- Oldest patient implanted was 84 years old

- Surgery takes about 1.5 to 2 hours
- Stimulator tested during implantation

- Generators are made of titanium
- Battery can last up to 7-10 years
- Limits on certain types of radiological studies and treatments

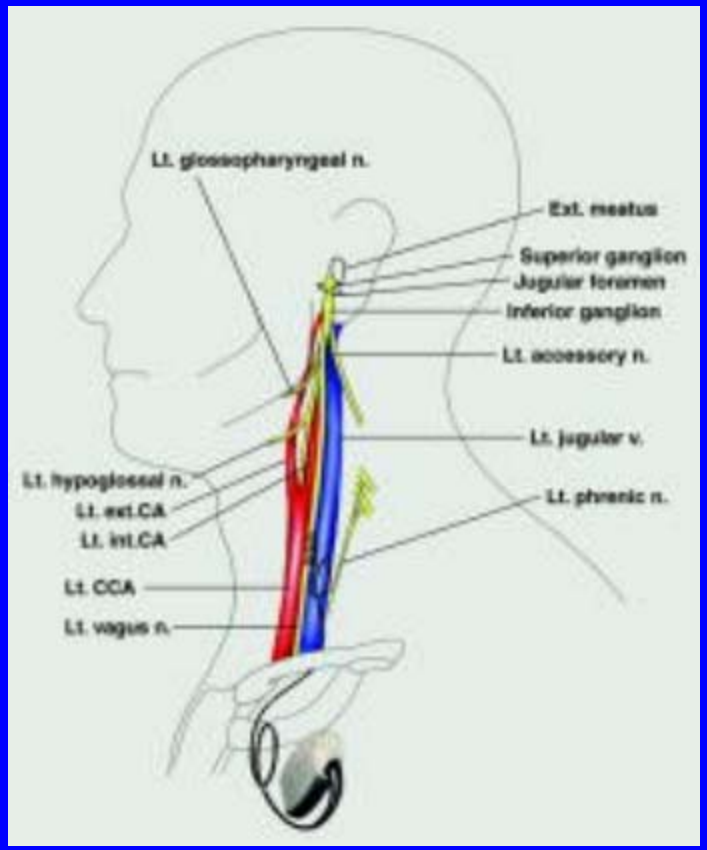


Figure 2. Use of programming wand to adjust generator stimulator parameters. Photo courtesy of Cyberonics, Inc.

Cyberonics, Inc.

Summary

- Depressive disorders are prevalent and diagnosable in older populations.
- Medical comorbidity can increase the challenges of accurate diagnosis.
- Look for psychological symptoms and signs to increase the specificity of diagnosis.
- Tools are available to assist in screening for depression across different settings and patient populations.
- Treatment strategies include psychotherapies, medications or brain stimulation approaches.