AAGP American Association for Geriatric Psychiatry

2022 Geriatric Psychiatry Review Course

This year's Review Couse held in August is now available for on-demaond viewing. Register at the link below to receive access to the recordings from the live event.

On-Demand!

CLICK HERE TO REGISTER

AAGP Members - $300
Non Members - $395

Content Areas

- Normal Aging
- Bipolar Disorder
- Dementias: From Risk Factors to Treatment
- Neurological Assessment and Common Neuropsychiatric Disorders
- Anxiety Disorders in Older Patients
- Psychotic Disorders in the Elderly
- Bereavement, Mood Disorders, and Suicide
- Substance Use Disorders
- Sleep Disorders in the Elderly
- Personality Disorders in the Elderly
- ECT and Neurostimulation Therapies
- Palliative Care
- Ethical and Forensic Issues

The American Board of Psychiatry and Neurology has reviewed the Review in Geriatric Psychiatry Self-Assessment Program and has approved it as part of a comprehensive self-assessment program, which is mandated by the ABMS as a necessary component of Maintenance of Certification.

Certification Exam: October 11-15, 2022
EXAM APPLICATION DEADLINE: March 24, 2022 | LATE DEADLINE: April 14, 2022
Learn more about the MOC exam at www.ABPN.com

AAGP
American Association for Geriatric Psychiatry

Review in Geriatric Psychiatry: Self-Assessment Program and Preparation for Subspecialty Exam

AGENDA

Introduction (10 min)
Adriana Hermida, MD, *Program Chair*

CME Information .....

Normal Aging (30 min) .....
Alicia Romeo, MD

Neurologic Exam & Review of Common Neuropsychiatric Disorders (60 min).....
Laura Marsh, MD

Bipolar Disorder (30 min) .....
Jennifer Gatchel, MD

Break (30 min)

Personality Disorders (30 min) .....
Chevelle Brudey, MD

Psychotic Disorders (30 min) .....
John Kasckow, MD, PhD

Depression, Bereavement and Suicide (60 min) .....
James Ellison, MD

<Continued on next page>

AGENDA

Dementia (60 min).....
Marie DeWitt, MD

Substance Use Disorders (30 min).....
Olivera J. Bogunovic, MD

ECT (30 min) .....
Adriana Hermida, MD

Break (30 min)

Anxiety Disorders (30 min) .....
Prasad Padala, MD

Ethical and Legal (30 min) .....
Lewis Krain, MD

Sleep Disorders (30 min) .....
Nery Diaz, DO

Palliative Care (30 min) ……
Maria I. Lapid, MD

Adjourn

Atrium Health

Geriatric Psychiatry: Normal Aging

Alicia Romeo, MD, DFAPA
Assistant Clinical Professor, Wake Forest School of Medicine

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Disclosures

None

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Overview

- Define normal aging
- Changes in
  - Neuro
  - Vision
  - Auditory
  - Cardiovascular
  - Pulmonary
  - GU
  - GI
  - Musculoskeletal
  - Sleep
  - Endocrine
  - Sexual function

Artist Unknown

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Aging is biological process, not a disease

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What Is Aging?

- A natural, non-pathological process affecting all organisms
  - Characteristic phenotypic features
  - Loss of reproductive capability
  - Decreased physiologic reserves and ability to maintain homeostasis
  - Increased susceptibility to disease
  - Factors influencing mood, perception, physiologic response to medication

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Neurological Changes

- Decrease in
  - Cortical gray matter
  - Neuronal volume
  - Complexity of neuronal connections
  - Neurotransmitter synthesis
- Increase in reaction time
- Spinal cord changes
  - Neuronal loss
  - Demyelination
  - Reduced reflexes
  - Reduced proprioception

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Neurological Changes

- Decreased adrenoceptor responsiveness
  - Increased concentration of circulating catecholamines
- Sensory decreases
  - Nerve endings on extremities
  - Taste buds
  - Sense of smell
  - Slowed nerve conduction

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Vision Changes

- Lens clouding
- Reduced accommodation
- Changes of lens curvature (presbyopia)
- Ciliary muscle weakening
- Decreased tear production
- Decreased pupil size (diminished night vision)
- Loss of cones (reduced color vision)

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Auditory Changes: Presbycusis

- Tympanic membrane thickening
- Structural thickening
- Nerve loss
- High frequency hearing loss
- Increased cerumen
- Reduced acuity
- Reduced noise localization

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Cardiovascular Changes

- **Decrease in**
  - Maximum heart rate
  - Cardiac output (CO = SV x HR)
  - Pacer cells
  - Myocytes
  - Catecholamine responsiveness
  - Volume
    - RBCs, Hematocrit, Hemoglobin
- **Increase in**
  - Fatty tissue accumulation at SA node
  - Thickening of valves, arteries > veins
  - Collagen
  - Systolic blood pressure
  - End-systolic and and end-diastolic volumes
  - Left ventricle size

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Pulmonary Changes

- **Increases in**
  - Residual volume
  - CO_2
  - Mucous
  - Work of breathing
- **Decreases in**
  - Vital & functional lung capacities
  - Chest wall compliance and elasticity
  - Cilial transport
  - Cough function
  - Secretory IgA
  - Maximal minute ventilation
  - Respiratory response to hypoxia (impaired chemoreceptor function)

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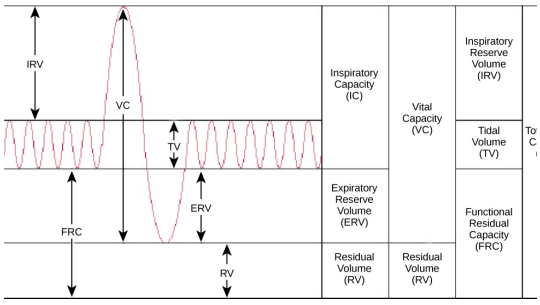
Pulmonary Changes



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Genitourinary Changes

- Decreases in
  - Renal blood flow (10% per decade after 50)
  - GFR/Creatinine clearance
  - Urinary concentration
  - Bladder capacity
  - Bladder wall elasticity
- Increases in
  - Prostate size
- Impaired functioning
  - Maintaining circulating blood volume
  - Maintenance of sodium homeostasis
  - Removing excess acid
  - Adjusting to hypovolemia, hemorrhage, low CO and hypotension

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Urinary Incontinence

- Transient
  - Reversible (delirium, UTI, meds, urethritis, vaginitis)
- Urge "overactive bladder"
  - Most common
  - Abrupt urgency, frequentcy, nocturia
  - Due to detrusor overactivity or local bladder irritation (infection, stone, tumor)
- Stress
  - Failure of sphincter to preserve closure during bladder filling
  - Often due to surgical procedures (anti-incontinence surgery, prostatectomy)
- Overflow
  - Due to detrusor underactivity or outlet obstruction
  - Symptoms include dribbling, weak urinary stream, hesitancy

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Gastrointestinal Changes

- Decreased
  - Saliva/taste buds
  - Gastric cells
  - Gastric acid (release of B12 from food)
  - Pancreatic enzymes (Fe, Ca, folic acid absorption)
  - Gut motility
  - Hepatic blood flow
  - Liver metabolism
- Increased GI contents due to decreased motility and obstruction

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Musculoskeletal Changes

- Decreased
  - Muscle mass
  - Bone density (calcium)
  - Height
- Increased
  - Cartilage erosion

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Drug Distribution and Metabolism

- Decreased albumin
  - Primary plasma protein that binds drugs
  - Increased proportion of free (active) drug
- Hydrophilic Drugs
  - Lower Vd due to increase body water/lower muscle mass
  - Quicker time to steady state
- Lipophilic Drugs
  - Higher Vd due to increase fat stores
  - Slower to steady state, longer elimination time
  - Examples: BDZs, TCAs, trazodone

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Sleep Architecture Changes

- Decreased
  - REM latency
  - Stages 3 and 4 sleep
  - REM amount
  - Sleep efficiency
- Increased
  - Sleep latency
  - Stages 1 and 2 sleep

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Endocrine Changes

- Basal ADH levels increase
  - Hyponatremia
- Decreased aldosterone
  - Dehydration and hyperkalemia
- Cortisol remains same
  - Secretion rate and clearance rate decline
- Norepinephrine increase
  - Increased sympathetic response but decreased receptor sensitivity

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Endocrine Changes

- Vitamin D levels decreased
  - Less sun exposure, dietary intake, absorption
  - Essential for calicium absorption
- PTH increases
  - Osteoclasts resorb bone to compensate for Ca loss
  - Bone density loss
- Thyroid less efficient
  - Increased TSH
  - T4 unchanged but iodination of T4 → T3 decreases

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Sexual Function Changes

Decreased

- Testosterone levels
- Ejaculate volume
- Vaginal lubrication and swelling
- Intensity of organsim

Increased

- Vaginal Pain
- Prostate size
- Stimulation required for orgasm
- Refractory period

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Conclusions


Tina Modotti

- Knowledge of basic principles of normal aging is expected on exam
- Questions often deal with changes related to decrease or increase in physiology
- Understand how age-related normal changes can impact mood and perceptions
- Understand how physiologic changes impact medication sensitivity

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Acknowledgements

Arnaldo Moreno, MD
Associate Professor of Psychiatry
University of California, San Francisco

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The Neurologic Exam in Geriatric Psychiatry, and Common Neuropsychiatric Disorders

AAGP Review Course in Geriatric Psychiatry:
Preparation for Subspecialty Examinations
AAGP Annual Meeting, Atlanta, Georgia
August 27, 2022

Laura Marsh, M.D.
Executive Director, Mental Health Care Line, Michael E. DeBakey VA Medical Center
Professor, Departments of Psychiatry & Neurology, Baylor College of Medicine

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Disclosures

- Consultancies (< 2 years)
  - None
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  - None
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  - Veterans Health Admin
- No discussion of off-label medications or treatments

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OUTLINE:The Neurologic Exam in Geriatric Psychiatry and Common Neuropsychiatric Disorders

I. General Principles

II. Taking a Neurological History

III. Elements of the Neurological Exam

IV. Common Neuropsychiatric Disorders

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General Principles of Assessment

1. The Neurological Hx and Exam are conducted in the context of the Psychiatric Presentation or Chief Complaint

	Psychiatric Assessment	Neurological Assessment
Theme	Mental State	Determine anatomical site of lesion and its underlying pathology
Goal	Develop hypotheses re contributing neurological conditions	Historical details focus the physical neurological exam so it targets specific neurological systems
Exam	• Confirm or refute hypotheses • Establish differential diagnoses	
Plan	• Formulation with appropriate investigations • Clinical management that accounts for overlap and interactions of neurological and psychiatric phenomena and treatments	

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General Principles

2. "The exam starts in the hallway/waiting room"
- Observe, observe, observe

3. Collateral information is essential for dx
- Is the possible neurological condition likely to limit recall of pertinent history?
- Family History, Personality changes, New Onset

4. "The money is in the history…"

Pay attention to timing
- Is there overlap in the temporal course of neuro and psych signs and symptoms?
- Dx clues: time of onset, progression, duration, recovery, frequency
- What neurological disorders present with psychiatric phenomena?

5. Collaboration is key
- Even if don't conduct the exam, appreciate neurological signs and be able to assess neurologist's conclusions

6. Examine systematically

5

Neurological History (Part 1)

- Usual history
  - HPI
  - FHx
  - Personal Hx
    - Incl. Developmental, Military, Legal, Substance Use Hx
  - Medications
  - Medical, Surgical, Injury Hx
  - Handedness
  - Review of Systems (ROS)
  - Psychiatric Hx
  - Premorbid Personality

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Neurological History (Part 2)

- Plus---Neurological review of symptoms
  - ROS provides screen for a prevailing, co-morbid, concurrent, or pre-existing Neurological Disorder?
    - Cognitive functions
    - Changes in consciousness
    - Motor sx
    - Sensory sx, Pain
    - Urogenital symptoms
    - Cranial nerve sx

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Neurological History (Part 3)

- Formulation of a Neurological Diagnosis
  - What are the symptoms of neurologic disease?
  - What are the signs of neurologic disease?
  - Where is the lesion?
  - What is the lesion?
  - Is there a systemic neurologic condition?

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Geriatric Psychiatry
Common Neurological Disorders

- Neurodegenerative disorders
  - Dementias, Movement disorders
- Cerebrovascular Disorders
- Other Movement Disorders
- Epilepsy
- Autonomic Dysfunction
- Peripheral Nerve disorders
  - Neuropathy
- Brain injury (recent or remote)
  - TBI, Substances, Infections, Inflammatory

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The Neurologic Exam

The objective is localization

- CNS vs PNS vs Muscle system
- Diffuse or discrete lesions

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Elements of the Neurologic Exam

- Mental State
- Speech
- Cranial Nerves I-XII
- Motor System
- Reflexes
- Sensation
- Gait

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The Mental State Component

- Appearance/behavior, Talk, Mood, Thought content, Delusions, Hallucinations, Insight, Cognition
- Plus, assess for localizing signs
  - Consciousness (reticular activating system)
    - Glasgow coma scale
      - Eye opening, Verbal and motor responses: nl=15
  - MMSE
    - Orientation, registration and recall, memory, attention/concentration, language (naming, repetition, comprehension, reading, writing), & visuospatial
  - Higher intellectual (cerebral) functions

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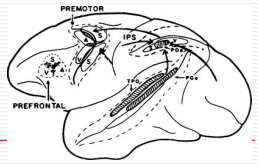
Localizing Higher intellectual (cerebral) functions

- Praxis
  - Formulation and performance of a skilled motor act
  - Pathway for skilled motor tasks: Temporal lobe → Wernicke's area (dominant posterior temporal lobe → Dominant Parietal lobe → Ipsilateral Frontal lobe premotor area → corpus callosum → contralateral motor strip of nondominant hemisphere



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Assessment of Praxis

- Evaluate ability to make gestures (symbolic acts) using buccofacial musculature and limbs, plus imagined and real acts

Actions	Gestures	Imagined	Real
Buccofacial	Kiss the air Repeat "pa"	Pretend to suck on a straw Pretend to blow out a match	Drink water through a straw Blow out a match
Limbs	Salute Stop traffic	Pretend to write Pretend to use a comb Pretend to fold a letter	Write on a piece of paper Comb the hair Use tools

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Apraxias

- Best localizing sign on Mental State Exam
- Ideomotor Apraxia

  Inability to convert an idea into action (intentional acts)
  - Dominant frontal or parietal lesion disconnects cognitive/language from motor regions
  - When pretend to use object, hands are used as if actual objects (e.g., brush teeth with finger vs pretend toothbrush)
  - Lesions
    - Often left CVA with aphasia, esp non-fluent
    - Corticobasal ganglionic degeneration (CBGD)- alien limb
  - Balint's syndrome –bilateral parietal damage
    - oculomotor apraxia
    - optic ataxia
    - visual simultagnosia

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Apraxias (Cont.)

- Ideational (conceptual)

Inability to plan & perform voluntary motor acts that require tools & sequential steps

- Inability to perceive an object's purpose and to plan and execute the correct function
  - e.g., Fold a letter and place in the envelope, then mailbox
- Lesions
  - Frontal lobe injuries, diffuse cerebral disease, dominant hemisphere
- Disorders
  - CVAs, TBI, Alzheimer's

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Apraxias (cont.)

- Constructional
  - Disruption in visuo-spatial functioning
  - Inability to draw or copy shapes, construct figures or patterns
  - Non-dominant parietal or frontal lesions CVAs, AD
- Other apraxia syndromes
  - Gait Loss of ability to alternate leg movements and shift weight to forward foot when walking (Normal pressure hydrocephalus)
  - Dressing Inability to clothe left-sided limbs (non-dominant parietal lesions; left neglect syndromes)

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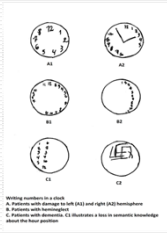

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Agnosias

- Non-recognition of relevant sensory stimulus in absence of other cues and in context of intact sensation
- Lesions involve sensory association areas
- Many types of agnosias
  - 5 senses
  - Form
  - Semantic
  - Time
  - Faces (prosopagnosia)
  - Pain
  - Visual motion
  - Text (alexia)

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Agnosias (cont.)

- Visual Agnosia
  - Dominant inferior parietal lobe-occipital lobe lesions
  - Gerstmann Syndrome (Angular Gyrus Syndrome)
    - Finger agnosia (inability to distinguish fingers on hand)
    - Dysgraphia/agraphia
    - Dyscalculia/acalculia
    - Left-right disorientation
    - Lesion at angular & supramarginal gyri (temp-parietal jxn)
    - ± aphasia
  - Alexia without agraphia
    - Pure word blindness, agnosic alexia
    - Can spell & write but cannot read
    - Left Posterior cbl artery CVA (Splenium, left visual ctx)

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Agnosias (cont.)

- Auditory Agnosia
  - Inability to recognize a sound without seeing it
  - Dominant temporal lobe
- Tactile (Somatosensory) agnosia (Astereognosis)
  - Inability to recognize an object by touch alone (contralateral parietal lobe)
- Anosognosia (usu part of Hemi-attention, Hemineglect):
  - Deficit of self-awareness (not same as lack of insight)
  - Usu Right-sided parietal, FTP lesions (CVA, TBI, others)
  - ± asomatognosia—denial of ownership & control of limbs
    - ~ Alien limb Syndrome variants (CVAs, CBGD, AD, CJD, tumors, post-surgical)

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The Neurologic Exam

- Mental State
- **Speech**
- Cranial Nerves I-XII
- Motor System
- Reflexes
- Sensation
- Gait

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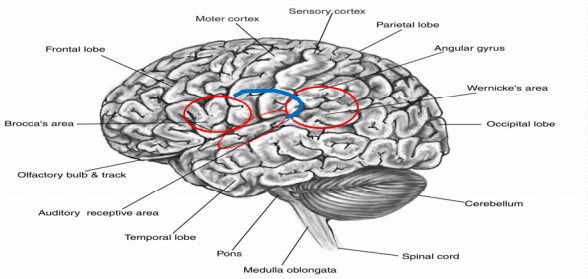
Neuroanatomy of Speech



Primary auditory cortex (Heschl's Gyrus) to Dominant Wernicke's (temp lobe/comprehension) via arcuate fasciculus to Broca's area (Speech expression) to precentral gyrus (controls speech musculature) to UMN VII, IX, X, XII.

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Elements of Speech

- Phonation: production of sound
  - Dysphonia: deficit of speech volume
- Articulation: manipulation of sound to produce single sounds
  - Dysarthria: impaired articulation w/ intact language functions
- Production of language: organization of sounds into words and sentences by speech centers (Broca's & Wernicke's areas)
  - Dysphasia: Abnl comprehension or production of speech

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Assessment of Speech

- Phonation:
  - volume, cough
- Articulation:
  - Repeat difficult phrases, "Methodist Episcopalian"
  - p, t, k sounds
- Spontaneous speech
  - Fluency, ability to produce phrases ≥ 5 words
- Repetition
  - Simple to complex phrases
- Naming & Word Finding
  - Familiar and unfamiliar objects

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Interpretation of Speech Deficits

- Dysphonia
  - Hypophonia w/ slow cough onset---vocal cord paralysis
- Dysarthria
  - UMN lesions—pseudobulbar palsy
    - Weakness of muscle groups
      - Speech slow, slurred, monotonous, high-pitched
      - Limited protrusion of tongue
      - Exaggerated jaw jerk
      - Emotional lability
  - LMN lesions—bulbar palsy
    - Weak individual muscles or groups; lesion location determines pattern
      - Indistinct, slow speech
      - Palatal paralysis
      - Tongue with wasting and fasciculations

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Interpretation of Speech Deficits

- Dysarthria (others)
  - Cerebellar lesions
    - Ataxic dysarthria—slow, slurred, scanning speech
  - Myopathies, neuromuscular junction disorders
    - Similar to bulbar palsy (indistinct, slow speech)
    - Myasthenia gravis---fatigability

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Interpretation of Speech Deficits

- Dysphasia
  - Various classifications
    - Expressive (motor) (Broca) vs Receptive (sensory) (Wernicke)
    - Fluent vs non-fluent

Type	Comprehension	Fluency	Repetition	Naming
Broca's	Good	Non-Fluent	Abnl	Abnl
Wernicke's	Abnl	Fluent	Abnl	Abnl
Conduction	Good	Fluent	Abnl	Abnl
Global	Abnl	Non-Fluent	Abnl	Abnl
Transcortical Sensory	Abnl	Fluent	Good	Abnl
Transcortical Motor	Good	Non-Fluent	Good	Abnl
Nominal (anomic)	Good	Fluent	Good	Abnl

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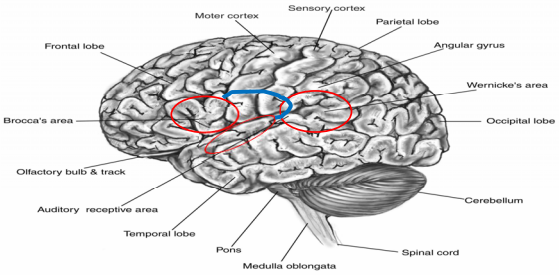
Neuroanatomy of Speech



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Dysphasias

Type	Lesion	Associated Features
Broca's	MCA, Frontal lobe	Right Hemiparesis (Arm,face>leg) Dysarthria, R Visual Field cut, Hemisensory loss, Buccal apraxia
Wernicke's	Temp-parietal CVAs, Alz Ds	Paraphasias; no weakness: Incr R DTRs; R sensory loss and field cut
Conduction	Arcuate Fasciculus Parietal/post temp lobe	Poor repetition and naming; minimal physical deficits
Transcortical Sensory	Spared AF; Perisylvian Watershed area of Temp lobe	Fluent Speech intact repetition, echolalia
Transcortical Motor	Spared AF; Perisylvian Watershed area of Ant Sup Frontal lobe	Nonfluent speech, Preserved repetition, comprehension

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Disorders related to Aphasia

- Often accompanied by Alexia and Agraphia
  - Alexia without agraphia
    - Can write and comprehend, but can't read
    - Transcribe dictation
    - Right Homonymous Hemianopsia
    - Lesion in Dominant occipital lobe, adj corpus callosum (Left visual cortex and splenium)
  - Gerstmann's Syndrome
    - Agraphia, alcalculia, finger agnosia, left/right confusion
    - Angular gyrus of Dominant parietal lobe
  - Alzheimer's disease/dementias
    - 4 A's: Amnesia, Aphasia, Agnosia, Apraxia (Also 5th-Affect)

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The Neurologic Exam

- Mental State
- Speech
- **Cranial Nerves I-XII**
- Motor System
- Reflexes
- Sensation
- Gait

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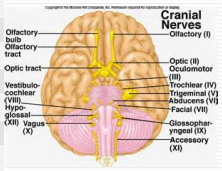
Cranial Nerves

#	Nerve	Mnemonic
I	Olfactory	On
II	Optic	Old
III	Oculomotor	Olympus'
IV	Trochlear	Towering
V	Trigeminal	Top
VI	Abducens	A
VII	Facial	Finn
VIII	Auditory/Vestibulocochlear	And
IX	Glossopharyngeal	German
X	Vagus	Viewed
XI	Spinal/Accessory	Some
XII	Hypoglossal	Hops



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Cranial Nerves

#	Nerve	Function
I	Olfactory	Smell
II	Optic	Visual Acuity, Fields, fundi
III	Oculomotor	With XI Pupillary response extraocular motion
IV	Trochlear	
V	Trigeminal	Corneal Reflex Facial sensation
VI	Abducens	With III,IV
VII	Facial	Facial muscles, taste
VIII	Auditory/Vestibulocochlear	Hearing
IX	Glossopharyngeal	IX-XI Articulation, palate, gag
X	Vagus	
XI	Spinal	
XII	Hypoglossal	Tongue Movement

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Visual Exam– Key Points

- Visual Acuity—lesions between cornea and visual cortex
- Visual Fields: Confrontation Technique
- Pupillary Responses:
  - Light response – Direct and Consensual constriction
  - Accommodation reflex – Convergence and constriction

Miotic Pupils	Light Reflex	Accommodation	Other features
Senile	Normal	Normal	Bilateral Small
Horner's Sd	Normal	Normal	Ptsosis, Enophthalmos Anhydrosis (SNS)
Argyll-Robertson	Absent	Normal	Irregular pupils Usu bilateral
Pontine lesion	Absent	Absent	CVA (Bil pinpoints-intrapontine lesion)
Miotics: Opiates PNS,cholinergics	Absent	Absent	Diff Dx for Pontine les.

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Visual Exam– Key Points (cont.)

Mydriasis	Light Reflex	Accommodation	Other features
III Lesion	Absent	Absent	Ptosis, eye 'down & out'
Mid-brain lesion	Absent	Absent	Bilat semi-dilated Impaired vertical gaze
Holmes-Adie Pupil	Slow	Slow	Absent ankle jerks Impaired sweating; young females
Mydriatic drugs: atropine, adrenaline	Absent	Absent	
Blown Pupil	Unilateral	Fixed	Incr Intracranial pressure
Anisocoria	Normal	Normal	Nl in 20% population

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Conjugate Gaze (Cr N. III, IV, VI)

- Saccadic (voluntary, frontal)
- Pursuit (Parieto-occipital)
- Positional: (vestibular and cerebellar nuclei

Lesion site	Component	Impact/Conditions		
Nuclear	Nucleus of Cr N II,IV, VI	Brainstem lesions: transtentorial herniation—III and brainstem—coma, dil pupil Diplopia + contralateral Hemiparesis/ataxia		
Internuclear	Medial Longitudinal Fasciculus	Internuc ophthalmoplegia (Multiple Sclerosis)		
Nerve	Midbrain: Cr N III, IV, Pons: Cr. N. VI	IV-Superior Oblique (no dwnd gaze on adduction; head tilt)	VI-Lateral rectus (diplopia)	III-all others; PNS, lev palpebrae Down & out Diplopia
Supranuclear	Cortex	Preserved conjugate gaze		

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Trigeminal Nerve (Cr N V)

- Sensory (Midbrain to medulla)
  - Facial sensation (3 sensory divisions)
- Motor (pons) --Innervate jaw muscles (Jaw jerk)
  - Hyperactive –UMN lesion vs Hypoactive –LMN (Cr N. Lesion)
- Corneal Reflex (V & VII)

Facial Nerve (Cr N VII)

- Sensory—taste (ant 2/3 of tongue)
- Motor—innervate facial muscles (of expression)
  - Upper face-crossed innervation
  - Lower face: uncrossed, unilateral innervation
    - Paresis suggests LMN (peripheral) lesion/Facial N. (Bell's) Palsy
      - Ipsi upper and lower face paresis
    - Versus UMN Lesion (R MCA thrombosis: paresis L lwr face,arm

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Acoustic (Cr N VII)

- Cochlear Division-hearing
  - Auditory impulses to middle/inner ear to Superior Temporal Gyrus bilaterally
  - Hearing sensitivity tested with whispered sound
  - Rinne's test
    - Compares bone conduction with air conduction
    - Tuning fork on mastoid bone then by ear (nl is Air > bone)
  - Weber's test
    - Fork on vertex/midline (nl is = sound bilaterally)
      - Conduction deafness: sound louder in affected ear
      - Nerve deafness: sound louder in normal ear.
- Vestibular Division – balance, t-mits labyrinthine impulses
  - Gait—pt walks toward vestibular lesion
  - Nystagmus

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Glossopharyngeal and Vagus (IX, X)

- Glossopharyngeal
  - Post 1/3 of toungue, pharnyx, middle ear
  - Motor innerv. to pharynx, middle ear
  - Mtr innerv. To stylopharygeus m. and ANS to parotid
- Vagus
  - Sensation to tympanic membrane, ext aud canal, ext ear
  - Motor innervation to palatal m, larynx, pharynx
- Assessment
  - Swallowing (coughing, spluttering)
  - Cough
  - Speech (Dysarthria and dysphonia)
  - Palatal movements
    - Say 'AAH"; vagal innerv to palate, uvula deviates contralaterally
  - Gag—intact in UMN (pseudobulbar), affected in LMN (bulbar palsy)

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Accessory Nerve (XI)

- Origins in Medulla, plus C2-C4
  - Innervates (Ipsilateral) Sternocleidomastoid and (contralateral) trapezius
- Assessment
  - Neck and shoulder for wasting, fasciculations
  - Strength: SCM-Resist neck flexion, turn head against resistance (L SCM turns head to R), TPZ-shoulder shrug
    - Weak Ipsi SCM, TPZ—LMN XI lesion; Ipsi/Contra-UMN lesion

40

Hypoglossal Nerve (Cr. XII)

- Motor supply to the tongue
- Affects
  - Swallowing (coughing, spluttering)
  - Cough
  - Speech (Dysarthria and dysphonia)
  - Palatal movements
  - Say 'AAH"; vagal innerv to palate, uvula deviates contralaterally
  - Gag—intact in UMN (pseudobulbar), affected in LMN (bulbar palsy)

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Hypoglossal Nerve (XII)

- Assessment
  - Inspect Tongue on floor of mouth
    - Wasting, fasciculations, involuntary movement
  - Protrude Tongue & move side to side
    - Deviation

Observation	Protrusion	Finding
Unilateral Wasting + Fasciculations	Deviates to side of wasting	Ipsi Unil LMN lesion (tongue points to the lesion)
Bilateral Wasting + Fasciculations	No Deviation	Bilat LMN
Normal Bulk, No Fasciculations	Slight deviation	Unilat UMN Contralat to side of deviation
Contracted	Limited protrusion	Bilat UMN lesion

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Bulbar vs Pseudobulbar Palsy)

Observation	Bulbar	Pseudobulbar
Location	Cranial N. IX-XII (medulla)	Frontal lobe damage UMN corticobulbar tracts
Also involves	Tracts: ↓ Corticospinal, ↑ sensory, SNS	Dementia, aphasia (Left hemisphere)
Dysarthria	Yes	Yes (explosive cadence)
Dysphagia	Yes	Yes
Palatal movement	Voluntary-No Reflex-No	Voluntary-No Reflex-Yes
Respiratory Imprt	Yes	No
Jaw Jerk	Hypoactive	Hyperactive
Emotional lability	No	Yes
Intellectual Imprt	No	Yes
Conditions	CVA-**Lat Med Infxt (Wallenberg Sd),** ALS, Polio, GB, MG, Meningitis, tumor	Alz Ds, MS, Multiple CVAs, Cerebral palsy, TBI, ALS

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The Neurologic Exam

- ☐ Mental State
- ☐ Speech
- ☐ Cranial Nerves I-XII
- ☐ **Motor System**
- ☐ Reflexes
- ☐ Sensation
- ☐ Gait

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The Motor Exam

Task	Elements		
Inspect	Posture	M. Wasting and Fasciculations	Involuntary Mvts
Tone:Resistance with passive mvt of limbs	Hypo/ Hypertonia	Clonus	Spasticity
Power: ability to contract agnst gravity	Compare side to side Scale: 0-5	UMN vs LMN	
Reflexes	Tendon	Cutaneous	
Co-ordination & Gait	Cerebellar signs: F-N; H-Shin, repetitive mvts; ataxia, dysarthria, eye signs	Ataxia	Hypo/Hyper active movements, gait patterns

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Tone Abnormalities

- **Lead Pipe Rigidity**
  - Increased resistance throughout ROM
- **Cogwheel Rigidity**
  - Increased tone intermittent and ratchety (superimposed tremor)
- **Spasticity**
  - Increased resistance throughout ROM after a sudden release
- **Gegenhalten (Paratonia)**
  - Patient opposes limb movements (Bilat frontal damage)
- **Myotonia**
  - Delay in M. relaxation after contraction (M. Dystrophy)
- **Dystonia**
  - Contraction of agonist and antagonist m., sustained limb postures.

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Limb Strength

- **UMN**
  - Weakness m. Groups in pyramidal distribution
    - Ext/Supinator Upper; Flexor/Abd Lower
  - Hemiparesis: contralateral hemisphere; incr DTRs, Extensor Plantar
- **LMN**
  - Wasting, fasciculations, hypotonia, decr DTRs, Flexor plantar
  - Weakness Indiv M. or groups based on side of lesion
    - Spinal cord-paraparesis
- **NMJ**
  - No wasting, nl tone, fatigues, bilat, proximal limb girdle weakness, nl DTRs, flexor plantar
- **Myopathy**
  - Wasting, decreased tone, Bilat, pxml limb girdle, decr tone, flexor plantar

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Upper vs Lower Motor Neuron Lesions

UMN	LMN
CNS	PNS
Cortical Neurons to Anterior Horn cells of Spinal cord Cortex, brain stem, spinal cord Pyramidal tracts Corticospinal and Corticobulbar tracts	Anterior Horn cells and beyond
UMN Injury: Paresis Muscle spasticity with no atrophy DTRs hyperactive Babinski signs Sensory loss patterns, eg hemisensory	LMN Injury: Paresis Muscle flaccidity and atrophy DTRs hypoactive No Babinski signs Sensory loss: stocking glove
Pseudobulbar palsy Damage to UMN corticobulbar tract UMN innervates brainstem motor nuclei and head and neck muscles	Bulbar (Brain Stem) palsy Cranial nerve IX-XII injury (medulla plus bit of pons) (also descending corticospinal (medial), ascending sensory, and SNS) Innervate soft palate, pharynx, larynx, tongue affects speaking and swallowing

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The Neurologic Exam

- Mental State
- Speech
- Cranial Nerves I-XII
- Motor System
- **Reflexes**
- Sensation
- Gait

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Reflexes

- Deep Tendon Reflexes
  - Hyperactive: corticospinal tracts
  - Hypoactive: peripheral nerve injury
- Pathological Reflexes
  - Babinski sign: brain or spinal cord damage
  - Frontal release signs
    - Grasp, snout, root, palmar-mental, glabellar etc.

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The Neurologic Exam

- Mental State
- Speech
- Cranial Nerves I-XII
- Motor System
- Reflexes
- **Sensation**
- Gait

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Sensation

- Elements
  - Light Touch
  - Pain
  - Vibration
  - Proprioception/Position
  - Temperature
  - Stereognosis
- Spinal Cord Ascending Sensory Pathways
  - Posterior Columns—Position & Vibration to thalamus
  - Lateral Spinothalamic tracts—Temp & Pain to thalamus
  - Anterior Spinothalamic tracts—Lt touch to thalamus
  - Spinocerebellar tracts—Joint position and mvt to cbllm

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Sensation

- Site of lesion determines pattern
  - Peripheral nerve
    - Sensory loss in glove and stocking distribution
  - Single nerve
    - Sensory loss in cutaneous distribution of nerve
  - Root
    - Sensory loss in distribution of root, several roots
  - Spinal Cord (see next slide)
  - Brain Stem
    - Loss of pain and Temp on Ipsi face, contralat body
  - Thalamic
    - Hemisensory loss of all modalities
  - Parietal lobe
    - Sensations are recognized but localization is poor (sensory inattention, astereognosis, loss of 2-point discrimination)

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Sensation

- Spinal Cord Lesions
  - Dorsal (Posterior) Column Lesion
    - Loss proprioception & Vibration with preserved pain, lt touch, temp
  - Anterior spinal Syndrome
    - Loss of Pain, Temp, Lt touch with preserved proprioception and vibration
  - Hemisection: Brown-Sequard Sd
    - Ipsi loss proprioc/vibration , CL loss pain and temp below lesion
      - Plus Ipsi paralysis (corticospinal damage)
  - Transection: loss all modalities below lesion
  - Central SC lesion: Dissociated sensory loss
    - Loss pain & temp at level of lesion (where spThal fibers cross)

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The Neurologic Exam

- Mental State
- Speech
- Cranial Nerves I-XII
- Motor System
- Reflexes
- Sensation
- **Gait**

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Gait - Assessment

- Walk barefoot, then Heel-to-toe
- Elements
  - Posture
  - Separation between feet
  - Size of each step (stride)
  - Height that knees are lifted
  - Manner that legs are swung
  - Movements of pelvis and shoulders
  - Extent of arm swing
  - Overall Symmetry of gait

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Gait - Assessment

- **Romberg Test** (Balance & Coordination)
  - Feet together
  - Eyes open: observe for steadiness
    - Severe unsteadiness: cbllr or vestibular Sd
  - Eyes closed: observe for steadiness
    - + Romberg: Steady with eyes open, not closed (loss of propioception)
    - Swaying back and forth: Cerebellar syndrome
    - Walk barefoot, then Heel-to-toe

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Patterns of Gait abnormalities

- **Parkinsonian**
  - Stooped posture, impaired initiation, cessation, turning; festination; decr arm swing
- **Ataxic (Cerebellar)**
  - Wide stance, uncoordinated (ataxic), unsteady, veers to lesion, (Heel-toe may elicit)
- **Apraxic (usu frontal lesions, NPH)**
  - Imprd initiation, Wide stance, small steps

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Patterns of Gait abnormalities

- **Hemiparetic (CVA)**
  - Flexed Upper limbs, Stiff, extended lower limbs with circumduction (so foot clears floor)
- **Spastic**
  - Adducted Legs at hips, may crossover when walking, slow, stiff
- **Steppage**
  - Foot drop (ankle does not dorsiflex); knees lifted high to clear foot from floor; foot slaps the ground when leg lowered

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Patterns of Gait abnormalities (cont)

- **Myopathic**
  - Proximal m. weakness of lower limb girdle (weak gluteals); waddling gait with weight placed alternately on each leg and hips and sides of trunk tilting upward to wt-bearing side, where hip sways out & opposite pelvis and trunk drop
- **Sensory ataxia**
  - Impaired proprioception; wide stance; unsteady; feet lifted high and stamp the floor; + Romberg
- **Antalgic**
  - Lower limb or pelvic pain; bear weight on unaffected side
- **Functional**
  - Astasia-abasia: inability to stand or walk without other abnl
  - Cautious gait--elderly

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Cerebellar signs

- **Ataxic Gait**
- **Nystagmus**
  - Fast phase points to lesion
- **Finger-nose, heel-shin tests**
  - Intention tremor, Dysmetria (Inaccuracy)
- **Repetitive Movements**
  - Dysdiadochokinesia (Irreg, lose pattern, uneven force)
- **Other signs**
  - Truncal Ataxia: Fall to side when lying to sitting
  - Ataxic dysarthria: slow, slurred, scanning speech, variable force of words, spoken in component syllables
  - Eye signs: Slow pursuits with 'catch-up' saccades
  - Pendular tendon reflexes: non-brisk, less damping of mvt

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Classification of Movement abnormalities

- **Hypoactive**
  - Akinesia
  - Bradykinesia
  - Rigidity (akinetic-rigid syndromes)
- **Hyperactive**
  - Tremor—resting, postural (action), intention
  - Dyskinesias - Chorea, athetosis
  - Ballism
  - Dystonia
  - Tics
  - Myoclonus
  - Akathisia

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Movement Disorder Screening Exam

Parkinsonism				
	Right		Left	
Tremors	UE	LE	UE	LE
Rest				
Postural				
Action				
Wing-beating				
Facial/Jaw				
Head				
Bradykinesia				
Arms				
Legs				
Face				
Finger tap				
Leg Lift				
Rigidity				

Other Hyperkinetic Movements	
Oral-buccal Lingual	
Other Stereotypies	
Akathisia (whole body)	
Restless Legs (Subjective)	
Chorea	
Dystonia	
Tics	

Gait		**Eye Movements**	
Parkinsonism		EOM Range	
Base		Saccades	
Tandem Stance		Smoothness	
Balance		Speed	

Comments:

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Other Common Neurological Disorders in Geriatric Psychiatry

- Parkinson's and related Disorders
- Epilepsy

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Movement disorders

- **Parkinson's Disease**
  - Tremor, Rigidity, Bradykinesia (Parkinsonism)
  - Asymmetric, starts unilaterally
  - Progressive, later gait dysfunction
  - Responsive to dopamine
  - Many non-motor features (psych, autonomic, sleep, olfactory
- **Parkinsonism**
  - Drug-induced
  - Parkinson-Plus Syndromes
    - Poor l-dopa response

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PD-related (PD-Plus) Disorders

- **Multiple System Atrophy (MSA)**
  - Parkinsonism, Ataxia, Autonomic Failure
  - Synucleinopathy with Glial Cytoplasmic Inclusions
- **Striatonigral Degeneration (MSA-P)**
  - Parkinsonism, Usu no tremor
- **Olivopontocerebellar Degeneration (MSA-C)**
  - Cerebellar ataxia, akinetic rigid sd
- **Shy-Drager Syndrome**
  - Parkinsonism
  - Autonomic neuropathy
    - Orthostasis, Constipation, Urinary retention and incontinence, impotence, loss of sweating

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PD-related (PD-Plus) Disorders

- **Progressive Supranuclear Palsy (PSP)**
  - Tauopathy
    - Pallidum, STN, SN, Pons
    - NFTs, neuropil threads, fibrillary gliosis
    - Variable neuronal loss and gliosis
    - No amyloid deposits or plaques
  - Clinical Features
    - Parkinsonism with Akinesia and rigidity
    - Early loss of postural reflexes
    - Pseudobulbar Palsy
    - Supranuclear ophthalmoplegia
    - Initial effect on down-gaze

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PD-related (PD-Plus) Disorders

- **Corticobasal Degeneration (CBGD)**
  - Pathology
    - Ballooning of neurons, gliosis, tauopathy
  - Deficits:Cortical Processing & Basal Ganglia Fxn
    - Asymmetric Signs
    - Parkinsonism (tremor, bradykinesia, rigidity, imbalance)
    - Limb dystonia
    - Apraxia (Ideomotor and Limb-kinetic)
    - Aphasia
    - Stimulus sensitive myoclonus
    - Cortical sensory loss
    - Alien limb phenomenon

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PD-related (PD-Plus) Disorders

- **Wilson's Disease**
  - Hepatolenticular degeneration
  - Abnormal Cu metabolism 2° autosomal recessive Chr. 13 gene
  - Akinetic-rigid sd, cbllr ataxia, dystonia
  - Dysarthria, dysphagia
  - Psychiatric sx, personality/behavioral dos

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PD and Cognitive Impairment

- **PD-Mild Cognitive Impairment**
  - ~19% - 39% Prevalence, include 19%-36% incident PD
  - Present in up to 1/3 at onset of PD-motor syndrome
  - Course: Variable course, usually insidious decline
  - Often subtly disabling
  - Cognitive Features
    - Fronto-striatal dysexecutive syndrome
    - Learning/encoding + visuospatial + verbal fluency deficits

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PD and Cognitive Impairment

- **PD-Dementia**
  - ~30% point prevalence, up to 80% Cumulative prevalence
  - Onset later in course of PD, ~10-15 years
  - Neuropathology
    - SN Lewy bodies, Nigrostriatal degeneration, limbic areas, AD pathology

  - Impairment ≥2 cognitive domains
    - Attention, executive functions, visuospatial functions
      - Memory Deficits involve retrieval
      - vs Alzheimer disease: Poor encoding/rapid forgetting
  - Behavioral sx support diagnosis
    - Apathy, depressed or anxious mood, hallucinations, delusions, daytime sleepiness, ICDs or Repetitive behaviors

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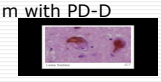
Dementia with Lewy Bodies

- 3rd most common dementia, Usual onset after age 60 years
- Neuropathologically: May be on continuum with PD-D
- Dementia at the onset



  - Prominent Attention deficits
  - Executive and visuospatial deficits
  - Later memory dysfunction

Plus:

- Spontaneous parkinsonism, onset ≤ 1 year of cognitive deficits
- Visual hallucinations—often severe, threatening
  - Delusions—Often complex, bizarre
- Fluctuating cognition
  - Alert, coherent, oriented periods alternate with periods when confused and unresponsive to questions, usually over a period of days to weeks but sometimes during the same interview or day
  - Stare into space for long periods
- Excessive daytime drowsiness
- REM Sleep Behavior Disorder
- Autonomic Dysfunction

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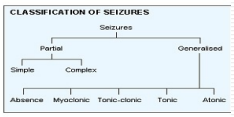
Seizures and Epilepsy

- Seizures
  - Intermittent, repetitive, stereotyped, synchronized electrical discharges from brain neurons
  - Manifestations of seizure (semiology) determined by origin, spread, and duration
    - Phases: Prodrome, Aura, Ictus, Postictal, Interictal
    - Anything brain or body can do can also occur during a seizure
      - Motor, sensory, autonomic, change in awareness or consciousness, or psychic phenomena



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Seizures and Epilepsy

- Epilepsy
  - Recurring tendency to have seizures
  - Prevalence 0.5-1%
  - Incidence greatest in children, and after age 55 years
    - 300,000 Seniors, most rapidly growing population with epilepsy
  - Types based on ± change in consciousness
    - Generalized
    - Partial/focal (Simple or Complex)
    - Partial with Secondary Generalization
  - Causes: Genetic, Congenital and Perinatal factors, Trauma, **Cerebrovascular ds**, Tumor, Head injuries, Infections, Inflammatory dos, Metabolic dos, **Degenerative dos (AD)**, Drugs/Toxins

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The Neurological Exam in Geriatric Psychiatry

- Critical for differential diagnosis, treatment planning, care coordination
- Much of Neurological Hx and Exam can be conducted during routine psychiatric interview and Mental Status Exam
- Neurological Differential Dx requires systematic consideration and application in clinical practice

75

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Bipolar Disorders in Older Adults

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Slides adapted from presentations by Drs. Brent P. Forester and Martha Sajatovic

1

Bipolar Disorders in Older Adults

Disclosures

- Jennifer R. Gatchel MD PhD
- --No relevant financial relationships to disclose
- Will discuss off-label medication use

2

Discussion of off-label use of therapies:

- This talk includes off-label use of antipsychotic, anticonvulsant, and antidepressant medications for bipolar disorder.

3

Outline

- Epidemiology
- Clinical Assessment
- Approach to pharmacological management
  - Bipolar mania, depression and maintenance
- Psychotherapy interventions
- Key treatment principles

4

Older Age Bipolar Disorder (OABD) is Common in Clinical Populations

- OABD: patients greater than 60 years of age with bipolar disorder
  - Dividing line between OABD and adult-age BD:≥60 years of age appears to be the consensual cut-off (the taskforce of the International Society for Bipolar Disorder (ISBD) suggests a cut-off of ≥50 years, given the reduced life expectancy in BD)
- 0.5-1% of population greater than age 50; 0.25% greater than age 65
  - Lower prevalence relative to younger adults (1.4%)
- In Community: 0.1-1.0% of elderly
- In Clinical populations:
  - 6% of geriatric outpatient visits
  - 8-10% of geriatric inpatient admissions
  - 3% of nursing home residents
  - 17% of geriatric patients presenting to psychiatric emergency department
- 10% of all patients with bipolar disorder present with first episode after the age of 50 (often associated with vascular changes or other brain disorders)
- Currently, of all BD patients, 25% are older than 60 years of age.
- By 2030, greater than 50% of all bipolar disease patients will be above 60.

Depp CA, et al. *Bipolar Disord.* 2004;6(5):343-367.
Depp CA, et al. *Am J Geriatr Psychiatry.* 2005;13(4):290-298.
Yassa R, et al. *Psychiatr Clin North Am.* 1988;11(1):117-131.
Jeste DV et al. *Archives of General Psychiatry*. 1999;56(9):848-53.
Dols A, Beekman A. *Psychiatr Clin N Am.* 2018; 41: 95-110.

5

Understanding Aging in Bipolar Disorder by Integrating Archival Clinical Research Datasets

- Integrated OABD database using the US National Institute of Mental Health Data Archive (NDA)
  - Combine data from three BD studies in the US with overlapping data elements
  - Investigate research questions related to aims of the original studies
  - Take an important first step toward combining existing datasets relevant to aging and BD.
- Despite heterogeneity, "integrated datasets are an opportunity to better understand how aging may impact the presentation and evolution of chronic mental health disorders across the lifespan."

Eyler LT. et al. *Am J Geriatr Psychiatry.* 2019; 27(10); 1122-1134.

6

GAGE-BD

Bipolar Disord. 2019 Nov;21(7):642-649. doi: 10.1111/bdi.12795. Epub 2019 May 30.

The Global Aging & Geriatric Experiments in Bipolar Disorder Database (GAGE-BD) project: Understanding older-age bipolar disorder by combining multiple datasets.

Sajatovic M[1], Eyler LT[2,3], Rej S[4], Almeida OP[5], Blumberg HP[6], Forester BP[7,8], Forlenza OV[9], Gildengers A[10], Mulsant BH[11], Strejilevich S[12], Tsai S[13], Vieta E[14], Young RC[15], Dols A[16].

- Lack of research about aging process in bipolar disorder Methods and start-up activities of first-ever initiative to create an integrated OABD-focused database.
  - 14 international investigators; broad geographic distribution; data on over 1,000 OABD.
- "The GAGE-BD project aims to advance understanding of associations between age, BD symptoms, medical burden, cognition and functioning across the life span and set the stage for future prospective research that can advance the understanding of OABD."

Sajatovic M. et al. *Bipolar Disord.* 2019;21(7):642-649

7

GAGE-BD

Bipolar Disord. 2022 Mar;24(2):195-206. doi: 10.1111/bdi.13119. Epub 2021 Aug 12.

Bipolar symptoms, somatic burden, and functioning in older-age bipolar disorder: Analyses from the Global Aging & Geriatric Experiments in Bipolar Disorder Database project

Martha Sajatovic [1], Annemiek Dols [2], Soham Rej [3], Osvaldo P Almeida [4], Alexandra J M Beunders [2], Hilary P Blumberg [5], Farren B S Briggs [6], Brent P Forester [7,8], Regan E Patrick [7], Orestes V Forlenza [9], Ariel Gildengers [10], Esther Jimenez [11], Eduard Vieta [11], Benoit Mulsant [12], Sigfried Schouws [13], Nadine Paans [14], Sergio Strejilevich [15], Ashley Sutherland [16], Shangying Tsai [17], Betsy Wilson [18], Lisa T Eyler [16,19]

- This first-ever analysis investigated associations among age, BD symptoms, comorbidity, and functioning.
- Harmonized, baseline, cross-sectional data from 19 international studies (N = 1377). Standardized measures included the Young Mania Rating Scale (YMRS), Hamilton Depression Rating Scale (HAM-D), Montgomery-Asberg Depression Rating Scale (MADRS), and Global Assessment of Functioning (GAF).

Sajatovic M. et al. *Bipolar Disord.* 2022 24(2):195-206.

8

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- Mean sample age: 60.8 years (SD: 12.2 years), 55% female, Mood symptom severity was low: mean total YMRS score of 4.3 (SD 5.4); moderate-to-severe depression: 22%.
- Manic and depressive symptom severity: lower among older individuals (p's < 0.0001).
- Somatic burden was high (mean =2.42, SD = 1.97)
- higher depressive (p < 0.0001) and manic (p < 0.0001) symptoms: associated with lower GAF, most strongly among older individuals.

Sajatovic M. et al. *Bipolar Disord.* 2022 24(2):195-206.

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GAGE-BD

› Bipolar Disord. 2022 Mar;24(2):195-206. doi: 10.1111/bdi.13119. Epub 2021 Aug 12.

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- Early findings support: attenuation of BD symptoms in OABD, despite extensive somatic burden.
- Strong association between depressive symptom severity and worse functioning in older individuals => need for effective treatments of BD depression in older people.
- Collaborative path for the development of a better understanding of aging in BD.

Sajatovic M. et al. *Bipolar Disord.* 2022 24(2):195-206.

10

II. Clinical presentations and assessment

- Early onset: those who have been ill for many years
  - Stronger family history, more depressive and mixed episodes
- Newly diagnosed (new mania) with a mood disorder history
- Onset later in life (after age 50 years)
  - More cognitive impairment and treatment resistance
- Secondary mania: illness associated with medical condition(s)
- Comorbidity complicates diagnosis and course of illness: substance use disorder (>20%), anxiety disorder (9.4%), PTSD (5.4%), neurocognitive disorder (4.5%)
- Clinical course: understudied; chronic and episodic; some evidence of increasing risk of recurrence after every new episode
  - Frequency of mood episodes constant through lifespan
  - Rapid cycling: comparable to younger ages
  - Long term outcomes: cognitive deficits, impaired functioning, increased risk of dementia, premature death

Sajatovic et al., 2006; Cassidy et al., 2001; Angst 2003; Al Jurdi 2008.
Chen P. et al. *Curr Psychiatry Rep*. 2017;19:46.
Dols A, Beekman A. *Psychiatr Clin N Am*. 2018; 41: 95-110.

Adapted from Sajatovic

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II. Clinical presentations and assessment

- OABD is a heterogenous population; two major groups—late onset and early onset (LOBD,EOBD)
- Few comparative studies: groups appeared to be distinct; within-group homogeneity in clinical symptomatology and genetic vulnerability
- Early onset: those who have been ill for many years
  - Stronger family history, more depressive and mixed episodes, rapid cycling and psychosis
- Newly diagnosed (new mania) with a mood disorder history
- Onset later in life (after age 50 years)
  - More cognitive impairment and treatment resistance
  - more frequent neurological disorders, cognitive decline, somatic conditions, vascular risk factors
- Secondary mania: illness associated with medical condition(s)
- Comorbidity complicates diagnosis and course of illness: substance use disorder (>20%), anxiety disorder (9.4%), PTSD (5.4%), neurocognitive disorder (4.5%)

Sajatovic et al., 2006; Cassidy et al., 2001; Angst 2003; Al Jurdi 2008.
Chen P. et al. *Curr Psychiatry Rep*. 2017;19:46.
Dols A, Beekman A. *Psychiatr Clin N Am*. 2018; 41: 95-110.
Strejilevich, S.; Int. J. Geriatr. Psychiatry 2019, 34, 950–956.

Adapted from Sajatovic

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Bipolar Disorder in DSM-5

- Criterion A for mania/hypomania slightly modified and include changes in energy as well as mood: "a distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy."
- Mixed episode: requirement for full depression or mania criteria not required
- No change specific to older age patients

http://www.dsm5.org/Documents/changes (APA press)

13

Bipolar Depression in Older Adults

- Depressed or irritable mood
- Disturbances in sleep, appetite and activity level
- Cognitive impairment: may resemble dementia

Shulman KI. *Can Fam Physician*. 1999;45:1229-1237.

Adapted from Sajatovic

14

Bipolar Mania in Older Adults

- Manic symptoms often milder; psychosis may be less common compared to younger patients
- May present with mixed mania, dysphoric, or agitated states
- More likely to have
  - Irritability
  - Treatment resistance (if new onset)
  - Mortality
- Somatic comorbidities common (with or without causal relationship to mania)
- May present with neurological signs (especially if later onset)
  - Confusion, disorientation, distractibility, agitation, ataxia, frontal release signs
    - >60% of patients with late-onset have comorbid neurological disorder; consider right hemispheric cerebrovascular events

Kessing LV. Bipolar Disord 2006; 8(1): 56-64.
Van Gerpen NW. *Am J Geriatr Psychiatry.* 1999;7:188-202.
Chen P. et al. *Curr Psychiatry Rep.* 2017;19:46.

Adapted from Sajatovic

15

Primary vs. Secondary Mania

Secondary mania: symptoms resulting from an underling medical illness in those without history of mood disorder or evidence of delirium[1]

Primary	Secondary
Onset early in life	Onset later life life (more common)
No obvious medical cause	Related medical cause
Higher familial rate of bipolar illness	Lower familial rate of bipolar illness
Better general response to lithium	Generally poor response to lithium

Forester

1. Krauthammer C, Klerman GL, *Arch Gen Psychiatry.* 1978; 35(11): 1333-9.

16

Secondary Mania: caused by an underlying somatic illness or medication

- **Neurologic**
  - Dementia/NCD
  - Traumatic Head injury
  - CNS tumor
  - Multiple sclerosis
  - CVA
  - Epilepsy
  - Huntington's; Wilson's disease
- **Sleep apnea**
- **Vitamin B12/niacin deficiency**
- **Endocrine**
  - Hypo- or hyperthyroidism
  - Hypercortisolemia
- **Infectious**
  - HIV encephalopathy
  - Neurosyphilis
  - Lyme disease
  - Viral encephalitis
- **Toxic**
  - Substances
  - Medications

Forester BP, et al. Geriatric Mania. *Directions in Psychiatry.* 2004; 24(1): 43-59.

Forester

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Assessment in OABD

- History: somatic and psychiatric history, medications; informant report; substance use, family history
- Physical and Neurological exam
- Clinical history; YMRS; PHQ-9/MADRS/GDS; MoCA; consider neuropsychological testing
- Laboratory evaluation:
  - CMP, Creatinine, GFR, CBC
  - TSH; free T3/T4 if TSH abnormal; liver function tests
  - Urinalysis and Urine drug screen
  - B12, folic acid
  - Serum blood levels of current medications
  - Infectious serologies if indicated
- MRI or CT (if new onset symptoms or change in baseline); consider functional imaging or EEG based on differential diagnosis

18

Medical complexity causes earlier death in BD

OABD: average 3-4 co-morbid medical conditions
- Most common: arthritis, cardiovascular disease, diabetes, endocrinopathies, hypertension, metabolic syndrome, respiratory illness, arthritis

Standardized mortality ratios (SMRs) in BD:
- 2.5 for men and 2.7 for women
- Death occurs 10 years earlier than general population
- Most frequent cause of death
  - Cardiovascular disease 31%
  - Suicide 19%
  - Cancer 14%
  - Life-style issues such as smoking, diet and substance abuse likely contribute
- Each 1-unit increase in BMI decreases BD treatment response by >7%
- Screening for side effects and general physical health evaluation: 2-4 times per year
- Integrated psychiatric and primary care is essential

Osby U, et al. *Arch Gen Psychiatry.* 2001;58(9):844-850.
Angst F, et al. *J Affect Disord.* 2002;68(2-3):167-181.
Newcomer J, Hennekens C. *JAMA.* 2007;298(15):1794-17964.
Kemp D and Fan J. *Bipolar Disorder* 2010.12: 404-413.
Fagiolini.A. *Bipolar Disord* 2005: 7: 424–430.
Ng F. et al. *Bipolar Disord* 2009; 11(6): 559-95.

Forester, Sajatovic

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Clinical course

- Inconclusive if OABD has a better, equal or worse course than in younger age populations
- Prospective follow-up of a cohort of OABD patients and a comparison to a cohort of younger-age BD patients: only subtle differences in the long-term course (The median follow-up was 5 years). OABD patients (61.6 ± 8.3 years) spent 15, 6 and 3% of their follow-up time with depressive, manic and mixed symptoms, respectively, and experienced 4.2 ± 2.6 episodes year.
- No significant differences between OABD and BD in working-age patients regarding episode density or mood instability (Strejilevich, S.; Int. J. Geriatr. Psychiatry 2019)
- In the short term, the response to acute treatment and recovery rates in OABD patients appear similar to that of younger patients [47 ,48]
- General evidence: of a progressive and deteriorating course over a life span: increasing sensitization leading to more relapses after every mood episode

- Fries GR et al. *Bipolar Disord.* 2019; epub ahead of print
- Sajatovic M. et al. *Bipolar Disord.* 2015; 17(7):689-704.
- Gildengers AG et al. *Psychol Med* 2013; 43(4): 801-11.
- Schouws SN. et al. *Bipolar Disord.* 2012; 14(7): 749-55.
- Schouws SN. et al. *Bipolar Disord.* 2016;18(2):148-54.
- Chen P. et al. *Curr Psychiatry Rep.* 2017;19:46.
- Oostervink, F.; Int. J. Geriatr. Psychiatry 2015, 30, 201–209.
- Strejilevich, S.; Int. J. Geriatr. Psychiatry 2019, 34, 950–956.

20

Cognitive Dysfunction in OABD

- Observed in greater than 30% of OABD, including in euthymic phase
- Multiple domains: attention, processing speed, cognitive flexibility (switching tasks), verbal fluency, episodic memory, working memory
- Multi-factorial etiologies: white matter degeneration, gray matter atrophy, neurochemical dysregulation, oxidative stress, neuroinflammation, mitochondrial dysfunction, ?neurodegneration
- Associated with worse outcomes; no effective treatments
  - Associated with higher severity of physical comorbidities, lower education
- Functional and cognitive remediation may hold promise but have not been tested in OABD

Gildengers AG et al. *Am. J. Psychiatry,* 2004; 161(4): 736 – 738.
Delaloye C, Moy G, Baudois S, et al. *Bipolar Disord.* 2009: 11: 735–743
Weisenbach S. In *Lehmann & Forester eds.* Springer Science. 2016.
Delaloye C. In J Geriatr Psychiatry. 2011; 26(12): 1309-18.
Burdick KE et al. *Acta Psychiatr Scand.* 2010; 122(6); 499-506.
Demant KM et al. *PLoS One,* 2015; 10(6):e0127955.
Belvederi Murri M et al. *J Affect Disord,* 2019; 1(257): 166-172.

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Cognitive Dysfunction in OABD

- Montejo et al. 2022: Meta-analysis: characterize the cognitive performance in euthymic older adults with OABD through a comprehensive neuropsychological assessment to obtain a detailed neuropsychological profile.
- 328 euthymic OABD patients and 302 healthy controls
- OABD: worse performance in comparison with healthy controls,
  - Large significant effect sizes: verbal learning, verbal and visual delayed memory.
  - Moderate sizes: processing speed, working memory, immediate memory, cognitive flexibility, verbal fluency, psychomotor function, executive functions, attention, inhibition, and recognition
- Cognitive dysfunction is present in OABD; important deficits in almost all cognitive domains, especially memory

Perform routine cognitive screening to assist with early detection of cognitive impairment

Montejo L. et al. *Bipolar Disord.* 2022 24(2): 115-136.

22

Elevated Risk of Dementia in Bipolar Disorder

- National Health Insurance Research Database, Taiwan: Study sample: 9,304 patients with incident dementia diagnosed between 2000 and 2009 and 55,500 gender-, age-, and index date-matched subjects without dementia.
  - Cerebrovascular disease, diabetes, hypertension, head injury, COPD, substance use disorders, health system utilization were covariates.
- A life-time history of bipolar disorder was significantly associated with an increased risk of subsequent dementia [adjusted odds ratio (aOR) = **4.32**, 95% confidence interval (CI):3.21–5.82]

Wu KY, et al. *Bipolar Disord*. 2013; 15(7):787-94.
Almeida OP et al. *Br J Psychiatry*. 2016; Aug:29(2): 121-6.

Adapted from Forester

23

TREATMENT OF OLDER AGE BIPOLAR DISORDER

24

III. Pharmacological Management: Treatment Guidelines of Older Age Bipolar Disorder

- Limitations of current evidence base:
  - No RCTs of treatments for:
    - Geriatric Bipolar depression
    - Maintenance therapy in geriatric cohorts
  - One RCT: Geriatric mania (Young et al. 2017)
- General principles: Mood stabilizer in all phases of treatment; start with atypical rather than typical antipsychotic when antipsychotic is indicated
- No treatment algorithms distinguishing early onset vs. late onset BD
- Current guidelines: first-line treatment of OABD; similar to that for younger populations, **but attention to the vulnerability to side effects, somatic comorbidities and specific risks in older adults**.

Sachs et al. Medication Treatment of Bipolar Disorder: 2000. The Expert Consensus Guideline Series. Postgrad Med Special Report, April 2000. APA 2002; Expert Consensus Guideline Series 2004.
Young RC et al. *Am J Psychiatry.* 2017; 174(11): 1086-1093.

25

Approved Agents for Bipolar Disorder

Acute Mania		Acute Depression		Maintenance	
Year	Drug	Year	Drug	Year	Drug
1970	Lithium	2003	Olanzapine + fluoxetine combination	1974	Lithium
1973	Chlorpromazine	2006	Quetiapine, XR (2008)	2003	Lamotrigine
1994	Divalproex, ER (2005)	2013	Lurasidone	2004	Olanzapine
2000	Olanzapine*	2019	Cariprazine	2005	Aripiprazole
2003	Risperidone*	2021	Lumateperone (Caplyta)	2008	Quetiapine, XR (adjunct)
2004	Quetiapine, XR (2008)*			2009	Risperidone LAI*
2004	Ziprasidone			2009	Ziprasidone (adjunct)
2004	Aripiprazole*			2021	Olanzapine/samidorphan
2004	Carbamazepine ERC				
2009	Asenapine				
2015	Cariprazine				

Ketter TA (ed). Handbook of Diagnosis and Treatment of Bipolar Disorder, Am Psych Pub, Inc., Washington, DC, 2010. Forester, Sajatovic

26

Lithium in OABD

- First-line treatment for maintenance monotherapy
- Reduces suicide risk; neuroprotective properties
  - Evidence suggests may reduce risk of dementia, and possibly of cancer
- Best studied medication for OABD
  - Roles with acute mania, bipolar depression, prophylaxis
  - 78% response rate in bipolar mania; RCT supports efficacy in mania/mixed states
- Narrow therapeutic window
- Reduce standard adult dose by 33-50%
- Usual dose does not exceed 900 mg per day, begin with low dose, 300 mg/day
  - Baseline screening: renal function, electrolytes, thyroid function, fasting blood glucose, EKG
  - Evaluate concomitant medications, (e.g. diuretics, NSAIDS, ACE inhibitors)

Chen P, Ahmed M, Sajatovic M. *Aging Health.* 2006; 2(2): 333-347.
Young RC et al. *Am J Psychiatry.* 2017; 174(11): 1086-1093.
Malhi GS et al. *J Affect Disord*. 2017; 217:266-280.
Song J. et al. *Am J Psychiatry*. 2017;174(8): 795-802.
Gerhard T. et al. *Br J Psychiatry.* 2015; 207(1): 46-51.
Huang RY et al. Br J Psychiatry. 2016; 209(5): 393-399.

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Lithium in OABD…

Target serum concentrations:
Low: 0.4-0.7 mEq/L
High: 0.8 mEq/L or higher
*Need for therapeutic drug monitoring

- Discordance between serum and cerebral Li levels[1]
  - Elevated cerebral Li associated with toxicity
  - **TREAT THE PATIENT NOT THE LEVEL**
- Discontinuation
  - 50% recurrence within 6 months
  - Gradual taper may reduce relapse rate
  - Consider discontinuation with renal insufficiency, otherwise proceed with CAUTION

1. Forester BP. *Am J Geriatr Psychiatry 2009*; 17(1): 13-23

Adapted from Forester

28

Adverse Effects of Lithium in OABD

- Weight gain, GI disturbance
- Cognitive slowing, sedation
- Ataxia
- Tremor
- Neurotoxic effects with minor overdose
- Polyuria, polydipsia, diabetes insipidus
- Urinary frequency, renal failure
- Peripheral edema
- Thyroid toxicity: hypothyroidism; goiter
- Cardiac toxicity: decrease in conduction => sick sinus syndrome
- Renal: chronic renal insufficiency, ARF, polyuria, polydipsia, diabetes insipidus

- Lithium toxicity: serum level 1.2: tremor, nausea, diarrhea, ataxia;
- 1.5-2.0: seizures; >2.0 acute renal failure (requires dialysis); >2.5: coma, death

Baldessarini RJ. *CNS Drugs*. 2002; 16(11):721-729

Adapted from Sajatovic

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Serum Lithium Level

Increase	No effect	Decrease
Loop diuretics	Aspirin	Mannitol
Thiazide diuretics	Paracetamol	Acetazolamide
Calcium blockers	Nefazodone	Theophylline
ACE inhibitors	Mirtazapine	Caffeine
AT II receptor blockers	Valproic acid	Aminophylline
COX2 inhibitors	Lamotrigine	Resonium
Trimethoprim	Amisulpride	
Metronidazole	Ziprasidone	
Spectinomycin	Risperidone	
Levofloxacin	Quetiapine	
NSAIDS		

Other: low sodium diet, dehydration, renal disease

Adapted from: Guideline Renal Side Effects of Chronic Lithium Use. Dutch Federation of Nephrology, 2013

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Predictors of Poor Lithium Response

- Rapid cycling
- Mixed or dysphoric mania
- > 3 previous manic episodes
- Depression-mania-euthymic (DME) sequence

- History
  - Lack of bipolar family history
  - Past Li non-response

- Co-morbidites
  - Substance use
  - Neurological comorbidity

Adapted from Forester

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Delphi Survey: Maintenance Lithium Treatment in Older Adults with Bipolar Disorder: An ISBD Task Force Report

- Evidence for efficacy in OABD remains high, but is use in OABD declining, and lack of specific guidelines
  - Concerns in older age population: chronic renal failure, hypothyroidism, hypercalcemia, neurotoxicity, parkinsonism
- Delphi method (systematic approach to expert consensus): focused on lithium maintenance therapy: place of lithium among preferred choices; clinical guidelines for safe and effective use
- Expert panel: 25 psychiatrists, 23 geriatric psychiatrists; 2 general psychiatrists with expertise in older age disorders;
- Oversight committee provided focus across 3 iterations of the survey completed by expert panel; response rate: 100% response rate across 3 iterations

- 100% consensus: lithium should be first line drug for monotherapy maintenance of OABD
  - Second line option for monotherapy maintenance: lamotrigine, olanzapine, valproate, quetiapine
  - Adjunctive treatments: lamotrigine, quetiapine, valproate

Shulman KI et al. *Bipolar Disord.* 2018;00:1-7.

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Delphi Survey: Maintenance Lithium Treatment in Older Adults with Bipolar Disorder: An ISBD Task Force Report

- Serum concentration 0.4-0.8 mmol/L for ages 60-79; 0.4-0.7 mmol/L for ages 80 and above; no consensus on once daily or twice daily dosing
- Assessment by clinician: at least every 3-6 months:
  - q3-6 months — Lithium level, serum creatinine, eGFR, BUN; tremor, gait
  - q6-12 months — TSH, fasting glucose, lipids, triglycerides, calcium; weight; waist circumference
  - q12 months — hematology; routine cognitive screening (MMSE/MoCA)
  - As concerns arise — general and comprehensive neurological assessments
- Signs of toxicity among OABD: impaired attention, delirium, tremor of extremities, ataxia, nausea/vomiting; no consensus reached: diarrhea, hyperreflexia, polyuria, polydipsia
- Areas for future study: long-term effect on renal and metabolic function; guidelines for use of other mood stabilizers in OABD; potential neuroprotective properties and protection from cancer
- Subsequent cross-sectional multi-center study among 281 older adults with OABD or MDD: long-term lithium use (mean: 12.5 years): lower intensity of depressive symptoms, reduced perceived clinical global severity; not linked to greater medical comorbidity, except hypothyroidism (Morlet et al. 2019)

Shulman KI et al. *Bipolar Disord.* 2018;00:1-7.
Morlet E et al. *J Affect Disord.* 2019; 259: 210-217.

33

Lithium use among GAGE-BD study participants

- Cross-sectional analysis of the GAGE-BD dataset to determine differences and similarities between lithium users and non-users.
- 986 participants aged 50 years or older (mean age 63.5 years; 57.5% females) from 12 study sites.
- Two subgroups ('Lithium'; 'Non-lithium') defined according to the current prescription of lithium.
- Lithium users: lower levels of depressive symptoms, better global cognitive/functional state, fewer comorbid psychiatric and cardio-vascular disorders, and less antipsychotic use.
- Two lines of explanation: lithium use is associated with better outcomes, vs. complex and difficult- to-treat patients less likely to be treated with lithium and more switched from lithium to other medications

"The present data do not support the notion that lithium use by OABD is necessarily associated with unacceptable risks and adverse outcomes".

Sajatovic M, Bipolar Disord. 2021;24(2):195-206.

34

Mood Stabilizing Anticonvulsants in OABD

- divalproex: 5 uncontrolled studies and 1 RCT[1] (in mania/mixed states) suggest efficacy.
  - Acute mania (dysphoric or rapid cycling), mixed states, bipolar maintenance
  - Side effects include sedation, ataxia, LFT elevation, hyperammonemia[2]; tremor, weight gain, alopecia, thrombocytopenia
- lamotrigine:
  - Secondary analysis of 2 pivotal maintenance studies[3]
    - 98 subjects 55 +, mean dose 240 mg/day
    - Delayed time to intervention for any mood episode vs. placebo
  - Open label, add-on treatment, 57 older adults, mean age 66.5 years[4]
    - Response: 64.8%; Remission: 57.4%
    - Mean dose: 150.9 mg/day
- Case Reports of gabapentin[5] and topiramate[6] in geriatric mania

1. Young RC et al. Am J Psychiatry. 2017; 174(11): 1086-1093.
2. Young RC, et al. Pharmacotherapy of Bipolar Disorder in Old Age. *Am J Geriatric Psychiatry* 2004; 12(4):342-357.
3. Sajatovic M, et al: Maintenance treatment outcomes in older patients with bipolar I disorder. *Am J Geriatr Psychiatry* 2005; 13(4):305-11.
4. Sajatovic M et al. *Bipolar Disord.* 2011; 13: 294-302;
5. Sethia et al: *J Geriatric Psychiatry Neurol.* 2003;16:117-120;
6. Madhusoodanan et al: *Am J Geriatric Psychiatry* 2002;10:759.

Adapted from Forester

35

Use of VPA in OABD

- Screening: liver enzymes, CBC with platelets
- Typical starting dose: 125-250 mg/day with gradual titration
- Usual daily dose of 500-1000 mg/day
- Therapeutic range for classic mania in the elderly: 65-90 mcg/mL
- Monitor for hepatic auto-induction /decrease in serum levels
  - Serum levels may be decreased by: carbamazepine, lamotrigine, phenytoin
  - VPA may increase concentrations of: amitriptyline carbamazepine-epoxide, clomipramine, diazepam, lamotrigine, nortriptyline, phenobarbital
- Retrospective chart review: VPA in older age psychiatric inpatients (without underlying liver disease): increased risk for hyperammonemia. Caveats: small sample, varied diagnoses, generalizability. (Adler and Regenold, 2015)

Chen P, Ahmed M, Sajatovic M. *Aging Health.* 2006; 2(2): 333-347.
Dunner DL. *J Clin Psychiatry* 2003;64(Suppl 5):38-43;
Fleming J, Chetty M. *Clin Neuropharmacol* 2005;28:96-101
Adler L and Regenold WT. *Prim Care Companion CNS Disord.* 2015; 17(2):10.4088/PCC.1401737.

Adapted from Sajatovic

36

GERI-BD: a Randomized Double-Blind Controlled Trial of Lithium and Divalproex in the Treatment of Mania in Older Patients with Bipolar Disorder

- **First age-specific randomized controlled trial for late life mania**
  - 9 weeks, lithium or divalproex (no placebo group); tolerability and efficacy
- Subjects: 224 older adults (age 60 and above) with bipolar I disorder, presenting with manic, hypomanic or mixed episodes
- Starting doses: lithium: 300 mg/day (target serum concentration: 0.80-0.99 mEq/L); divalproex: 500 mg/day (target serum concentration: 80-99 micrograms/mL).
- Results: lithium and divalproex both adequately tolerated and similarly efficacious; greater reduction in manic symptoms over 9 weeks in lithium treated group
- less than 20% of all participants required adjunctive antipsychotic medication
- Authors' opinion: "treatment of older adults with bipolar I mania.. lithium and divalproex should be given consideration, perhaps emphasized, relative to antipsychotics." (but no head-to-head comparison to antipsychotics in this study).

Young RC et al. *Am J Psychiatry*. 2017; 174(11): 1086-1093.

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Use of lamotrigine in OABD

- Bipolar maintenance (FDA); bipolar depression (APA guidelines)
- Dosing: increase by 25 mg/q1-2 weeks or more slowly if history of allergies
- Interaction with enzyme-inducing anticonvulsants (carbamazepine, phenytoin phenobarbital, primidone--**More rapid lamotrigine elimination)**
- Interaction with enzyme-inhibiting anticonvulsants (valproate)
  - **Doubling of the elimination half-life of lamotrigine (lamotrigine clearance reduced)**
- Rash (including rare Stevens-Johnson syndrome)
  - Low starting dose, slow up-titration
- Weight-neutral

Bowden CL et al. *Drug Saf*. 2004;27(3):173-184.
Goldsmith DR et al. *Drugs*. 2003; 63(19):2029-2050.
Keck PE, McElroy SL. *J Clin Psychiatry*. 2003; 64(12):1426-1435.

Adapted from Sajatovic

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Use of carbamazepine in OABD…

Acute mania and maintenance
--Also: trigeminal neuralgia, partial seizures
Adverse effects include
- Dizziness, drowsiness, ataxia
- Hematologic: anemia, neutropenia, agranulocytosis
- Hepatic toxicity
- Numerous drug-drug interactions: strong inducer of 3A4

Guidelines for Dosing:
- Initial: 100 mg BID
- Titration: ↑ to 200 mg over 3–5 days as tolerated
- Usual range 400–800 mg/d
- Target level 6–12 µg/mL

Wilder BJ, et al. (eds.) In: *Antiepileptic Drug Interactions*. New York, NY: Demos Publications;1989:65-72;
Fast DK, et al. *Am J Psychiatry*. 1986;143:117-118.
Arana GW, et al, *J Clin Psychiatry*. 1988;49:448-449.

Adapted from Sajatovic

39

Use of carbamazepine in OABD…

- Drug Interactions
  - carbamazepine **decreases levels of**: alprazolam, buproprion, clonazepam, clozapine, haloperidol, olanzapine
  - **carbamazepine levels are increased by**: cimetidine, fluoxetine, isoniazid, ketoconazole, macrolides, valproate, verapamil

Dunner DL. *J Clin Psychiatry* 2003;64(Suppl 5):38-43.

Adapted from Sajatovic

40

Atypical Antipsychotics in OABD: Mania

- Open-label and retrospective reports[1]
- Clozapine, olanzapine, quetiapine, lurasidone, risperidone, asenapine reported to benefit OABD[1,2]
- Olanzapine, risperidone, aripiprazole, ziprasidone, asenapine and quetiapine all FDA approved for mania (adults studied)[3]
- Clozapine for treatment of refractory illness and severe mania[1]

FDA = US Food and Drug Administration.
1. Sajatovic M. *Int J Geriatr Psychiatry.* 2002;17:865-873.
2. Sajatovic M. *Int J Geriatr Psychiatry.* 2015; 30(7): 710-9.
3. Sajatovic M, et al. *Drugs Aging.* 2005;22:39-54.

Adapted from Forester

41

Atypical Antipsychotics in OABD: Bipolar Depression

- Quetiapine: Post-hoc analysis found similar efficacy treating bipolar depressive episodes in older adults as in younger adults[1]
- Aripiprazole: Adjunctive treatment improves depressive symptoms in bipolar older adults (age 55-65) who are sub-optimally responsive to traditional mood stabilizers[2]
- lurasidone: Post-hoc analysis of two double—blind placebo-controlled trials, monotherapy but not adjunctive (lithium or valproate), 6 week treatment effective for OA Bipolar Depression, age 55+, doses 20-60 mg/d, 80-120 mg/d, placebo; both monotherapy and adjunctive therapy safe and well-tolerated[3]
  - Safety and efficacy maintained over a 6-month, open-label extension study (in both monotherapy and adjunctive therapy groups)[4]
    - minimal effects on weight/metabolic parameters, low rates of switching to hypomania or mania over 7.5 months[4]

1. Sajatovic M. Poster presentations, AAGP Annual Meeting. New Orleans, LA. March, 2007.
2. Sajatovic M., et al. *J Clinical Psychiatry.* 2008; 69:41-46.
3. Sajatovic M, Forester BP, Tsai J, et al. *J. Clinical Psychiatry.* 2016. 77(10): 1324-1331.
4. Forester BP., Sajatovic M, Tsai J. et al. *Am J Geriatr Psychiatry.* 2018. 26(2): 150-159.

Adapted from Forester

42

Antipsychotic Dosages for BD Elders

Drug	Starting dose (mg/day)	Healthy elderly (mg/day)	Frail elderly (mg/day)
clozapine†	**6.25-25**	**50-400**	**6.25-50**
risperidone	**0.25-0.5**	**1-3**	**0.25-1**
olanzapine†	**2.5-5**	**5-20**	**2.5-5**
quetiapine	**12.5-25**	**100-750**	**25-100**
ziprasidone	**20-40**	**40-160**	**20-80**
aripiprazole	2.5-5	10-30	5-15
asenapine	2.5-5	10-15	5-10
lurasidone	20-40	60-100	20-60

† Higher dose especially in chronic smokers.

Adapted from Sajatovic

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Use of Atypical Antipsychotics in BD Elderly

- Somnolence, orthostatic hypotension, gait disturbance[1]
- ADA warning for risk of diabetes with all atypical antipsychotics[2]
- ECG abnormalities (ziprasidone)[3]
- Extrapyramidal symptoms; tardive dyskinesia[1]
- FDA warning of increased mortality (1.6-1.7x higher) in elderly patients with dementia[4]
  - Causes of death varied—(heart failure, sudden death, or infections)
- Warning for elevated risk of cerebrovascular adverse events in dementia[5]
- **Implications for older adults (non-demented) with serious mental illness are unclear**

ADA = American Diabetes Association; CVAEs = cerebrovascular adverse events.

Sources: 1. McDonald WM. *J Clin Psychiatry.* 2000;61(suppl 13):3-11.
2. American Diabetes Association, et al. *Diabetes Care.* 2004;27:596-601.
3. Geodon package insert. Pfizer
4. Wang PS, et al. *N Engl J Med.* 2005;353:2335-2341.
5. Schneider LS, et al. *JAMA.* 2005;294:1934-1943.

Adapted from Forester

44

Mortality Risk with Atypicals in OABD

- 4717 VA patients with OABD (65 years old or above), newly started on risperidone, olanzapine, quetiapine or valproic acid during 2001-2008
- 6-month Mortality rates /100 person years:
  - risperidone: 11.8
  - olanzapine : 10.3
  - quetiapine: 5.3
  - valproic acid: 4.6

Bhalerao S et al. *Journal of Geriatric Psychiatry and Neurology* 2012;25(1):29-36.

45

Other Treatments

- Antidepressants
  - No benefit from adding antidepressant in bipolar depression, no destabilization either (STEP-BD)[1]
  - Maintenance treatment with antidepressants: risk for increasing the number of mood episodes[2]
  - Aizenberg et al: 10 year retrospective study of BD elders on mood stabilizers and antidepressants: may decrease risk of suicide (2006)[3]
- Other medication treatments (Omega-3, Vitamin D, etc.)
- 70 OABD patients in acute mania compared memantine vs. a placebo add-on to valproic acid: significant reduction in YMRS scores for this combination, but there was no difference in improving cognition (Omranifard, V.. Adv. Biomed. Res. 2018)
- ECT/TMS
  - ECT—treatment of choice for both mania and depression; can also be used in continuation treatment
- Psychotherapeutic and Psychoeducation Approaches
  - Enhancing treatment adherence

1. STEP BD: Sachs et al, *NEJM* 2007
2. Schneck et al, *AJP* 2008; 165: 370-377.
3. Aizenberg D et al. *J Affect Disord* 2006; 91: 91–94

Adapted from Sajatovic

46

ECT and OABD

- The majority of BD treatment guidelines do not provide specific recommendations on OABD
- Extrapolating from results of ECT in adults with BD and older adults with MDD: favorable effect of ECT in OABD can be expected. Indications for treatment include treatment resistance, previous ECT response, or urgent safety concerns
- Older patients may experience more pronounced cognitive side effects during an ECT course
- Case report: ECT as a viable option to treat depression in older adults with bipolar disorder who are vulnerable to cognitive side effects (Blanken et al., Bipolar Disorders (23(2): 2021.

47

IV. Psychotherapy in BD Elders

- No controlled psychotherapy trials in geriatric bipolar disorder
- Current practices: extrapolation from mixed-age studies & experience
  - Empirical examination with IPT, CBT[1]
  - Hopelessness (associated with suicide) may be targeted with cognitive restructuring
- Cognitive changes may require adaptation, monitoring and structure
- Psychosocial interventions may be improve health and functioning
  - Psychosocial skills training efficacious in older adults with severe mental illness: 12-month RCT (including 36 OABD subjects)[2]
  - Helping Older People Experience Success (HOPES) compared to treatment as usual: improved social skills, self-efficacy, community functioning, leisure and recreation in older adults with severe mental illness[3]

1. Forester BP, et al. Geriatric Mania. *Directions in Psychiatry.* 2004; 24(1): 43-59.
2. Bartels SJ et al. *Am J Geriatr Psychiatry.* 2014; 22(11): 1251-61.
3. Mueser KT et al. *J Consult Clin Psychol* 2010; 22(4): 381-5.

Adapted from Forester

48

V. Treatment Recommendations

- Geriatric Bipolar Mania or Mixed States
  - 1st line: Monotherapy - divalproex or lithium
  - Partial responders - add atypical antipsychotic medication - olanzapine, risperidone, quetiapine (possibly aripiprazole or asenapine)
  - For "Treatment Resistant" – Consider Clozapine or ECT
  - No evidence-based guidance on duration of treatment, time to wait before augmentation, or use of other mood stabilizing anticonvulsants
- Geriatric Bipolar Depression
  - Monotherapy with mood stabilizer or antipsychotic
  - Consider quetiapine (monotherapy or adjunctive), aripiprazole (adjunctive) and lurasidone (monotherapy or adjunctive), combination of olanzapine with fluoxetine
  - Partial responder: cautious addition of antidepressant (SSRI, bupropion)
  - ECT: suicidal patient or patient with inadequate food/fluid intake
- Maintenance
  - 1st line: lithium; second line: lamotrigine, olanzapine, valproate, quetiapine

Young RC, et al., *Am J Geriatric Psychiatry* 2004; 12(4):342-357.
Shulman KI et al. *Bipolar Disord.* 2018;00:1-7.
Dols A, Beekman A. *Psychiatr Clin N Am.* 2018; 41: 95-110.

Adapted from Forester

49

V. Treatment Recommendations: Co-morbidity Management

- BD is multi-system disease that is chronic and progressive
  - Begin co-morbidity management as early in life as possible
  - Aim for NO mood relapses—relapse may damage brain
- Coordinate with other medical providers to manage/reduce risk. (HgbA1c< 7, BP and lipid control)
- Evaluate concomitant medications (i.e. drugs that alter sodium excretion with lithium)
- Incorporate non-pharmacological approaches that promote self-management

Aarre TF., 2008; Sajatovic M, 2011; Leboyer M. & Kupfer D. J., 2010

Adapted from Forester

50

SUMMARY

- Geriatric BD is common in clinical populations.
- Differential diagnosis: mood episode vs. delirium vs. dementia => rigorous work-up
- Medical co-morbidity and cognitive dysfunction are the rule.
  - Cognitive screening and monitoring; early co-morbidity management
- FDA-indicated medications studied in adult aged populations without significant co-morbidities
- Mood stabilizers are mainstay of treatment; therapies with evidence in older adult populations : lithium, valproic acid, quetiapine, lamotrigine, lurasidone
- Monitor closely for drug-drug interactions and adverse effects; judicious dosing in frail elderly
- Treat the patient, not the serum level.
- Coordinate care with medical providers to minimize risk of adverse events
- Psychosocial interventions modified for challenges to adherence and cognitive change are valuable components of treatment.

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PERSONALITY DISORDERS IN OLDER AGE

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1

Disclosures

- No conflicts of interest
- I will mention the off-label use of medications in personality disorders.

2

Personality Disorder

- "An enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual's culture. This pattern is manifested in two (or more) of the following areas: cognition, affectivity, interpersonal functioning, impulse control."
- Onset by adolescence or early adulthood

Personality Disorders. American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.)

3

Personality Disorder Clusters

Cluster A	Paranoid, Schizoid, Schizotypal
Cluster B	Antisocial, Borderline, Narcissistic, Histrionic
Cluster C	Avoidant, Dependent and Obsessive-Compulsive

4

Dimensional Classification

- Dysfunctional personality traits in these domains:
  - Negative affectivity
  - Detachment
  - Antagonism
  - Disinhibition
  - Psychoticism
- Dysfunctional personality functioning

Personality Disorders. American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.)

5

Challenges in Assessment

- Limited research
- Older adults may be less likely to endorse certain symptoms
- Limited collateral information
- Medical and psychiatric comorbidity
- Sense of therapeutic futility

Am J Geriatr Psychiatry. 2007 September; 15 (9): 742-753.
J Psychiatr Res. 2010 January; 44(1): 1. doi:10.1016/j.jpsychires.2009.06.009
Psychol Aging. 2007 March ; 22(1): 171–185

6

Challenges in Assessment

- Some criteria appear irrelevant in older age:
  - Physical aggression
  - Impact on work
  - Lacking close friends or confidants other than first-degree relative

7

Challenges in Assessment

- Difficult to confirm pattern of behavior over decades
- Maladaptive behaviors may be dismissed in older adults
- Questions about stability of personality disorders over time
- Multimorbidity

8

Screening Tools

- Gerontological Personality Disorder Scale
- Hetero-Anamnestic Personality Questionnaire

Curr Psychiatry Rep 2015; 17:538

9

Differential Diagnosis

- Neurocognitive disorder
- Autism spectrum disorder
- Substance use disorder
- Personality disorder due to general medical condition
- Transient decline in functioning due to another mental health disorder
- Traumatic brain injury, concussion, structural brain lesion
- Sequelae of critical illness

FOCUS 2021; 19 (3): 303-307
Journal of Gerontology: PSYCHOLOGICAL SCIENCES 2007, Vol. 62B, No. 6, P353–P361
CNS Drugs. 2010 May 1; 24(5): 375–398
DEPRESSION AND ANXIETY 32:919–926 (2015)

10

General demographics

- Among the most common mental health diagnoses
- General population prevalence is 15% in the United States
- Similar prevalence in older age
- Mood, anxiety and substance use disorders are frequently comorbid
- Declining prevalence with older age

Curr Psychiatry Rep 2020; 22:14
Br J Psychiatry 2018; 213: 709-715

11

General Demographics

- Most common:
  - Obsessive compulsive personality disorder
  - Narcissistic personality disorder
- Least common:
  - Dependent personality disorder
  - Histrionic personality disorder
- Overall, more common in older men
- Paranoid, avoidant, dependent more common in women

Curr Psychiatry Rep 2020; 22:14
Br J Psychiatry 2018; 213: 709-715

12

Adverse Outcomes

- Increased healthcare utilization
- Reduced work productivity
- Impaired role functioning
- Increased absences from work

Br J Psychiatry. 2006;188:13.
Cognitive Behaviour Therapy Vol 36, No 3, pp. 145–155, 2007
J Clin Psychiatry 2008; 69: 259-265.
Psychiatr Clin N America 31 (2008) 395-403.

13

Health outcomes – mental health

- Decreased response to treatment and/or prolonged time to treatment response for depressive and anxiety disorders
- Decreased functional status and quality of life among depressed older adults even after depression remission

Am J Geriatr Psychiatry 2001; 9:67–71
Am J Geriatric Psychiatry 2005 Sep;13(9):808-14
Psychiatr Clin N America 31 (2008) 395-403.

14

Health Outcomes - general

- Premature mortality in the general population
- Increased smoking, alcohol use disorder
- Associated with both severe obesity and being underweight
- Increased risk of stroke and heart disease
- Associated with diabetes, arthritis, GI disorders

Soc Psychiatry Psychiatr Epidemiol (2015) 50:807–820
J Clin Psychiatry 2007 68: 69-74
Journal of Personality Disorders, 27(3), 411-424, 2013 Journal of Gerontology: PSYCHOLOGICAL SCIENCES Vol. 62B, No. 5, P295–P299
Psychosomatic Medicine 70:1012–1019 (2008)

15

Antisocial Personality Disorder

- Associated with increased risk of:
  - Accidental injury
  - Hepatitis C
  - HIV

Can J Psychiatry 2015; 60:309-314

16

Risk of Suicide

- Elderly patients with personality disorders generally have increased suicide risk
- Narcissistic PD is likely a risk factor for late-life suicide among depressed older adults

Aging Ment Health. 2015; 19(12): 1071-7.
Am J Geriatr Psychiatry 2007; 15(9): 734-41

17

Personality Change Over Time

- Personality traits are thought exhibit about 50% heritability
- Environmental influence
- Changes with aging
  - Increased use of mature coping mechanisms
  - Exacerbation of underlying deficits with stressors of aging

Lancet 2015; 385: 727-34.

18

Cognitive Deficits

- Personality disorders are associated with subtle impairments:
  - Executive function
  - Memory
  - Processing speed
  - Visuospatial abilities

Clin Psychol Rev 2016; 44:1-12

19

General trends

- Limited evidence
- Increasing frequency of schizoid and cluster C personality disorders over time
- Clusters A and C tend to worsen over time
- Decreasing frequency of cluster B personality disorders

Annu Review Clinical Psychology 2011; 7: 321-349.
Journal of Personality Disorder 2003; 17(4): 447-459.
Psychopathology 2003; 36(2): 78-83

20

Cluster B

- General decline in severity over time
- Borderline personality disorder
  - Decreased impulsivity, identity disturbance
  - Anger, dysphoria and feelings of emptiness remain stable
  - Increased use of mature defenses
  - Impairment may persist despite symptom improvement

Acta Psychiatr Scand 2009; 119(2): 143-8
Am J Psychiatry 2013; 170(1): 111-120
J Women Aging 2007; 19(1-2): 173-191

21

Treatment

- Limited data
- Psychotherapy
- Off-label medication trials for specific target symptoms

Int J Geriatr Psychiatry 2007; 22(2): 131-143.

22

Treatment - Therapy

- DBT in patients with comorbid MDD
- Schema-based therapy

Int J Geriatr Psychiatry 2007; 22: 131-143
Aging Ment Helath 2018; 22: 738-747

23

Treatment - Medications

- No FDA-approved medications
- Off-label medications for specific target symptoms
- No data specific to older adults

24

Guidelines for Medication Use

- Identify target symptons
- Determine duration of trial
- Discontinue if unhelpful

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Medications for Borderline PD

- Topiramate
- Naltrexone
- Atypical antipsychotics (most data for olanzapine and aripiprazole)
- Divalproex
- Omega-3 fatty acids

Int J Neuropsychopharmacol 2011; 14:1257–1288
J Clin Psychiatry 1996; 57:233–237
Br J Psychiatry 2010; 196:4–12

26

Omega-3?

Two small randomized controlled trials of omega-3 fatty acids showed:

- Decreased aggression
- Decreased parasuicidal behaviors
- Improved affect
- Decreased stress reactivity

J Clin Med 2017; 5(8): 67

27

Medications for Borderline PD

Helpful for:

- Interpersonal problems
- Impulsivity
- Affective instability
- Anger
- Psychotic symptoms

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PSYCHOTIC DISORDERS IN ELDERLY PERSONS

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1

No potential conflicts of interest

Will discuss off label medication use

2

Two Preliminary Points

In older adults, for all conditions: think "Comorbidity"

For any new psychiatric conditions/change in symptoms:

Assume a physical cause until proven otherwise

3

Psychosis in the Elderly

1. Can be primary (due to psychiatric disorder) or secondary (due to medical/neurological disorder)

2. No reliable pathognomonic signs to distinguish primary or secondary psychosis (dx of exclusion: need to rule out secondary causes).

3. Every new onset psychoses or notable change in symptoms needs a medical work-up.

4

A) Primary psychotic disorders:

Schizophrenia and related disorders
Schizophrenia
Schizoaffective disorder
Schizophreniform disorder
Delusional disorder
Brief psychotic disorder

Affective psychoses
Bipolar disorder with psychotic features
Unipolar depression with psychotic features

Freudenreich (2010); Karim & Byrne (2005)

5

B) Secondary psychotic disorders:
Psychotic symptoms associated with dementia

Alzheimer's Disease with psychoses
Vascular dementia with psychoses
Lewy Body Disease with psychoses
Other dementing disorders with psychoses

Psychotic symptoms during delirium ("toxic psychoses")

Psychotic symptoms associated with medications and substance abuse
Psychotic symptoms due to medical and surgical disorders

Freudenreich (2010); Karim & Byrne (2005)

6

Lifetime Risk

Up to 23% of the older adult population will experience psychotic symptoms at some time, with dementia being the main contributing cause

Khouzam & Emes (2007)

7

Etiology of Psychosis in Older Adults

1. Alzheimer's disease and other dementias (40%)
2. Depressive disorder (33%)
3. Medical/toxic causes including substances (11%)
4. Delirium (7%)
5. Bipolar Affective Disorder (5%)
6. Delusional disorder (2%)
7. Schizophrenia spectrum disorders (1%)

Manepalli et al. (2007); Webster & Grossberg (1998; 1999)

8

Risk Factors for Psychosis in Older Adults

1. Sensory deficits
2. Social isolation
3. Cognitive decline
4. Medical comorbidities
5. Polypharmacy
6. Age related changes in pharmacokinetics and pharmacodynamics
7. Comorbid psychiatric illnesses such as dementia and delirium
8. Age-related changes in cerebral structures such as frontotemporal cortices
9. Neurochemical changes associated with aging

Psychosis may be multifactorial; occurs in the context of frailty, limited reserve capacity, increased vulnerability to stressors.

Targum & Abbott (1999); Targum (2001)

9

Alzheimer's Disease

Prevalence of psychotic symptoms: 12% to 74%; Median: 41%

Rates of psychoses: 20% in early stages to 50% by 3rd or 4th years of illness.

Hallucinations: visual> auditory> other.

Paulsen et al. (2000); Ropacki & Jeste (2005)

10

Delusions: most likely theft, infidelity of one's spouse, abandonment, house not one's home, and persecution; decreases in later stages.

Some evidence that psychotic symptoms are associated with a more rapid decline.

Schneiderian 1st rank symptoms and disorganization of speech rare

Jeste et al. (2001); Burns et al. (1990a; 1990b)

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Psychoses in AD

Presence of hallucinations and/or delusions of at least one month duration, even if intermittent, not explainable by delirium, drug effects, schizophrenia or other psychiatric disorders.

AD diagnosis preceded those of psychosis

Jeste & Finkel (2001)

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Lewy Body Dementia

1. About half have **visual** hallucinations (up to 80% in some studies); an early sign in 43%

2. Auditory hallucinations (20%) and paranoid delusions(65%) are also common

3. Psychotic symptoms may be more common than in AD.

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Parkinson's disease

Overall rates: 20 to 60% --- about ¼ have hallucinations in PD, but ¾ have hallucinations with Parkinson's Disease with Dementia (PDD). Thus, psychosis is more common in later stages of PD.

Hallucinations more common than delusions.

PD without cognitive decline:

(a) No medication: psychotic sx may occur but rare.

(b) On medication: minor psychotic sx, with or without insight may occur (10-20%) such as:

Visual illusions (distorted perceptions)

Benign visual hallucinations/sense presence (someone is nearby when there is no one)

Passage hallucinations (fleeting imagery in peripheral vision)

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- **PD and Dementia**: often experience psychotic symptoms in the absence of medications; dopaminergic therapies may trigger or exacerbate symptoms
  (75% prevalence of psychosis in this category)

- REMEMBER:
  Extrinsic causes > Intrinsic causes, i.e., hallucinations in PD most commonly secondary to dopaminergic agents (extrinsic).

Need to assess onset of symptoms. Medications produce vivid visual hallucinations.

Fenelon et al. (2000); Sanchez Ramos et al. (1996); Zahodne et al. (2008)

15

Unipolar Depression

1. Psychotic depression occurs in 20% to 45% of hospitalized elderly depressed patients

2. Delusions are more commonly mood-congruent, including delusions of guilt, delusions of deserved punishment for moral or personal inadequacies, delusions of nihilism, somatic delusions, delusions of poverty.

3. Auditory hallucinations are less common.

4. Catatonia in severe depressive episodes

Blazer et al. (2009); Meyers (1995); Shanmugham et al. (2005)

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Bipolar Illness

1. Psychotic symptoms occur in the context of manic or depressive episodes.
2. Bipolar depression is similar to unipolar depression in having predominantly mood-congruent delusions.
3. Bipolar mania also presents with predominantly mood-congruent delusions such as grandiosity, erotomania, delusions about possessing special powers.

Depp & Jeste (2004)

17

Substance Induced Psychosis

1. Psychotic symptoms may occur during alcohol (e.g., DTs), sedative, or barbiturate withdrawal, whereas stimulants (amphetamines, cocaine, OTC weight –reducing drugs) can cause symptoms with intoxication.

2. Opiates such as narcotic analgesics, heroin, codeine, and methadone may induce delirium, and consequently, psychoses

3. Prescribed medications. Most common causes of psychosis are the "anti's": anti-inflammatories (including steroids), antiparkinsonian drugs, anticholinergic drugs, antiarrhythmic agents, antivirals, antibiotics, anti-malarials.

4. If **tactile hallucinations** occur, consider drug withdrawal states, toxic, or metabolic disturbances.

Targum (2001)

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Medical Illness

1. Medical illnesses can cause psychosis with and without delirium.

2. DSM criteria require prominent hallucinations or delusions, with evidence from the history, physical examination, or laboratory findings that the disturbance is physiological consequence of the general medical condition. It should not be better accounted for by another mental disorder and does not occur exclusively during the course of a delirium.

3. Typical medical causes of psychosis are neurological, infectious, metabolic, and endocrine.

4. Elderly persons are more at-risk because of high rates of physical illness, polypharmacy, and susceptibility to disruption of brain function

Cardinal & Bullmore (2011)

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Older Patients who had Early-Onset Schizophrenia

Greater numbers of schizophrenia patients are surviving into old age.

Between 80-85% of persons aged 55 and over developed schizophrenia before age 45. Prevalence estimates for schizophrenia in adults aged > 64 are as high as 0.5%.

By 2025, about 1/4 of persons with schizophrenia will be age 55 and over.

Broadway & Mintzer (2007); Jeste & Twamley (2003); Khouzam et al. (2005); Howard et al. (2000)

20

There is heterogeneity of outcome in schizophrenia into later life.

Long-term studies observing the symptoms and functioning in early-onset schizophrenia suggest that the course of schizophrenia may not be as pessimistic as previously thought, and such findings challenge the notion implied in the term *dementia praecox*.

Jeste et al. (2009)

Excess mortality seen in older patients with schizophrenia compared to age matched controls. In a cohort of 157 older patients with schizophrenia/ schizoaffective disorder (mean age = 68 years) the standardized mortality rate overall = 1.89; higher in men (2.60) than women (1.78)

Meesters et al (2016)

21

Based on long-term studies carried out in Europe ranging from 22 to 37 years, Ciompi (1980) found:

*20 to 27% of patients attained complete symptomatic remission

*22 to 33% attained mild end states,

*24% to 29% attained intermediate end-states, *14 to 18% attained severe end-states.

Thus, roughly half of persons exhibited recovery or mild end-states, and half showed moderate or severe end states.

Ciompi (1980)

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1.Outcome from earlier life (depends on definitions): About half improve in psychopathology, one-third remain unchanged, and about 15% get worse.

20% remission in positive and negative symptoms; 60% largely unchanged; 20% worsening of symptoms (Jeste et al., 2009)

2. "Social recovery" was observed in about half of subjects.

3. Looking at a more comprehensive definition of recovery, Auslander & Jeste (2004) found only 8% of older outpatients attained "sustained remission," based on symptom remission, social functioning, and medication dosage.

4. Better prognosis: female, later development of illness, better premorbid functioning, married, acute-remitting course

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Late-Onset Schizophrenia

A review of studies of late-onset schizophrenia found that approximately 23% of patients with schizophrenia were reported to have experienced the onset of the disorder after age 40, with 13% in the fifth decade of life, 7% in the sixth decade, and 3% in later decades: **roughly 15% onset over age 44**.

Howard et al. (2000)

24

The International Late-Onset Schizophrenia Group has proposed that schizophrenia with an **onset between age 40 and 60 be termed "Late-Onset Schizophrenia"** and be considered a subtype of schizophrenia.

The authors believe that schizophrenia with onset in middle age is a neurodevelopmental disorder, and that differences with early-onset schizophrenia are more of degree than of kind.

Howard et al. (2000)

25

No differences between early and late onset groups in:

positive symptoms, family history, brain abnormalities, memory retention, or minor physical abnormalities.

The late-onset group is more likely to:
1. Be female versus no gender differences in early-onset,
2. Have the paranoid subtype of schizophrenia,
3. Have lower levels of negative symptoms,
4. Have less impairment in learning, abstraction, and flexibility,
5. Better premorbid functioning with respect to work and marriage.

Howard et al. (2000); Chen et al. (2018)

26

The International Late-Onset Group also proposed the term, **"Very Late Onset Schizophrenia-Like Psychosis" for disorders that begins after age 60.** This disorder has features that suggest a neurodegenerative component including more brain abnormalities and neuropsychological deficits.

Howard et al. (2000); Sharma et al (2014)

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This disorder is also distinguished from the other two types by:

1. many more females;
2. greater prevalence of persecutory and partition delusions;
3. higher rates of visual, tactile and olfactory hallucinations;
4. lower genetic load;
5. more sensory abnormalities;
6. absence of negative symptoms or formal thought disorder.

Howard et al. (2000)

28

Delusional Disorder

1.Non-bizarre delusions which involve situations that may occur in real life, such as theft, suffering from a disease, spousal infidelity, or being followed. Schizophrenia has more bizarre delusions and auditory hallucinations. Poor psychosocial functioning in delusional disorder is directly related to the delusional beliefs.

2. Prevalence: 0.03%

3. Risk factors: Persons with schizotypal or paranoid personality disorders

4. Tends to be chronic, especially in those with the persecutory type.

Kendler & Davis (1981); Jeste et al. (2009)

29

6 "Ds" of Psychiatric Diagnoses in Older Adults that Co-Occur with Psychoses

Think of these possibilities and consider course:

- **Delirium: days to weeks**
- **Drugs: days to months**
- **Disease: days to months**
- **Depression: weeks to months**
- **Dementia: months to years**
- **Delusional disorder and schizophrenia: months to decades**

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Pharmacologic Treatment of Older Patients with Psychosis

Antipsychotics that have been well studied:

1. Risperidone
2. Olanzapine
3. Quetiapine
4. Aripiprazole

Start with lower doses and titrate slowly

Gareri et al. (2014); Tariot et al. (2000); Madhusoodan et al. (2004); Kohen et al. (2010)

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Pharmacologic Treatment of Older Patients with Psychosis

TABLE 2
ANTIPSYCHOTICS: SAFETY AND TOLERABILITY[1]

Item	Typical Neuroleptic	Clozapine	Risperidone	Olanzapine	Quetiapine	Ziprasidone	Aripiprazole
EPS	+ to +++	±	± to +++*	± to +*	±	± to +*	± to +
TD	+++	±	± to ++	± (?)	± (?)	± (?)	± (?)
Somnolence	± to +++	+++	±	++	++	±	±
Prolactin	+++	±	+++	±	±	±	±
Weight	± to ++	+++	+	+++	++	±	±
Dyslipidemia	± to +	+++	+	+++	++	±	±
DM	± to +	+++	+	+++	++	±	±
QTc	+	++	+	+	+	++	±
Orthostatic BP↓	± to +++	+++	++	+	++	±	±

*Dose-related.

Key: ±=none-to-minimal; +=mild; ++=moderate; +++=marked; ?=no data, compared to placebo rates.

EPS=extrapyramidal symptoms; TD=tardive dyskinesia; DM=diabetes mellitus; QTc=corrected Q-T interval; BP=blood pressure.

Glick ID, He X, Davis JM. *Primary Psychiatry.* Vol 13, No 12. 2006.

Note: Antipsychotics are not FDA approved to treat Dementia related psychosis

Retrospective chart review on 115 geriatric inpatients: 14.3% olanzapine patients had > 7% weight gain; aripiprazole group -2.3% change compared to olanzapine (Yeung et al 2017)

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Pharmacologic Treatment of Older Patients with Psychosis

Other FDA approved Antipsychotics:

1. Asenapine
2. Lurasidone
3. Paliperidone
4. Brexpiprazole
5. Cariprazine
6. Iloperidone
7. Pimavanserin
8. Lumaterperone

Note: Antipsychotics are not FDA approved to treat Dementia related psychosis

33

Pharmacologic Treatment of Older Patients with Psychosis

Other Studies of FDA approved Antipsychotics:

Asenapine – elderly bipolar patients; n = 11; side effects: rash, peripheral edema, mild sedation; dose: 10 mg bid

Barcuh et al. (2013)

Lurasidone – bipolar I depression; n = 88 monotherapy and n = 54 adjunctive therapy; monotherapy group significantly different from placebo; discontinuation rates in both groups did not differ from placebo; monotherapy dose: 35 mg/day (mean modal dose) for the 20-60 mg/day group and 96 mg/day for the 80-120 mg/day group

Sajatovic et al. (2016)

34

Pharmacologic Treatment of Older Patients with Psychosis

Lurasidone

6 month open label follow up study in older adults with a diagnosis of bipolar I depression (n = 141) who completed 6 weeks of double blind placebo controlled treatment of lurasiodone as monotherapy or adjunctive treatment lithium or valproate; minimal changes in weight, lipids, HA1c; improvements in MADRS noted; dose range: 20-120 mg daily.

Forester et al (2017)

Paliperidone – limited dosing and safety data

Madhusoodanan and Zaver (2010)

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Pharmacologic Treatment of Older Patients with Psychosis

Other FDA approved Antipsychotics:

Brexpiprazole

2 studies in patients with dementia; dose range – 0.5 – 2 mg /day;

Side effects noted: study 1: headache (9.3% vs 8.1% with placebo), insomnia (5.7% versus 4.4%), dizziness (5.7% vs 3.0%), and urinary tract infection (5.0% vs 1.5%).

Study 2: headache (7.6% versus 12.4% with placebo) and somnolence (6.1% vs 3.6%).

Cariprazine

Package insert recommends lower doses; dose range 1.5-6 mg/day

Iloperidone

1 study in dementia patients- dose used up to 6 mg a day which was generally tolerated; dose titration included 0.5 – 1.0 mg increases every 3 days.

Grossberg et al, 2020; Lepola et al, 2018; El-Bizri et al. 2002

36

COVID-19 and Antipsychotic Use

Mortality study:

56 outpatients in NYC clinic in 2020

Mean age: 76 +/-

Increased mortality risk in patients prescribed at least 1 antipsychotic:

(OR = 11.1, 95% confidence interval: 1.4–96.0; Fisher's exact test P = 0.009).

Logistic regression adjusted for age, gender, housing situation, dementia (p = 0.035)

88% of survivors returned to pre infection levels of baseline psychiatric symptoms

Another study demonstrated increased risk of COVID-19 infection in individuals treated with clozapine compared to those on another antipsychotic (HR = 1.76; 95% CI: 1.14-2.72)

Austria et al et al (2021); Govind et al (2020)

37

Large-scale randomized, double-blind controlled trial comparing 2nd generation antipsychotics—risperidone (1-3 mg/day) and olanzapine (5 mg to 20 mg/day)-- in adults older than 60.

Improvements seen in both groups with (+) symptoms, (-) symptoms, disorganized thoughts, and symptoms of anxiety/depression.

More weight gain in the olanzapine group.

Jeste et al. (2003)

Lack of published data specifically examining antipsychotics in late-onset schizophrenia (LOS); Open studies of typical antipsychotics in LOS indicated that 48%–61% of patients demonstrated full remission of psychotic symptoms.

Cognitive behavioral therapy and social skills training also have shown promise.

Essali & Ali (2012)

38

Randomized controlled trial in patients with very late onset schizophrenia like psychosis

Hypothesis: Is low-dose amisulpride (100 mg daily) superior to placebo in reducing psychosis symptoms over 12 weeks and is it maintained by continuing treatment after 12 weeks?

Criteria: Brief Psychiatric Rating Scale [BPRS] score of ≥ 30

Randomization to 1 of 3 groups in a 2 stage trial:

1. Amisulpride in both stage 1 and 2
2. Amisulpride in stage 1 then placebo in stage 2
3. Placebo in stage 1 then amisulpride in stage 2

Stage 1: Treatment (100 mg oral amisulpride daily *vs* placebo) given for 12 weeks
Stage 2: Compares continuation of amisulpride to withdrawal to placebo

101 participants; 92 (91%) of 101 participants took trial medication

59 (64%) completed stage 1; 34 (58%) of these 59 participants completed stage 2 treatment.

Howard, et al (2018)

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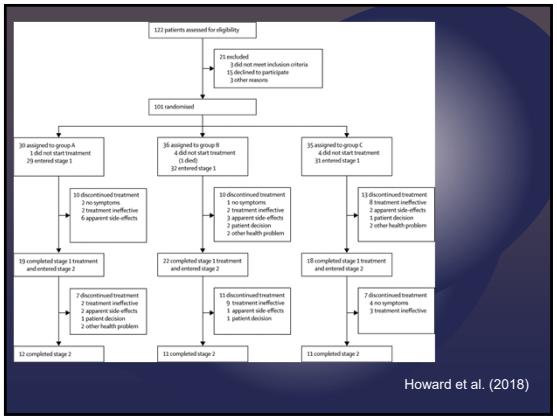


Howard et al. (2018)

40

Despite suboptimal compliance, improvements in BPRS scores at 12 weeks were 7.7 points greater with amisulpride

In stage 2, BPRS scores improved by a mean of 1.1 points from 12 weeks to the final assessment in those who continued amisulpride but deteriorated by 5.2 points in those who switched from amisulpride to placebo.

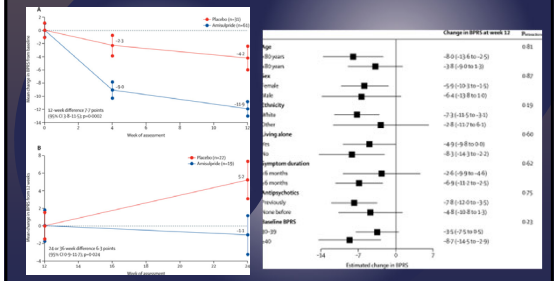
Fewer participants who were allocated amisulpride than placebo stopped treatment because of non-efficacy in stage 1 and stage 2.

Most common serious adverse events with amisulpride treatment: Infection and extrapyramidal side-effects.

Five patients died during the study. No deaths were related to treatment.

Howard, et al (2018)

41



Howard et al. (2018)

42

Meta-analysis analyzing antipsychotics in elderly patients with schizophrenia

Reviewed all randomized controlled trials; Primary Outcome: overall symptoms

Secondary Outcome- positive symptoms, negative symptoms, response, dropouts, quality of life, social functioning, side effects

29 references from 18 RCT's

Elderly- minimum age 46; mean age: 57-73

Conclusions

- Paliperidone – fewer dropouts due to inefficacy vs placebo
- Olanzapine- superior to haloperidol in overall symptoms, negative symptoms and response; had fewer dropouts relative to risperidone
- Risperidone and haloperidol- more prolactin increase than olanzapine
- Olanzapine – less use of anti-parkinsonian medicine than haloperidol

Krause et al (2018)

43

Psychosocial Treatments for Older Patients with Schizophrenia

1. Integrated Psychological Therapy (IPT; Mueller et al., 2013): cognitive remediation therapy (CRT) and social skills therapy (SST)
2. Functional Adaptation Skills Training (FAST; Patterson et al., 2003):SST
3. Helping Older People Experience Success (HOPES; Pratt et al., 2008)
4. Cognitive Behavioral Social Skills Training (CBSST; Granholm et al., 2005)
5. Cognitive Remediation Therapy (McGurk & Mueser, 2007; Greenwood et al., 2005)

44

Delusional Disorders

Commonly, persons deny their illness; thus non-adherence to antipsychotics is a common problem

Lack of robust clinical trials

- Antipsychotic agents often are effective, especially in agitated delusional patients.
- For refractory cases, modified electro-convulsive therapy has been reported as successful.

Cognitive-behavioral therapy has been demonstrated as an effective treatment approach.

Jumaa & Brown (2006)

45

Parkinson's Disease

Critical to first adjust anti-parkinsonian medication

Quetiapine: 12.5 mg to 150mg has been used for psychotic symptoms; however, a recent systematic review of 7 trials in patients with Parkinsons' disease or related neurodegenerative disorders indicated it failed to reduce psychotic symptoms relative to placebo

Goldman et al. (2011); Desmares et al. (2016)

46

Parkinson's Disease

Aripirprazole

open label study by Friedman et al 2006; dose: 1-5 mg/day; n = 14

Improvement seen with BPRS; 8 discontinued due to worsening parkinsonism (3), worsening of both (2), and lack of efficacy (1)

Clozapine: 6.25mg to 125 mg has been effective.

Friedman et al. (2006); Goldman et al. (2011); Desmares et al. (2016); Reddy et al (2018)

47

Pimavanserin: Drug approved to treat hallucinations and delusions associated with psychosis in Parkinson's disease.

6-week clinical trial of 199 participants. Pimavanserin was superior to placebo in decreasing the frequency and/or severity of hallucinations and delusions without worsening the primary motor symptoms of Parkinson's disease.

Serious adverse reaction: QTc prolongation
Common adverse reactions: peripheral edema, nausea, and confusion

Selective serotonin inverse agonist (SSIA) – an agent that binds to the serotonin receptor but induces a pharmacological response opposite to the agonist.

Recommended dose: 34 mg po q day without titration.

Endpoint	Mean Baseline Score	Δ from Baseline in Placebo	Δ from Baseline in pimavanserin	Difference (95% CI; p value)
SAPS-PD	15.9	-2.73	-5.79	-3.06 (-4.91 to 1.20; p = 0.0014)
SAPS-PD Hallucinations	11.1	-1.80	-3.81	-2.08 (-3.46 to -0.71; p = 0.0032)
SAPS-PD Delusions	4.8	-1.01	-1.95	-1.16 (-2.22 to -0.10; p = 0.0325)

Cummings et al. (2014)

48

New Tardive Dyskinesia Drugs
Valbenazine

Data pooled from three 6-week, randomized, double-blind, placebo-controlled studies (DBPC) and two long-term studies.

Week 6 end of DBPC: % participants who met AIMS response threshold higher with valbenazine versus placebo in both subgroups:

> 55 years: (80 mg/d, 39.7% [P < .001]; 40 mg/d, 28.6% [P < .01]; placebo, 9.7%)

<55 years: (80 mg/d, 39.5% [P < .001]; 40 mg/d, 20.0% [P > .05]; placebo, 10.8%).

CGI-TD response higher with valbenazine versus placebo:

> 55 years: (80 mg/d, 41.3% [P < .01]; 40 mg/d, 30.2% [P > .05]; placebo, 19.4%)

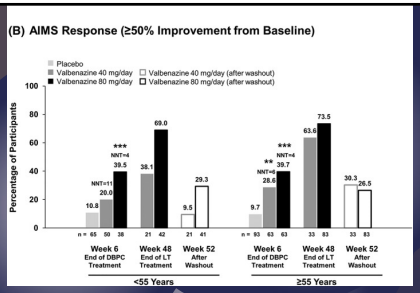
< 55 years (80 mg/d, 39.5% [P < .05]; 40 mg/d, 35.3% [P < .05]; placebo, 18.5%).

Week 48 (end of long-term treatment, combined doses):
> 55 (AIMS, 70.7%; CGI-TD, 82.8%)
< 55 (AIMS, 58.7%; CGI- TD, 72.3%).

No differences between older and younger subgroups were found for AIMS or CGI-TD. No new safety signals or TEAEs of clinical concern were found in older participants who received long-term treatment

Sajatovic et al (2020)

49



Sajatovic et al (2020)

50

New Tardive Dyskinesia Drugs

Deutetrabenazine

119 younger (< 55) and 218 older (> 54)

Drug initiated at 12 mg/day and titrated once weekly by 6 mg/day using a response-driven dosing regimen until adequate dyskinesia control was reached or a clinically significant adverse event occurred.

Multi-site trial: 337 participants with TD; 3 years of open-label treatment,

Mean deutetrabenazine dose: ~39.5 mg/day in both groups.

Mean±SE change in total motor AIMS score: -6.7 ± 0.62 and -6.5 ± 0.47 in younger and older participants, respectively (percent changes: -61.4% ± 4.10% and -54.6% ± 3.01%)

76% of younger and 62% of older participants achieved ≥50% AIMS response.

Deutetrabenazine - generally well tolerated in both groups.

QTC prolongation also a concern; other adverse events: insomnia, nasopharyngitis

Citrome et al (2017); Sajatovic (2022)

51

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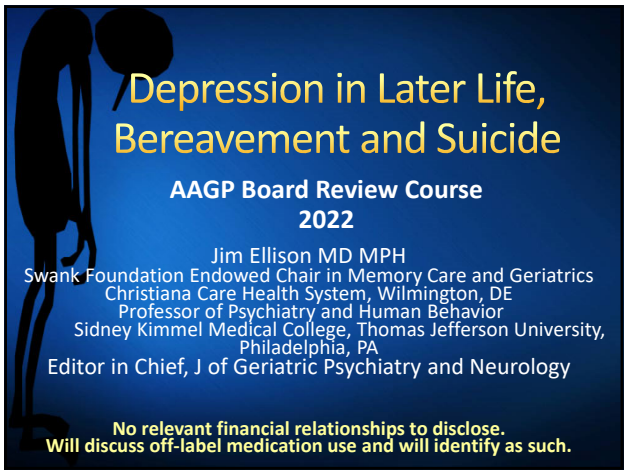

Depression in Later Life, Bereavement and Suicide

AAGP Board Review Course
2022

Jim Ellison MD MPH
Swank Foundation Endowed Chair in Memory Care and Geriatrics
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Editor in Chief, J of Geriatric Psychiatry and Neurology

No relevant financial relationships to disclose.
Will discuss off-label medication use and will identify as such.

1

Late-Life Depression: The Essentials and Essential Differences

2

Key Points

1. MDD not a "normal part of aging"
2. Depressive symptoms/syndromes in later life are significant and treatable!
3. Age influences demographics, etiology, presentation, assessment, acute and maintenance treatment, and outcome
4. Recent advances in psychotherapies and somatic therapies improve treatment effectiveness

3

Prevalence of Depressive Syndromes in Later Life

	Clinically Significant Depressive Symptoms[1]	Major Depressive Disorder[1]
Community	8-15% 9.7-26.1% for 75+[3] 6.1% for men age 60+[3], 9.6% for women age 60+[3]	1-3% 4.4-10.6% for 75+[2]
Primary Care		6-9%[3]
Long Term Care	30-50%	6-25%
Bipolar Disorder		0.1-0.4%[4]

1. Ellison JM, Gottlieb G: Recognition and management of late life mood disorders. In: Sirven JI, Malamut BL (eds): Clinical Neurology of the Older Adult, 2nd Edition. Philadelphia, Lippincott Williams & Wilkins, 2008; 2. Luppa et al. J Aff Dis 2012;136:212-221; 3. National Health and Nutrition Survey 2013-2016; 4. Unutzer et al. Milbank Q 1999;77:225-6

4

Some Risk Factors for LLD

- Demographic Risk Factors
  - Older age
  - Female sex
  - Lower income
- Health
  - New/chronic medical illness
  - Vascular disease
  - Psychiatric illness history
  - Cognitive impairment
  - Sleep disturbance
  - Pain
  - Functional limitations
- Coping/Social Support
  - Recent negative life events
  - Lack of social support
    - Small social network
    - Unmarried
    - Bereaved
    - Loneliness
- Habits
  - Alcohol problem
  - Smoking
  - Low exercise level

Vink et al. Journal of Affective Disorders 2008;106:29–44.

5

Social Determinants/Late Life Depression

- A cross-sectional study of 25,503 participants in the Vit D and Omega-3 Trial (Cancer and CVD prevention) found, after controlling for confounding factors:
  - Black participants had a 10% higher severity level of PHQ-8 scores; Hispanic 23% higher; "other" group 14% higher vs non-Hispanic white subjects.
  - Anhedonia, sadness, psychomotor symptoms were more prevalent in minority groups than in white participants.
  - Among the depressed, black participants were 61% less likely to report any treatment (meds, counseling) than non-Hispanic white participants.

Vyas et al. JAMA Network Open 2020;3(3):e2601606. doi:10.1001/jamanetworkopen.2020.1606

6

Adverse Outcomes of Untreated LLD[1-7]

- Increased use of non-mental health services
  - 2x the medical appointments, 2x likelihood of polypharmacy
- Reduced adherence to medical treatment
- Functional Decline / Increased disability
- Increased morbidity/mortality:
  - CVA/MI/Hypertension/Diabetes/Dementia/SUD/Suicide
- Increased health care costs[7]
- And yet – more than ½ of depressed elders go untreated.[8]

1. Beekman et al. Psychol Med 1997;27:1397-409; 2. Bruce and Leaf. Am J Public Health. 1989;79:727-30; 3. Romanelli et al. J Am Geriatr Soc 2002;50:817-22; 4. Alexopoulos GS. *Lancet* 2005; 365): 1961–70; 5. Katon et al. Arch Gen Psychiatry 2003;60:897-903; 6. Hall and Reynolds. Maturitas 2014;79:147-52; 7. Beyer and Johnson Current Psychiatry Reports 2018;20:34-;8. Barry et al. J Affect Dis 2012;136:789-96.

7

Diagnosis: The Definitions

8

DSM-5-TR MDD = DSM-4-TR Minus Bereavement Exclusion and Depressed

- **Change from previous function, of the 5 required symptoms (present at least 2 weeks) depressed mood OR loss of interest/pleasure must be included**
- **At least 4 additional symptoms present most or all days:**
  - weight loss or decrease in appetite/weight gain
  - insomnia/hypersomnia
  - psychomotor agitation or retardation
  - fatigue/loss of energy
  - worthlessness/guilt
  - diminished concentration/decision-making
  - thoughts of death/suicide/attempt
- Distress or functional impairment
- Medical/Substance/Psychiatric exclusions
- There has not been a manic/hypomanic episode

MDD = "Major Depressive Disorder"
American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Text Revision. Washington DC, American Psychiatric Association, 2022.

9

New for DSM 5 (and TR): Persistent Depressive Disorder (aka Dysthymia)

- Incorporates 2 DSM IV disorders: Chronic Major Depressive Disorder and Dysthymic Disorder
  - Depressed mood more days than not, for at least 2 years
  - Two or more symptoms: appetite, sleep, energy, self-esteem, concentration, hopelessness
  - No remission more than 2 months at a time in 2 year period
  - Major Depressive Disorder criteria may also be met
  - Symptoms not explained by manic, hypomanic, cyclothymic, other psychiatric, substance, medical
  - Significant distress (social, occupational, other)

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Text Revision. Washington DC, American Psychiatric Association, 2022.

10

What Is Exceptional About LLD?

- Etiologies
  - Recurrence of early onset mood disorder
  - Psychosocial stressors of late life
  - Affective consequences of medical burden:
    - Disease sx can mimic depressive sx
    - Vascular depression hypothesis[1]
    - Inflammation hypothesis[2]
- Help is sought by Elders in Primary Care
  - Higher medical burden (illnesses, symptoms)
  - Fewer than half of cases are recognized[3]
  - Untreated/undertreated patients are common.

1. Alexopoulos et al. Dialogues Clin Neurosci 1999;1:68-80 ;2. Maes et al. Metab Brain Dis 2009;24:27-53; 3. Mitchell et al. Psychother Psychosom 2010;79:285-94.

11

Special Symptomatic Presentations of LLD

- Subthreshold: Beneath the "Major Depression"
- Different symptoms:
  - "Depression without sadness"[1]
  - Somatic (sometimes cognitive) focus
  - Depression with psychotic features
- Concomitant medical concerns:
  - Depression with cerebrovascular disease
  - Depression with cognitive impairment [2,3]

Gallo and Rabins. Am Fam Physician 1999;60:820-6; 2. Butters et al. Am J Psychiatry 2000;157:1949-54; 3. Sáez-Fonseca et al. J Affect Disord 2007;101:123-9

12

Depression with Psychotic Features

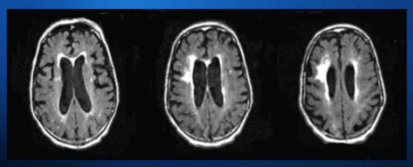
- Delusions (mood-congruent)/hallucinations (auditory) with MDD symptoms.
- Higher prevalence in older depressives.[1]
  - 20-45% of hospitalized older depressed adults
  - 15% of community older depressed adults
- Associated with:[2,3]
  - Later onset
  - Poorer response to monotherapy/maintenance
  - Higher recurrence rate/suicide risk
- ECT or combination ADD/APD are best treatments.[4]

1. Reinhardt and Cohen. Curr Psychiatry Rep 2015;17:1; 2. Gournellis et al. Int J Geriatr Psychiatry 2001;16:1085-91; 3. Flint and Rifat Am J Psychiatr 1998;155:178-83; 4. Meyers et al. Arch Gen Psychiatry. 2009;66:838–47.

13

Vascular Depression: Neuropsychological Correlations[1]

- Presence of moderate to severe white matter hyperintensities in depressed patients has been linked with increased psychomotor retardation and disability, and Neuropsychological Correlations[1];
  - Poorer Executive Functioning
  - Slower response to citalopram treatment[2]
  - Greater relapse risk



MRI Courtesy of Martin Goldstein MD

1. Kelly Jr and Alexopoulos. In Ellison et al (eds). Mood Disorders in Later Life. Informa Healthcare 2008; 2. Manning et al. Am J Geriatr Psychiatry. 2015 May:23(5):440-5.

14

Post-Stroke depression

- More than 795,000 CVAs per year in US[1]
- About 1/3 of CVA patients have Post-Stroke Depression[2]
  - Compared to Va Depression, PSD is disorder of larger blood vessels
  - Correlation of PSD with lesion location is controversial, and Current research approaches are moving beyond location of lesion to effect on larger brain networks.
- Treatment
  - Risk of PSD after CVA is reduced with use of prophylactic escitalopram or active rehabilitation program.[3]
  - SSRIs and TCAs have been shown more effective than placebo.[4]
  - Side effects can be significant.[4]
  - Change treatment if no response after 6 weeks.[4]
  - Treat at least 4 months beyond initial recovery.[4]
  - Treatment of PSD is associated with significant increase in survival.[5]
  - Preventive tx with SSRI was associated with decreased rate of PSD.[5]

1. Benjamin EJ et al. Circulation 2017;135:e229-e445; 2. Nickel A and Gotz T. Front Neurol 2017;Vol 8:Article 498. doi: 10.339/fneur2017.00498;3.Xiao-Min X et al. Medicine 2016;95(45):e5349. doi: 10.1097/MD.0000000000005349;4. Alexopoulos GS, Kelley Jr., RE: World Psychiatry 2009;8:140-9; 5. Robinson RG and Jorge RE. Am J Psychiatry 2016;173:221-231.

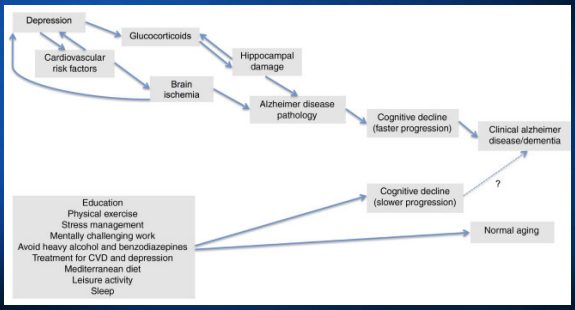
15

Depression With Cognitive Impairment

- Risk factor?
- Prodrome?
- Consequence?
- Manifestation of shared etiology?

16

Relationshi p Between Depression and Cognitive Decline



Chen et al. Am J Ger Psychiatry 2019;27(3):213-36.

17

"Masked Depression" Associated With Dementia

- Likelihood that depression is present is increased in the presence of:
  - Delusions[1]
  - Verbal/physical aggressive behaviors[2]
  - Suicidal or self-destructive behaviors
  - Disruptive vocalizations[3]
  - Weight loss[4]

1. Bassiony et al. Int J Geriatr Psychiatry. 2002;17:549-56; 2. Menon et al. Int J Geriatr Psychiatry 2001;16:139-46; 3. Dwyer and Byrne Int Psychogeriatr. 2000;12:463-71; 4. Morley and Kraenzle J Am Geriatr So 1994;42:583-5.

18

Assessment: Best Practices

19

1. Detection: Screening tools for LLD

- SELFCARE-D (Self-administered)
- Center for Epidemiological Studies – Depression Scale (CES-D)
- ***Geriatric Depression Scale (GDS)**
- ***PHQ-2, PHQ-9**
- ***Cornell Scale for Depression in Dementia (CSDD)**

1. Diagnosing, Screening, and Monitoring Depression in the Elderly: A Review of Guidelines. Canadian Agency for Drugs and Technologies in Health. Accessed 12/27/15; https://www.cadth.ca/sites/default/files/pdf/htis/sep-2015/RC0691_Diagnosing%20depression%20in%20elderly_Final.pdf
2. Phelan et al. BMC Fam Pract. 2010;11:63.

20

Assessment: GDS 15

1. **Are you basically satisfied with your life ?**
2. **Have you dropped many of your activities and interests ?**
3. **Do you feel that your life is empty ?**
4. **Do you often get bored ?**
5. **Are you in good spirits most of the time ?**
6. **Are you afraid that something bad is going to happen to you ?**
7. **Do you feel happy most of the time ?**
8. **Do you often feel helpless ?**
9. **Do you prefer to stay at home, rather than going out and doing new things ?**
10. **Do you feel you have more problems with memory than most?**
11. **Do you think it is wonderful to be alive now ?**
12. **Do you feel pretty worthless the way you are now?**
13. **Do you feel full of energy ?**
14. **Do you feel that your situation is hopeless ?**
15. **Do you think that most people are better off than you are ?**

GDS is in the Public Domain, can be freely reproduced and used. Score 1 pt for each "Yes" on 2,3,4,6,8,9,10,12,14,15 or "No" on 1,5,7,11,13. A score of 6 or higher suggests need for definitive diagnostic evaluation. (http://www.stanford.edu/~yesavage/GDS.html)

21

Psychometrics of GDS

- Appears to be most widely used screen
- In public domain, with multiple translations
- 4 versions: range from 4 to 30 questions
- GDS15 with cut-off of 5/6:
  - Sensitivity overall 86%
  - Specificity 79%
  - Figures are lower in outpatient and nursing home settings

1. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2015 Sep 8. Diagnosing, Screening, and Monitoring Depression in the Elderly: A Review of Guidelines [Internet]. https://www.ncbi.nlm.nih.gov/books/NBK321381/ accessed 12/31/18; 2. Krishnamoorthy et al. Arch Gerontol Geriatr 2019 Dec 19;87:104002. doi: 10.1016/j.archger.2019.104002

22

PHQ-2 for MDD or "Dysthymia"

Over the past 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
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed or hopeless	0	1	2	3

Score Cut-Off	Sensitivity	Specificity
≥1	99%	28%
≥2	97%	48%
≥3	64%	85%
≥4	44%	93%
≥5	23%	98%

Staples et al. Gen Hosp Psychiatry 2019;56:13-18.

23

PHQ-9 (Each point multiplied by 0,1,2,3 for not, several days, more than ½ of days, nearly all days in past 2 wk):

1. Little interest or pleasure in doing things
2. Feeling down, depressed, or hopeless
3. Trouble falling or staying asleep, or sleeping too much
4. Feeling tired or having little energy
5. Poor appetite or overeating
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down
7. Trouble concentrating on things, such as reading the newspaper or watching television
8. 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
9. Thoughts that you would be better off dead or of hurting yourself in some way

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

http://www.phqscreeners.com/sites/g/files/g10016261/f/201412/PHQ-9_English.pdf

24

PHQ-9 Psychometric Properties

- Diagnostic validity established in studies involving 8 primary care and 7 obstetrical clinics
- Scores:
  - 5 = mild
  - 10 = moderate
  - 15 = moderately severe
  - 20 = severe
- Sensitivity and specificity for PHQ9 score ≥ 10 in major depression both equal 88%.

Kroenke et al. JGIM 2001;16:606-16.

25

Cornell Scale for Depression in Dementia

Scoring System
A = unable to evaluate 0 = absent 1 = mild or intermittent 2 = severe
Ratings should be based on symptoms and signs occurring during the week prior to interview
No score should be given in symptoms result from physical disability or illness.

A. Mood-Related Signs	
1. Anxiety: anxious expression, ruminations, worrying	a 0 1 2
2. Sadness: sad expression, sad voice, tearfulness	a 0 1 2
3. Lack of reactivity to pleasant events	a 0 1 2
4. Irritability: easily annoyed, short-tempered	a 0 1 2
B. Behavioral Disturbance	
5. Agitation: restlessness, handwringing, hairpulling	a 0 1 2
6. Retardation: slow movement, slow speech, slow reactions	a 0 1 2
7. Multiple physical complaints (score 0 if GI symptoms only)	a 0 1 2
8. Loss of interest: less involved in usual activities	a 0 1 2
(score only if change occurred acutely, i.e. in less than 1 month)	

Alexopoulos et al. Biol Psych 1988;23:271-284.

26

C. Physical Signs	
9. Appetite loss: eating less than usual	a 0 1 2
10. Weight loss (score 2 if greater than 5 lb. in 1 month)	a 0 1 2
11. Lack of energy: fatigues easily, unable to sustain activities	a 0 1 2
(score only if change occurred acutely, i.e., in less than 1 month)	
D. Cyclic Functions	
12. Diurnal variation of mood: symptoms worse in the morning	a 0 1 2
13. Difficulty falling asleep: later than usual for this individual	a 0 1 2
14. Multiple awakenings during sleep	a 0 1 2
15. Early morning awakening: earlier than usual for this individual	a 0 1 2
E. Ideational Disturbance	
16. Suicide: feels life is not worth living, has suicidal wishes, or makes suicide attempt	a 0 1 2
17. Poor self esteem: self-blame, self-depreciation, feelings of failure	a 0 1 2
18. Pessimism: anticipation of the worst	a 0 1 2
19. Mood congruent delusions: delusions of poverty, illness, or loss	a 0 1 2

Alexopoulos et al. Biol Psych 1988;23:271-284.

27

Psychometrics of CSDD

	Cutoff	Sensitivity (%)	Specificity (%)	Accuracy (%)
DSM-IV-TR (n=231)	6/7	84	61	67
	7/8	77	69	71
	8/9	74	74	74
	9/10	69	82	78
	10/11	63	86	79
Nursing Home (DSM-IV-TR)	6/7	85	64	68
	7/8	80	70	72
	8/9	75	77	76
	9/10	70	82	79
Hospital Patients (DSM-IV-TR)	6/7	83	58	67
	7/8	75	68	70
	8/9	73	72	72
	9/10	69	81	77
	10/11	65	88	80

Data from Barca et al. Dement Geriatr Cogn Disord 2010;29:438-447

28

2. Assessing Effect of Medical Burden

- Medications, Alcohol, Drugs
- Endocrinopathy
- Malignancy
- Infection
- Metabolic disorders
- Nutritional deficiencies
- Sleep disorders
- Vascular disease
- Neurological disorders

- Depressive episode should be treated while managing the comorbid medical condition

29

"Masked Depression" Associated With Dementia

- Likelihood that depression is present is increased in the presence of:
  - Delusions[1]
  - Verbal/physical aggressive behaviors[2]
  - Suicidal or self-destructive behaviors
  - Disruptive vocalizations[3]
  - Weight loss[4]

1. Bassiony et al. Int J Geriatr Psychiatry. 2002;17:549-56; 2. Menon et al. Int J Geriatr Psychiatry 2001;16:139-46; 3. Dwyer and Byrne Int Psychogeriatr. 2000;12:463-71; 4. Morley and Kraenzle J Am Geriatr So 1994;42:583-5.

30

3. Assessing Laboratory Results

- **Hematology**
  - CBC with indices/differential
  - ESR
- **Chemistry**
  - Lytes, BUN, Creatinine
  - Liver function tests
  - Thyroid function tests
  - Fasting glucose level
  - Folate, B12[1]
- **Urine**
  - Urinalysis
  - Culture and sensitivity
- **Additional tests, e.g.**
  - Electrocardiogram
  - Chest X-Ray
  - Neuroimaging (?)

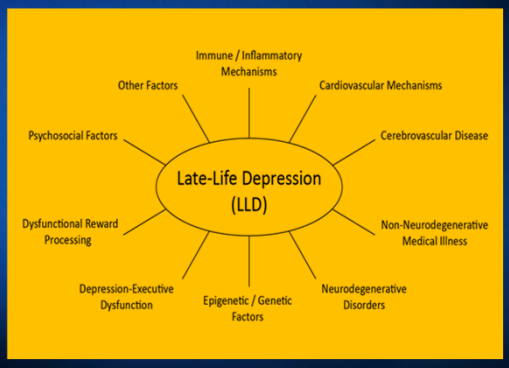
1. Petridou et al. Aging Ment Health 2015 Jun 8:1-9 epub.

31

Treatment Approach

32

Assess Contributing Factors



Husain-Krautter and Ellison. Focus 2021;19:282-93.

33

Consider Non-pharmacological treatments

- Non-pharmacological strategies, alone or with antidepressants, are effective in treating Late Life Depression and should be strongly considered when planning treatment.

Reynolds CF 3rd, Dew MA, Martire LM, *et al*. Treating depression to remission in older adults: a controlled evaluation of combined escitalopram with interpersonal psychotherapy versus escitalopram with depression care management. Int J Geriatr Psychiatry 2010; 25:1134–1141.

34

1. Psychotherapy: Several Are Evidence-Based Treatments for Late Life Depression

- RCTs support[1]
  - Cognitive Behavioral Therapy (CBT)
  - Interpersonal Therapy (IPT)
  - Problem Solving Therapy (PST)
  - ENGAGE

1. See Antognini and Liptzin in Ellison et al. Mood Disorders in Later Life. Informa 2008.

35

CBT Premises

- People, environment, social situations trigger cognitive reactions
- Cognitive reactions trigger emotional and behavioral responses
- Response depends on past experience and the skills we have to cope and react.
- These thoughts and plans can change with new cognitive and behavioral experiences.

36

CBT Strategies

- Collaborative framework
- Educational principles
- Skill building
- Questioning and inductive reasoning
- Behavioral activation

37

Interpersonal Therapy

- Based on Sullivanian interpersonal psychoanalysis
- Depression results from interactional style associated with attachment issues.
- Focuses on four areas of conflict
  - Grief
  - Role transition
  - Interpersonal deficits
  - Interpersonal conflict

38

Problem Solving Therapy

- Problem solving is a component of all psychotherapies.
- PST formulates depression as a function of:
  - Insufficient problem solving skill
  - Abandonment of skill
  - Perceived complexity of problems

39

PST techniques

- Problem Orientation
- Definition
- Brain storming
- Decision making
- Planning
- Implementation
- Evaluation
- Use of "forms"

40

ENGAGE: A New Evidence-Based Psychosocial Treatment for LLD

- An RDOC-domain based approach
  - Easily learned behavioral approach
  - Addresses dysfunction of positive valence system
    - Reward exposure: repeated activation of networks
    - Stepped
    - Personalized
- Preliminary positive results: Behavioral activation predicted depression improvement

Alexopoulos et al. J Affect Disord 2017;221:192-7.

41

2. Physical Activity

- Greater midlife physical activity is associated with lower depressive symptomatology in later life[1]
- Physical inactivity in older adults is associated with both depression and cognitive deficits[2]
- Meta-analysis supports benefit of Physical Exercise, less evidence supporting use over 80 years old or with MMSE < 23/30.[3]
- Higher and faster remission in LLD linked with exercise augmentation of sertraline (24 wk of PAE).[4]

1. Chang et al. J Gerontol A Biol Sci Med Sci 2015 Nov 2.pii: glv 196 (epub);
2. Paulo et al. J Aging Phys Act 2015 (epub); 3. Klil-Drori et al. J Clin Psychiatry 2020 Jan 21;81(1). Pii: 19r12877. doi: 10.40888/JCP. 19r12877.
4. Belvederi Murri et al. Br J Psychiatry 2015;207:235-42.

42

3. Pharmacologic Treatment Antidepressant Efficacy

- All FDA-indicated antidepressants treat LLD[1]
- Response rate (50% symptom decrease)[2]
  - 50 – 65% in ITT* trials, 25 – 30% respond to placebo
  - Number Needed to Treat (NNT*): 2.5 to 5
- Remission (≥90% symptom decrease)[2]
  - Typically 30 – 40% with medication vs 15% for placebo, NNT: 4 to 7
- Most important barrier = undertreatment![3,4]

***ITT*: Intention to Treat, *NNT*: Number Needed to Treat**

1. See Ellison et al. Mood Disorders in Later Life. Informa Health Care 2008; 2. Shanmugham et al. Psychiatr Clin North Am. 2005;28:821-35;3.Wang et al. J Clin Psychopharmacol 2005;25:118-26; 4. Barry et al. J Affect Disord 2012;136:789-96.

43

Pharmacodynamic Basis of Adverse Effects

Medication Property	Possible Clinical Consequences
NE reuptake blockade	Tremors, tachycardia, erectile/ejaculatory dysfunction, elevated blood pressure
Serotonin reuptake blockade	GI symptoms, sexual dysfunction, EPS, bruising/bleeding, bone mass density loss
Dopamine reuptake blockade	Activation, aggravation of psychosis
Histamine H_1 receptor antagonism	CNS depressant potentiation, sedation, weight gain, hypotension
Muscarinic receptor antagonism	Blurred vision, dry mouth, constipation, urinary retention, cognitive dysfunction, sexual dysfunction
NE α_1 receptor antagonism	Potentiation of some antihypertensives, postural hypotension, dizziness, reflex tachycardia

Adapted/modified from http://www.cpgnews.org/DEP/tools.cfm

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Antidepressant Side Effects: TCAs

- Anticholinergic side effects: blurred vision, urinary retention, constipation, cognitive dysfunction, delirium
- Postural hypotension
- Cardiac side effects
- Risk in overdose

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Antidepressant Side Effects: SRIs

- Discontinuation is less common with SSRI treatment (17%) than with TCA treatment (24%).
- Significant side effects with SRIs:
  - Sedation
  - Weight gain
  - GI symptoms
  - Hyponatremia
  - Risk for bruising
  - Risk for GI bleeding
  - Sexual dysfunction
  - Falls?

46

SRIs and Cardiac Safety

- SADHART[1] reported no adverse effects on LV EF, HR, BP, ECG with sertraline; ENRICHD[2] found decreased cardiac life threatening events among SSRI treated cardiac patients.
- Newer findings show risk of QTc prolongation with citalopram, escitalopram (less), amitriptyline[3,4]
- Demonstrated low risk for QTc prolongation in older adults:
  - Vilazodone[5]
  - Vortioxetine[6]

1. Shapiro et al. Am Heart J. 1999;137:1100-6;; 2. Taylor et al. Arch Gen Psychiatry. 2005;62:792-8; 3. Castro et al. BMJ 2013;346:f299. doi: 10.1136/bmj.f288; 4. Maljuric et al. Br J Clin Pharmacol 2015;80:698-705;5. Edwards et al. Int J Clin Pharmacol Ther 2013;51:456-65; 6. Katona et al. Int Clin Psychopharmacol 2012;27:215-23.

47

Antidepressant Drug/Drug Interactions

- Age exacerbates potential for adverse effects and interactions
  - Hepatic inactivation of drugs ↓
  - Renal elimination of drugs ↓
  - Anticholinergic vulnerability ↑
- Average adult > 65 years old is on 5 prescribed medications
- Many interactions are possible
  - Pharmacodynamic
  - Pharmacokinetic

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Antidepressant Cost

- Adherence can depend upon affordability
- Limitations of Medicare Part D
- Range of generically available antidepressants
- Avoid first line use of brand name drugs:
  - Trintellix (vortioxetine)
  - Fetzima (levomilnacipran)
  - Viibryd (vilazodone)
  - Emsam (transdermal selegiline)
  - Spravato (intranasal ketamine isomer)

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Predictors of Antidepressant Response [1]

- Age or Sex do not predict response
- Recurrent vs single episode doesn't predict response
- Executive Function is a predictor
  - Cognitive Control system – important for response inhibition, planning, problem solving, working memory - tested by Stroop test or (in office) trail-making test.
  - Intact CC predicted better response to escitalopram in LLD.[2]

1. Beyer and Johnson. Current Psychiatry Rep 2018;20:34;2. Alexopoulos et al. Psychol Med 2015;45:3111-20.

50

SRIs – Still 1st Choice in LLD

- Several well-tested, generic, well-tolerated, with limited drug interactions, appropriate elimination half-lives:
  - **Sertraline = best overall safety&efficacy[1]**
  - **Duloxetine – mixed findings, bonus=analgesic**
  - Paroxetine – considered effective/problematic
  - Citalopram is not more effective than other SRIs (Note FDA dosage warning to not use with QTc above 500 or with dose > 20 mg/d). Escitalopram may be less likely to prolong QTc.

1. Beyer and Johnson. Current Psychiatry Rep 2018;20:34.

51

SNRIs

- SNRIs share potential adverse effects of:
  - Hypertension
  - Anxiety
  - Insomnia
  - Share with SSRIs the potential for discontinuation symptoms

52

Other Antidepressants to Consider

- Bupropion
  - Less sedation and sexual side effects
  - Less help with anxiety/psychosis
  - Special contraindications: seizures, eating disorder
- Mirtazapine
  - More anxiolytic, less sexual side effects, less nausea
  - More weight gain and sedation
  - Could exacerbate REM sleep behavior in PD[1]
  - Associated with small/significant risk for neutropenia, agranulocytosis; minimal interaction with warfarin

1. Onofrj M, Luciano AL, Thomas A, Iacono D, D'Andreamatteo G. Mirtazapine induces REM sleep behavior disorder (RBD) in parkinsonism. Neurology 2003;60:113–5.

53

The Newer Antidepressants

- Trintellix (Vortioxetine)
  - SSRI, agonist 5HT1a, partial agonist at 5HT1b antagonist 5HT3a/5HT7
- Viibryd (Vilazodone)
  - SSRI and partial agonist at 5HT1a
- Fetzima (Levomilnacipran)
  - Balanced SNRI
- Spravato (esketamine)
  - Different mechanism and effects

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Old But Not Forgotten:

- Tricyclic antidepressants
  - Nortriptyline – validated as effective
  - Drawbacks of TCAs in late life depression
    - Anticholinergic effects
    - Postural hypotension
    - Cardiac effects
- MAO Inhibitors
  - May be appropriate for selected patients
  - Drawbacks of MAOIs in late life depression
    - Lifestyle
    - Adverse effects
    - Drug interactions

55

Stimulants*

- Limited data on use in LLD
- Small RTC showed MPH well-tolerated, effective in treating apathetic depression in medically burdened elders[1]
- MPH (mean 16 mg) + Citalopram (mean 32 mg) associated with faster and greater improvement in RTC of LLD with anxiety.[2]
- Stimulants alone or with TRD not promising[3]

*stimulants are used off label in treatment of depression

1. Padala et al. Methylphenidate may treat apathy independent of depression, Ann Pharmacother 39:1947–1949. 2. Lavretsky et al. Am J Psychiatry 2015;172:561-9; 3. Nelson JC. Am J Psychiatry 2015;172:505-7.

56

Ketamine*?

- Limited data in elderly
  - Early open trial (n=4) and more recent case series (n=6): limited benefit, significant relapse, dissociative adverse effects.[1,3]
  - RTC showed subq ketamine up to 0.5 mg/kg in 16 older TRD adults superior to midazolam. At 6 months, response+remission = 68.8%.[2]

*Subq ketamine is still investigational or off label in the treatment of depression but intranasal esketamine has been given an FDA indication for use WITH an Oral antidepressant in adults with treatment-resistant depression.

1. Szymkowicz et al. J Clin Psychopharmacol 2014;34:285-6; 2. George et al. AJGP 2017;25:1199-1209; 3.Bryant et al. J Clin Psychopharmacol 2019;39:158-61;

57

Esketamine (intranasal)?

- Esketamine plus antidepressant was studied in older adults with TRDOA (TRANSFORM-3), flexible dosing up to 84 mg x 2/wk for 4 wk.[1]
- Although the study failed to meet endpoint of significant decline in MADRS, secondary analyses suggested benefit in subjects with earlier onset (≤55) or younger age (65-74 vs ≥75).[1]
- Delivery of this treatment is challenging because of requirement for post-use observation and enrollment in Spravato REMS.
- National Institute for Health and Care Excellence has chosen not to recommend this for TRD.[2]

1. Ochs-Ross et al. Am J Geriatric Psychiatry 2020;28:121-141; 2. Mahase. BMJ
2. 2020;368:m329 doi: 10.1136/bmj.m329 (published 28 January 2020)

58

And now for something completely different… Quetiapine monotherapy

- Quetiapine XR monotherapy tested in a 9 week double-blind placebo controlled study, n=338, ages 66 and older with MDD
- Flexible dosing of 50-300 mg/d (mean dose 159 mg/d) vs placebo showed improvement on MADRS
- Sleep improved on PSQI. Excessive sleepiness was predominant adverse effect.

Katila et al. Am J Geriatr Psychiatry 2013;21:769-84

59

Electroconvulsive Therapy

- Underused modality, especially suitable with:
  - Antidepressant intolerance or non-response
  - Prior positive response to ECT
  - Delusions
  - Catatonia
  - Mania
  - Emergency

Flint and Rifat. Int J Geriatr Psychiatry 1998;13:23-8; Manly et al.
Electroconvulsive therapy in old-old patients Am J Geriatr Psychiatry. 2000 Summer;8(3):232-6.

60

ECT Efficacy

- Greater in older adults[1]
  - RUL: for ≥60 yr old, 70.4% remission vs 46% in <60
  - BT: for ≥60 yr old, 75% remission vs 58.3% in <60
- Better than meds in recent comparison:*
  - 3.1 +/- 1.1 wk to ECT remission vs 4.0 +/- 1 wk with meds[2]
  - Remission rate: 63.8% at 6 wk vs 33.3% at 12 wk in med group[2]
- Cognitive effects: stable or improved in recent study[3], mixed findings in earlier studies attributed to technique and/or underlying disease.[4]

1. Sanghani et al. Am J Geriatr Psychiatry 2014;22:S114. 2. Spanns et al. Br J Psychiatry 2015;206:67-71; 3. Verwijk et al. Int Psychogeriatr 2014;26:315-24. 4.Galvez et al. Curr Psychiatry Rep 2015;17:59-74
*This study contrasted results from two possibly noncomparable RCTs

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Transcranial Magnetic Stimulation

- TMS (rTMS) is considered safe and well-tolerated in LLD.
- May be suitable for individuals unable to accept ECT.
- Modifications:
  - Adjusted treatment schedule
  - Deep rTMS achieved efficacy in LLD of 40% vs 14.8% in control group.
  - There is interest in assessing for TR LLD

Kaster et al. Neuropsychopharmacology 2018;43(11):2231-8.

62

Additional Neurotherapies[1]

- Repetitive Transcranial Magnetic Stimulation[2]
  - 20-50% response rate open label, older adults
  - Poorer response associated with cortical atrophy
  - Better response with higher intensity stimulation?
- VNS– limited data in elderly
- *Transcranial Direct Current Stimulation
- *Magnetic Seizure Therapy
- *Deep Brain Stimulation

*these neurotherapies are used investigationally or off label in treatment of depression

1. Alexopoulos GS, Kelly Jr RE. Research advances in geriatric depression. World Psychiatry. 2009; 8(3): 140–149; 2. Galvez et al. Curr Psychiatry Rep 2015;17:59-74

63

Treatment of Depression in Dementia

- Multiple antidepressants studied, including
  - Citalopram[1]
  - Sertraline[2,5]
  - Clomipramine[3]
  - Moclobemide[4]
  - Mirtazapine[5]
- Large controlled trial (DIADS) failed to show superiority of sertraline over placebo
- Side effect assessment - more difficult in dementia
- Clinical approach – try, but discontinue if ineffective

1. Nyth et al. Acta Psychiatr Scand 1992;86:138-45; 2. Lyketsos et al. Am J Psychiatry. 2000;157:1686-9;
3. Petracca et al. J Neuropsychiatry Clin Neurosci.1996;8:270-5;4. Roth et al. Br J Psychiatry 1996;168:149-57.
5. Banerjee et al. Health Technology Assessment 2013;17(7):1-166.

64

HTA-SADD: Sertraline vs Mirtazapine vs Placebo in depressed patients with AD

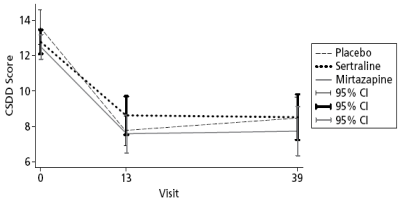

FIGURE 4 The CSDD scores by treatment group, unadjusted means with 95% CI (a lower CSDD score means fewer depressive symptoms).

Banerjee et al. 2013. Health Technol Assess. 17(7):1-166.

65

Antidepressant Treatment in Depressed, Demented Patients: What's A Clinician To Do?

- Assess symptoms severity, "masked" depression, and differential diagnosis including: pain, neuropsychiatric symptoms, cognitive decline, social isolation, quality of life[1]
- Choose target symptoms and medication and monitor improvement and adverse effects
- Based on outcome, modify approach and/or discontinue antidepressant.

1. Kubo et al. Psychogeriatrics 2018 Sep 23.doi: 10.1111/psyg.12371.

66

Treatment Resistant Depression and the "ABCD" Review

- **A**dequacy of prior treatment
  - Duration of treatment
  - Dosage of medication
- **B**ehavioral/Environmental factors
  - Personality disorder
  - Psychosocial stressors
- **C**ompliance/Adherence
  - Patient education
  - Treatment intolerance
- **D**iagnosis
  - Missed medical diagnosis or adverse medication effect
  - Missed psychiatric diagnosis

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Spotlight on Substance Use

- Benzodiazepines:
  - Chronic use (daily>3 months): 12% of elderly [1]
  - 9.5% of users are dependent[1]
- Alcohol (>7 drinks/wk is considered excessive)
  - 25% of elderly are daily drinkers
  - 10% of elderly alcohol users "binge drink"[2]
- Other drugs of concern: analgesics, hypnotics
- Illicit and nonmedical prescription drug use much greater among 50-64 year olds.[1]

1. Wu and Blazer 2010 (in press) J Aging and Health; 2. Culberson 2006;Geriatrics 61:23-27.

68

Spotlight on Pain

- Pain often accompanies MDD[1]
  - Chronic painful physical conditions are increased fourfold in MDD patients.
  - Headache, neck and back, abdominal, and musculoskeletal pain are common.
- Chronic painful physical conditions are an independent risk factor for MDD and poor treatment response.[1]
  - Pain affects other depressive symptoms adversely (exacerbates sleep, energy, anxiety symptoms).
  - MDD+pain is associated with worse outcome to SSRI treatment proportional to pain severity.
- The presence of pain is associated with increased help-seeking[2]

1. Brannan et al. J Psychiatr Research 2005;39:43-53; 2. Bonnewyn et al. J Aff Dis 2009;117:193-6.

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The Next Step in Treatment Resistant Depression

- Optimize
- Switch
- Augment/Co-prescribe
- ECT

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To Switch or To Augment?

Switch

- Slower
- Simpler, less costly
- Fewer drug interactions
- Can reduce side effects
- Introduces "new mechanism"
- Outpatient setting

Augmentation

- Quicker
- More complex, costly
- More drug interactions
- Can increase side effects
- Avoids loss of earlier partial response
- Inpatient setting

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SWITCH after SSRI-Nonresponse: What Is the Next Medication to Try?

- Some popular strategies:
  - Change drug "mechanism"?
  - Target different depressive symptoms?
  - Address depressive subtype?
    - Atypical
    - Melancholic
    - Bipolar

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Rational Polypharmacy[1]

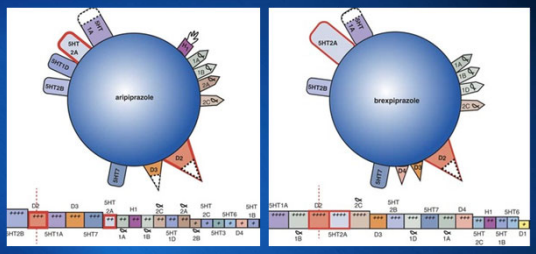
- Augmenters:
  - Lithium carbonate+*
  - Triiodothyronine+*
  - Atypical antipsychotic+
    - Aripiprazole augmented venlafaxine in TR LLD[2]
      (better than adding or switching to bupropion in OPTIMUM)
    - Brexiprazole (open label in older adults)[3]
  - Testosterone+*
- Co-Prescribed Antidepressants:
  - Mechanisms/interactions+*

+ signifies presence of credible evidence base for use/ *signifies "off label" in this use

1. See Ellison et al, in Ellison et al (eds): Mood Disorders in Later Life. New York, Informa 2008; 2. Lenze et al. Lancet 2015;Sep 24. pii: S0141-6736(15)00308-6. doi: 10.1016/SO140-6736(15)00308-6; see also the OPTIMUM study; 3. Lenze EJ et al. Lancet. 2015 Dec 12;386(10011):2404-12.

73

Aripiprazole VS Brexiprazole



Aripiprazole: greater intrinsic DA receptor agonistic activity, Accounting for activating effect.

Brexiprazole: lower DA agonistic activity and greater binding affinity for 5HT1A, 5HT2A, and alpha 1B than does aripiprazole. Less akathisia?

*Both are indicated as adjunctive treatments for depression.
Illustrations are from Stahl S. CNS Spectrums 2016;21(1);1-6

74

Atypical Antipsychotic Medications: Safety Issues

- Somnolence, orthostatic hypotension, gait disturbance[1]
- Extrapyramidal symptoms; tardive dyskinesia[1]
- ADA warning for risk of diabetes with all atypical antipsychotics[2]
- FDA warning of increased CVAEs and increased mortality is for older adults with dementia and psychosis[3,4]
- Mortality risk may include depression augmentation use[5]

1. McDonald WM. J Clin Psychiatry. 2000;61(suppl 13):3-11; 2. American Diabetes Association, et al. Diabetes Care. 2004;27:596-601; 3. Wang et al. N Engl J Med. 2005;353:2335-2341; 4. Schneider et al. JAMA. 2005;294:1934-1943;5. Gerhard et al. PLOS One 2020 Sep 30;15(9):e0239206. doi: 10.1371/journal.pone.0239206.

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Tardive Dyskinesia: Rates in Adult vs. Elderly

- Conventional Antipsychotic Medications[1,2] :
  - Year 1: Adult 5% Elderly 33%
  - Year 2: Adult 10% Elderly 50%
  - Year 3: Adult 15% Elderly 60%
- Atypical Antipsychotic Medications[3,4]
  - Year 1 Adult: 0.3-0.6%
  - Year 1 Elderly: 2.6%
- More VMAT2 inhibitor data needed in elderly.

1. Kane et al. J Clin Psychopharmacol 1988;8[4 Suppl]:52S-56S; 2. Jeste 1: J Am Geriatr Soc. 1999 Jun;47(6):716-9; 3. Csemansky et al. N Engl J Med. 346:16-22.; 4.Jeste DV. J Clin Psychiatry 2000;61[Suppl 4]:27-32.

76

Cerebrovascular Adverse Events in Dementia Trials

- Class warning for elevated risk of cerebrovascular adverse events
  - Risperidone (3.8%) vs. Placebo (1.5%); N=1230
  - Olanzapine (1.3%) vs. Placebo (.4%); N=1882
  - Aripiprazole (1.3%) vs. Placebo (.6%); N=938
  - Quetiapine (0.3%) vs. Placebo (1.9%); N=568

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FDA Warning on Mortality

- Announced April 11, 2005
- Boxed Warning: atypical antipsychotics used to treat dementia-related psychosis carry an "increased risk of death compared with placebo"
- Rate of death in drug treated patients was 4.5% vs. 2.6% in placebo group
- Risk of death 1.6 to 1.7 times that seen in placebo group
- Cause of death - heart related or infectious

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Popular Coprescriptions

Augmenter	Evidence in Adults	Evidence in Late Life Depression
TCA + SSRI/SNRI	+	+ Nortriptyline/paroxetine[1]
SSRI/SNRI + bupropion	+	+ Bupropion/paroxetine[1] +VAST-D, OPTIMUM
SSRI/SNRI + mirtazapine	+	No specific study
SSRI+Stimulant		+limited but credible data for citalopram plus methylphenidate

+ signifies presence of credible evidence base for use

1. See Ellison et al, in Ellison et al (eds): Mood Disorders in Later Life. New York, Informa 2008.

79

Combined Treatments: Who should Receive Medication AND Psychotherapy?

- Expert consensus (Alexopoulos, 2003):
  - For geriatric minor depression:
    - Psychotherapy first; meds only if unimproved at 2-3 mos.
  - For geriatric major depression:
    - Combined treatment or medication
- 3 year follow-up study
  - IPT alone: 64% recurrence
  - Nortriptyline alone: 43% recurrence
  - IPT plus nortriptyline: 20% recurrence

Reynolds et al. JAMA 1999;281:39-45.

80

The Importance of Maintenance

- Even with maintenance, there is a high recurrence rate
- Maintenance pharmacotherapy reduces recurrence risk
  - Nortriptyline + IPT[1]
  - Citalopram[2]
  - Paroxetine[3]
- Slower initial responders may do better with combined therapy in maintenance[4]

1. Reynolds et al. JAMA 1999;281:39-45; 2. Klysner et al. Br J Psychiatry 2002 Jul;181:29-35. ;
3. Reynolds et al. N Engl J Med. 2006;354:1130-8; 4. Dew et al. J Affect Disord 2001;65:155-66.

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Bereavement: Similar to but Different from Depression

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Definitions

- 11% of men, 34% of women 65 and older are "widowed".[1]
- Bereavement = loss, grief = associated feelings and behaviors. Mourning is behavioral manifestation of grief. Integrated or abiding grief develops with acceptance.[2]
- Grief can include sadness, insomnia, poor appetite, sense of the deceased's presence or voice - proceeds in waves, mixed with positive feelings, NOT typically associated with feelings of worthlessness, persistent social/occupational dysfunction, suicidality.

1. Davidow et al. AJGP 2022;30(3):404-18; Zisook and Shear. World Psychiatry 2009;8:67-74

83

Healing of Normal Grief[1]

- 4 stages: Predeath, Acute, Adaptation, Integration[1]
- 4 major tasks for integration: Accepting reality of the loss; Processing the emotional pain; Adjusting to life without the deceased; Establishing an enduring connection with deceased while moving forward.
- Peer support groups: efficacy not shown except in participants with "low interpersonal and emotional competencies".
- Symptom and self-care improvement has been shown with structured groups, specialist leaders, mindfulness techniques/spirituality.

1. Meichsner et al. AJGP 2020;28:560-9; 2. Davidow et al. AJGP 2022;30(3):404-18

84

Grief with Depression

- Two conditions can co-exist
- Interpersonal Therapy (IPT):
  - Effective treatment for grief-related depression in one study[1]
  - In another nortriptyline was superior to IPT=placebo, however combined IPT/nortriptyline participants had highest rate of treatment completion.[2]
- Citalopram, as adjunct to CGT, helped depressive, not grief symptoms.[3]

2. Reynolds et al. Am J Psychiatry 1999;156:202-8; 3. Miller et al. J Psychother Pract Res 1994;3:149-62;

85

Prolonged Grief Disorder in DSM-5-TR

(Under Trauma- and Stressor- Related Disorders)

Diagnosis (summarized)

A. Death of close relationship at least 12 months ago.

B. For more days than not, nearly every day in past month, clinically significant, intense yearning for deceased and/or preoccupation with thoughts/memories

C. At least 3 of these symptoms most days, nearly every day for last month:
  - Identity disruption, disbelief, avoidance of reminders, emotional pain, difficulty reintegrating, emotional numbness, feeling life is meaningless, intense loneliness

D. Significant functional impairment/distress

E. Duration of grief too long for cultural/religious/age-appropriate norms

F. Not substance, medical condition, or other mental disorder

American Psychiatric Association (Ed.). (2022). Diagnostic and statistical manual of mental disorders: DSM-5-TR (Fifth edition, text revision). American Psychiatric Association Publishing.

86

Complicated Grief's Complications

- Complicated Grief develops in about 7% of bereaved people.[1]
- Negative Health Consequences of complicated grief include increased risk for [2]
  - Impaired self-care
  - Disturbed sleep
  - Substance use
  - Increased suicidality
  - Worse executive function
  - Increased brain atrophy
  - Increased cognitive decline

1. Zisook and Shear. World Psychiatry 2009;8:67-74; 2. Meichsner et al. AJGP 2020;28:560-9.

87

Complicated Grief: Risk Factors

- Pre-loss factors:
  - Dysfunctional attachment
  - History of anxiety or depression
  - Female sex, older age, lower educational level, lower socioeconomic status, lower social support
- Loss-related factors:
  - Type of loss (e.g. spouse/child, stigma)
  - Suddenness
  - Immediate response
- Post-loss factors:
  - Negative coping strategies (e.g. avoidance, alcohol)
  - Lack of social support, Negative consequences

Shear et al. Curr Psychiatry Rep 2013;15:406; Bui et al. Bereavement, grief, and depression: clinical update and implications. Psychiatric Times 2017;34:31-3.

88

Interventions for Complicated Grief

- Prolonged grief disorder symptoms can be "prevented" or diminished in high-risk individuals by interent-based, therapist-assisted CBT intervention addressing education, stress management, behavioral activation, accommodation of loss, relapse prevention.[1]
- In established Complicated Grief, Complex Grief Therapy (CGT) does better than CBT, focusing on history, grief experience, situation revisiting, and personal goals e.g. coping strategies and social connections. Exposure, IPT and motivational interviewing are included in CGT.[2]

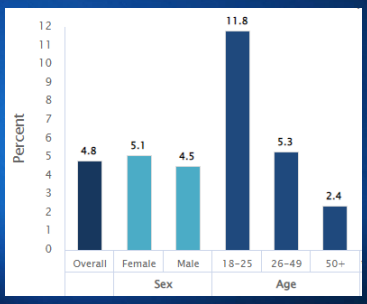
1. Litz et al. Behav Res Ther 2014;61:23-34;
2. Shear et al. JAMA Psychiatry 2014;71:1287-95.

89

Suicide in Later Life

90

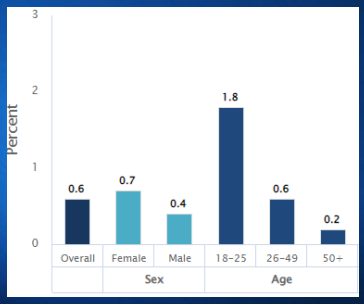
Past Year Prevalence of Suicidal Thoughts Among U.S. Adults 2019 Data Courtesy of SAMHSA



https://www.nimh.nih.gov/health/statistics/suicide.shtml accessed 1/03/22

91

Past Year Prevalence of Suicide Attempts Among U.S. Adults 2019 Data Courtesy of SAMHSA



https://www.nimh.nih.gov/health/statistics/suicide.shtml accessed 12/31/18

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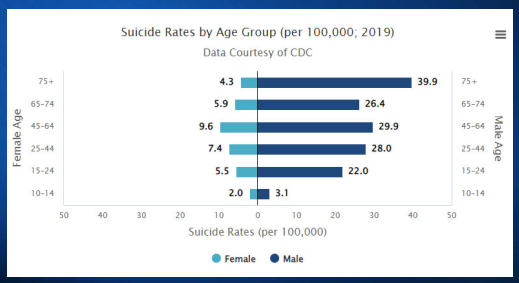
Age and Demographics of Suicide

- 2019 data:



https://www.nimh.nih.gov/health/statistics/suicide.shtml accessed 1/03/22

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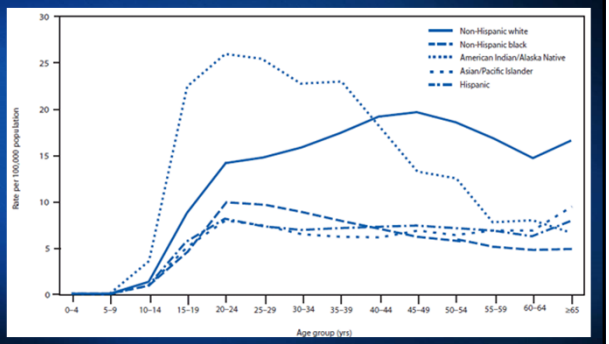
Suicides in US 1999-2007 by Age/Ethnicity



Crosby et al. Suicides — United States, 1999–2007. CDC. Morbidity and Mortality Weekly Report (MMWR), January 14, 2011 / 60(01);56-59

94

Epidemiology of Suicide in Later Life

- In older adults, one of 4 suicide attempts is fatal.[1]
- Increased risk with[2]:
  - Older, white, male
  - Widower, living alone, isolated, loss of social support, financial stress
  - Pain, Perceived poor health
  - Greater functional impairment
  - Acute stressful event, bereavement
  - Access to lethal means
  - DEPRESSION!

1. Crosby et al. Suicide Life Threat Behav 1999;29: 131-140; 2. Blazer and Friedman. Am Fam Physician 1979;20:91-6; also see Conwell et al. Completed suicide at age 50 and over. J Am Geriatr Soc 1990;38: 640-644; Conwell et al. Completed suicide among older patients in primary care practices: a controlled study. J Am Geriatr Soc 2000;48: 23-29.2000

95

Illness Risk Factors

- Major depression[1]:
  - Among depressed elderly seen in primary care during 12 months preceding suicide attempt, fewer than 1/10 received appropriate depression dx.
- Medical illnesses[2]:
  - Cancer, neurological diseases and cardiovascular diseases are the most frequently reported disorders associated with suicide. Associated Relative Risk = 1.5 to 4.
  - Recent data suggest increase in older adult suicide associated with COVID19 pandemic.[3]

1. Suominen et al. Int J Geriatr Psychiatry 2004;19:35-40; 2. Juurlink et al. Arch Intern Med 2004;164:1179-1184; 3. Liang et al. J Ger Psych Neurol 2022;35(2):245-51.

96

Assessment/Intervention: The 5 D's

Characteristic	Description	Potential Intervention
Deadly means	Firearm in home (used in 7% of late life suicides)	Firearm safety legislation, weapons removal, disposal of expired medications
Depression	Depression in 87% of older adults who die by suicide	Depression care managers in primary care, adequate treatment of late life depression
Disease/ Disability	Physical illness as well as functional disability is important	Improved health care maintenance, education, access
Disconnected	Lack of structural, functional, emotional supports	Identification and intervention for those at risk
Developmental	Vulnerability is increased by lack of safe upbringing, supports, lack of early safe, trusted relationships	Bolstering social support to modify attachment anxiety

Modified from Conwell and Lutz. Int Psychogeriatr 2021;33(2):117–119.

97

Treatment of Depression in Primary Care Settings

98

Depression and Medical Illness

- Medical burden in the elderly is great, and illnesses complicate the diagnosis of depression because of overlapping symptoms.
- Many illnesses are linked with increased depression risk: e.g. Coronary Artery Disease (15-23%), Diabetes Mellitus (17-25%), ESRD with dialysis (25%), Cancer (25%)
- Disease mechanisms can be synergistic; treatment requires attention to adverse effects / interactions.
- In general, the medical disorder and depression are both treated.

see Harnett and Pies, in Ellison et al (eds). Mood Disorders in Later Life..Informa Health Care 2008.

99

How Can Late Life Depression Be Detected and Treated More Effectively in Primary Care Settings?

- Primary Care settings are optimal site for detecting and initiating treatment of late life depression.
- Several model programs have demonstrated efficacy:
  - IMPACT
  - PROSPECT
  - PRISM-E
  - TIDES

100

"Improving Mood-Promoting Access to Collaborative Treatment": IMPACT

- 1801 patients, 25 sites, 60 or older, with major depression and/or dysthymic disorder excluding substance abuse, psychosis, high suicide risk, cognitive impairment
- "Depression Care Manager" (CM) supervised by primary care expert and psychiatrist
- Step 1: PST or AD; Step 2: alternate; Step 3: combo; Step 4: Specialty care or ECT

Unutzer et al. JAMA 2002;288:2836-2845

101

IMPACT Results

- At 12 months, 45% of intervention patients vs 19% of "usual care" had at least 50% reduction of depressive symptoms (OR=3.45, NNT=4-5)[1]
- Intervention was associated with:
  - Greater rates of depression treatment
  - Higher treatment satisfaction, Greater quality of life
  - Reduced functional impairment
  - Low increment in health care costs[2]
  - Better depression outcomes in cognitively impaired[3]

1. Unutzer et al. JAMA 2002;288:2836-2845; 2. Katon et al. Arch Gen Psych 2005;62: 1313-20; 3. Steffens et al. Am J Geriatr Psychiatry 2006;14:401-9.

102

"Prevention of Suicide in Primary Care Elderly: Collaborative Trial": PROSPECT

- Goal: better recognition and treatment of late life depression, reduction of suicide risk in primary care settings.
- Subjects: 60 or older, major/minor depression, not cognitively impaired
- Masters-level clinician collaborates with PCP in disease management program driven by algorithm:
  - Psychoeducation of patient and family
  - SSRI or, if requested or preferred, IPT
  - Treatment monitoring

Bruce and Pearson. Dialog Clin Neurosci 1999;1:100-112

103

PROSPECT Results

- For Major Depression, intervention patients benefited from:
  - More frequent remission
  - Earlier remission[1]
    - At 8 months, 43% "intervention" vs 28% "usual care"
    - NNT = 7
  - Better outcome for patients experiencing hopelessness
  - More rapid resolution of suicidal ideation[2]
  - Better outcome in cognitively impaired depressed[3]

1. Alexopoulos et al. Am J Psychiatry 2005;162:718-24;
2. Bruce et al. JAMA 2004;291:1081-91;
3. Bogner et al. Int J Geriatric Psychiatry 2007;22:922-9.

104

"Primary Care Research in Substance Abuse and Mental Health for the Elderly": PRISM-E

- Multisite randomized trial at 10 primary care and specialty MH/SA clinics randomly assigned depressed, anxious, at-risk alcohol users, or dual diagnosis patients (mean age 73.5 years) to integrated (co-located) primary and MH/SA care vs enhanced referral to specialty care.
- Treatment engagement was greater with co-located vs specialty clinic treatment
- High rate of engagement for suicidal-ideation patients (83%) in integrated model

1. Bartels et al. Am J Psychiatry 2004;161:1455-62

105

Comments On Collaborative Treatment of LLD in Primary Care Settings

- Evolving model of late life depression increases the emphasis on medical factors.
- Evolving care models demonstrate value of integration of medical with mental health care.
  - Outcome in PC setting similar to MH/SA clinic
  - Superior engagement, coordination of care
  - Possible advantage for high-risk subpopulations
  - Opportunity to integrate preventive, medical and mental health care effectively

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Conclusions

- Depression: Not a normal part of aging
- Age affects LLD:
  - Risk
  - Etiology
  - Presentation
  - Assessment
  - Treatment
  - Prognosis
- Remember to look for LLD and to treat actively!

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Good luck!

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For Questions:
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Dementia

2022 AAGP Review in Geriatric Psychiatry

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1

Dementia

Disclosures

- Marie DeWitt
  - Financial interest: None
  - Will discuss off-label medication use

2

Outline

- Background information
- DSM 5 diagnostic criteria
- Specific etiologies
- Evaluation & management
- Neuropsychiatric behaviors

3

GENERAL EPIDEMIOLOGY, RISK FACTORS & ECONOMIC BURDEN

4

General Epidemiology

- Dementia prevalence estimates
  - 1-2% at age 65+
  - Up to 30% by age 85
  - Incidence doubles with age every 5 years beginning at age 65
- MCI prevalence estimates
  - 2-10% age 65
  - 5-25% by age 85

Djh	XVD Ghp hqwld
9809<	517
:30:7	813
:80:<	4318
;30;7	4:1:
;80;<	5:18

Jorm AF, Jolley D. Neurology 1998;51:728-733

5

General Epidemiology

- The Aging, Demographics, and Memory Study (ADAMS)

	All Types of Dementia		
Age	Female	Male	Both
71-79	4.8	5.3	5.0
80-89	17.8	17.7	24.2
90+	34.7	44.6	37.2
Total	15.5	10.8	13.7

Brookmeyer et al. Alzheimers Dement. 2011; 7:61-53

6

General Epidemiology

- Increased risk of developing dementia in Amnestic MCI
  - 10-15% per year compared to 1-2% in healthy controls
  - Considered to be a prodromal form of AD

Albert et al. 2011; Alzheimers Dement. 7:270–79

7

General Risk Factors

- Age
- Female gender
- Family history (65-80%)
- Environment (20-35%)

Fratiglioni et al. Neurology 2000; 54:S10-S15; Zandi et al. JAMA 2002; 288:2123-2120

8

Economic Burden

- 5343#Frvw#lq#XV
  - '4;6#elobrq#gluhfw#frvw
  - '535#elobrq#xqsdlg#fduh
  - '414#Wulobrq#e|#5383

Stefanacci, 2011 Am J Manag Care

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DSM 5 DIAGNOSTIC CRITERIA

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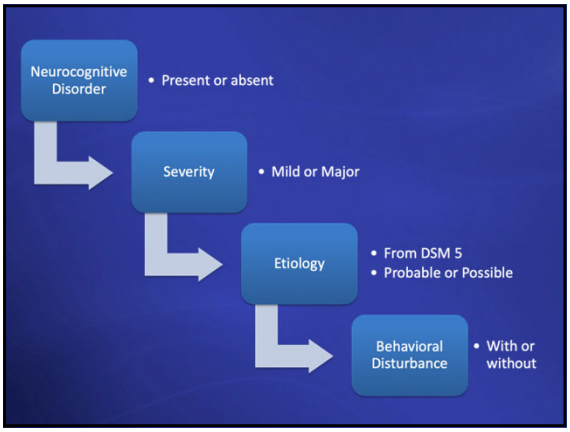

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DSM 5 Neurocognitive Disorder

Impairment in at least one cognitive domain:

- Complex attention
- Executive function
- Learning and memory
- Language
- Perceptual-motor
- Social cognition

Based upon both
- Subjective concern
- Objective evidence (determines mild versus major)

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DSM 5 MAJOR Neurocognitive Disorder

- *Significant* decline from previous functioning
- *Interferes* with independence in everyday activities

Exclusions

- Not exclusively in the context of delirium
- Not better explained by another mental disorder

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DSM 5 MILD Neurocognitive Disorder

- *Modest* decline from previous functioning
- *Does NOT interfere* with independence

Exclusions

- Not exclusively in the context of delirium
- Not better explained by another mental disorder

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Neurocognitive Disorder Specifiers

Major NCD

- –With or without behavioral disturbance
- –Severity
  - •Mild- difficulty with IADLS
  - •Moderate- difficulty with ADLS
  - •Severe- fully dependent

Mild NCD

- –With or without behavioral disturbance

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CORTICAL VERSUS SUBCORTICAL

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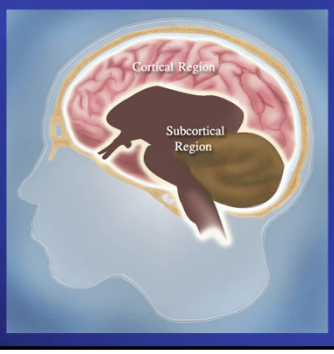
Cortical versus Subcortical



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	Cortical	Subcortical
Symptoms	• Memory encoding impairment • Aphasia • Apraxia • Agnosia	• Memory retrieval impairment • Executive dysfunction • Slowed processing speed • Reduced attention
Findings	• Recent memory is usually notably affected • Cortical release signs • Perseveration • Disinhibition	• Memory may appear normal or only mildly affected • Emotional lability • Pyramidal or extrapyramidal motor signs
Anatomy	• Neocortical association areas • Hippocampus	• Thalamus • Basal ganglia • Hypothalamus • Limbic system • Rostral brain stem

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Cortical & Subcortical Etiologies

Cortical Dementias
- Alzheimer's disease
- Large vessel vascular disease

Subcortical Dementias
- HIV associated dementia
- Small vessel vascular disease
- Parkinson's disease

Mixed Cortical-Subcortical Dementias
- Frontotemporal dementia
- Dementia due to trauma

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SPECIFIC ETIOLOGIES

20

Neurocognitive Disorder Subtypes

- Alzheimer's disease
- Frontotemporal lobar degeneration
- Lewy body disease
- Vascular disease
- Traumatic brain injury
- Substance/medication use
- HIV infection
- Prion disease
- Parkinson's disease
- Huntington's disease
- Another medical condition
- Multiple etiologies
- Unspecified

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NCD DUE TO ALZHEIMER'S DISEASE

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NCD due to Alzheimer's Disease

- Decline in memory and learning and at least one other cognitive domain
- Steadily progressive, gradual decline in cognition without extended plateaus

OR

- Causative genetic mutation from family history or genetic testing

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Cognitive Deficit	Significance	Symptom manifestation
Recent episodic memory	• Difficulty learning new information	• Forgetful • Repetitive • Losing objects
Orientation	• Disoriented sense of time	• Loses track of time
Executive function	• Poor planning or judgment • Impairment on complex tasks	• Trouble managing finances • Unsafe driving
Visuospatial	• Poor object or person recognition	• Problems navigating • Getting lost
Language	• Anomnia	• Word finding difficulty • Limited speech content
Praxis	• Ideomotor apraxia • Limb-kinetic apraxia	• Trouble getting dressed • Inability to demonstrate a task

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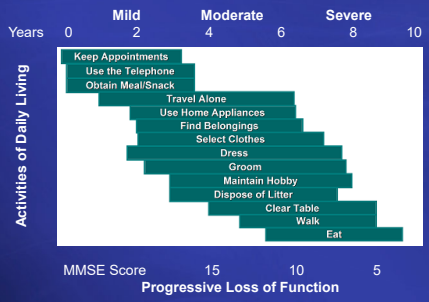
NCD due to Alzheimer's Disease



Adapted from Galasko D, et al. *Eur J Neurol*. 1998; 5 (suppl 4); S9-S17.

25

Neuropsychiatric Behaviors in AD

- Occur in 80-90% of people with AD

Dysphoria, anxiety, apathy

↓

Irritability

↓

Agitation, wandering, psychosis

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NCD due to Alzheimer's Disease

- Death due to AD most commonly from aspiration, dehydration, or sepsis
- Mean duration of survival is 10 years after diagnosis
  - Younger age at onset likely to live longer

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Epidemiology of NCD due to Alzheimer's Disease

- 60-90% of all dementias

Age	AD prevalence
65+	6%
80+	20%
95+	45%

- 50% diagnosed ages 75-83
- 40% diagnosed age 85+

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Pathology of Alzheimer's Disease

- Depletion of acetylcholine (Ach) and decline in choline acetyltransferase (ChAT) activity
- Neuronal degeneration and synaptic loss
- Loss of acetylcholine, serotonin, and norepinephrine inputs to cortex contribute to the cognitive and behavioral symptoms
- Diffuse cortical atrophy (esp. medial temporal lobes and hippocampus) resulting in hydrocephalus ex vacuo

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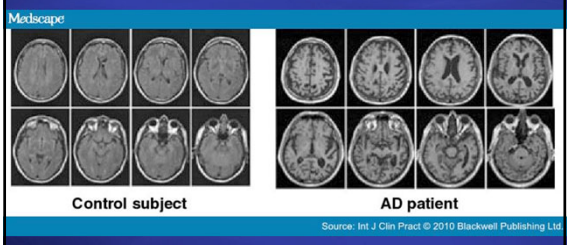
Cortical Atrophy/Synaptic Loss



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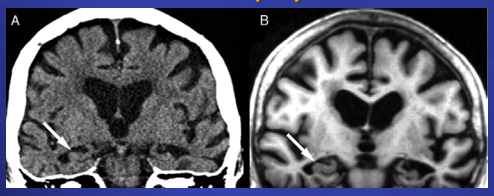
Bilateral medial temporal lobe atrophy



(A) 64 detector row computed tomography scanning

(B) 1.5 tesla MRI volumetric T1 weighted sequence

Jonathan M Schott et al. BMJ 2011;343:bmj.d5568

31

Pathology of Alzheimer's Disease

- Amyloid neuritic plaques
- Tau neurofibrillary tangles
- Cerebral amyloid angiopathy (CAA)

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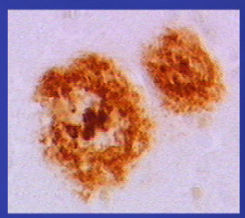
Beta Amyloid (Aβ) Plaques

- Extracellular neuritic plaques
- Composed primarily of amyloid and cellular elements
- Most concentrated in hippocampus
- Amyloid burden seen on PET using PiB



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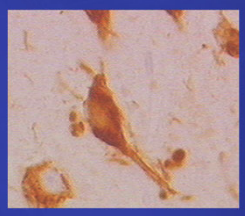
Tau Neurofibrillary Tangles

- Dense intraneuronal cytoplasmic aggregates of paired helical filaments (bifilar helices)
- Hyperphosphorylation of tau protein
- Cluster among dystrophyic neurites of senile plaques
- Found throughout neocortex and limbic nuclei



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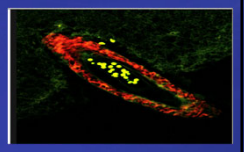
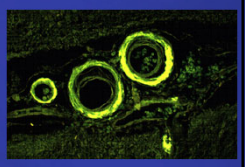
Cerebral Amyloid Angiopathy (CAA)

- Amyloid deposits in small and medium meningeal and cortical vessel walls
- Progressive loss of smooth muscle cells → weakens vessel walls, increasing the risk of hemorrhage
- Amyloid is congophilic (red)
- Under polarized light, affected arterioles show yellow-green birefringence





Weller et al. Alzheimer's Research & Therapy 2009 1:6

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Genetics

Chrom	Gene	Clinical
1	Presenilin 2 (PSEN2)	• Early onset familial • Autosomal dominant • <10% of early-onset cases
14	**Presenilin 1 (PSEN1)**	• Early onset familial • Autosomal dominant • **30-50% of early-onset cases**
19	APO ε4	• **RISK FACTOR** (susceptibility gene) • Late onset familial and sporadic • Dose-related
21	**β Amyloid Precursor (APP)**	• Early-onset familial • Autosomal dominant

Additional susceptibility genes/risk loci: CLU, PICALM, CR1, BIN1

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Cognitive Reserve/Vulnerability

Risk

- Age
- Female
- Lower level of education
- History of head injury
- Genetics
  - Familial AD accounts for <5%
  - Down Syndrome- about 30% over age 35 develop AD
- Vascular disease and risk factors

Protective

- Higher level of education
- Mediterranean diet
- Physical activity
- Social engagement

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NCD DUE TO VASCULAR DISEASE

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NCD due to Vascular Disease

- Onset of cognitive deficits is temporally related to one or more cerebrovascular events

OR

- Evidence for decline is prominent in complex attention (including processing speed) and frontal-executive function

---

- Presence of cerebrovascular disease sufficient to account for neurocognitive deficits

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NCD due to Vascular Disease

- Post-stroke dementia
  - Large vessel vascular disease
- Subcortical vascular dementia
  - Small vessel vascular disease
- Alzheimer's disease plus cerebrovascular disease
  - Mixed dementia (common)

40

Epidemiology and Course of NCD due to Vascular Disease

- Second most common cause of *dementia*
- More prevalent in men and African Americans
- Course varies

	Large Vessel	Small Vessel
Onset	Acute onset	Insidious onset
Progression	Stepwise progression with plateaus +/- fluctuations	Gradual/insidious progression +/- fluctuations

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Risk for NCD due to Vascular Disease

Cerebrovascular
- Hypertension
- Diabetes
- Smoking
- Obesity
- Elevated cholesterol
- Elevated homocysteine
- Atrial fibrillation
- Cerebral amyloid angiopathy

Genetic
- CADASIL

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Binswanger's Disease

- Binswanger's (subacute arteriosclerotic encephalopathy)
  - Widespread, microscopic areas of damage to the deep layers of white matter in the brain
  - Due to atherosclerosis of small vessels
  - Begins late in 4th decade

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CADASIL

- CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy)
  - Autosomal dominant
  - Notch 3 mutation
  - Thickening of blood vessels muscular walls blocks blood flow
  - Symptoms usually start in 4th decade

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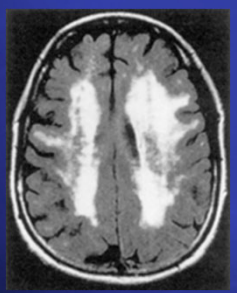
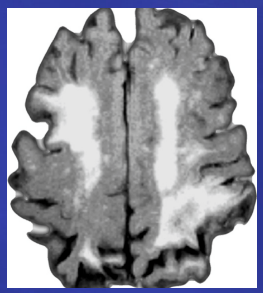
Subcortical Vascular Dementia



FDGDVLO



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NCD DUE TO LEWY BODY DISEASE

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NCD due to Lewy Body Disease

Core Features
- Fluctuating cognition with pronounced variations in attention and alertness
- Well formed and detailed visual hallucinations
- Spontaneous features of parkinsonism *after* cognitive decline

Suggestive Features
- REM sleep behavior disorder
- Severe neuroleptic sensitivity

Probable
- 2 core OR
- 1 core and 1 suggestive

Possible
- 1 core OR
- 1 suggestive

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NCD due to Lewy Body Disease

- Repeated falls
- Syncope or transient episodes of unexplained loss of consciousness
- Autonomic dysfunction
- Auditory and nonvisual hallucinations
- Systematized delusions and delusional misidentification
- Depression

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Epidemiology and Course of NCD due to Lewy Body Disease

- 2nd most common *neurodegenerative disorder* (about 20% of dementias starting after age 65)
- 1.5-2 males: 1 female ratio
- Average duration 5-6 years
- Onset 6th-9th decade, most in mid-70s, rare before 55
- Insidious onset
- Occasional plateaus with eventual progression

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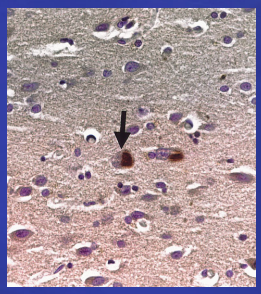
Pathology in Lewy Body Disease

- Synucleinopathy
- Not specific- Lewy bodies are found in 20-35% of all dementia cases
- DLB Lewy bodies are primarily *cortical*



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Imaging Findings in Lewy Body Disease

- SPECT/PET
  - Low/reduced striatal DAT uptake
  - Generalized low uptake with reduced occipital activity
- CT/MRI: relative preservation of medial temporal structures
- MIBG myocardial scintigraphy: low uptake
- EEG: prominent slow-wave activity, transient waves in temporal lobe

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NCD DUE TO PARKINSON'S DISEASE

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NCD due to Parkinson's Disease

- Disturbance occurs in the setting of established PD
- Insidious onset and gradual progression of impairment

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NCD due to Parkinson's Disease

- Executive dysfunction is common
- Apathy
- Depressed mood
- Anxious mood
- REM sleep behavior disorder
- Excessive daytime sleepiness
- Hallucinations
- Delusions
- Personality changes
- As cognitive impairment progresses, recognition is more affected and impairments in remote memory may emerge

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Epidemiology of NCD due to Parkinson's Disease

- 3-4% of dementia is due to PDD
- 75-80% of individuals with PD will develop dementia during lifetime
- *~10% of PD patients/year will develop dementia*
- More common in males
- Onset in 6th-9th decade; mean in early 60s

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Risk for NCD due to Parkinson's Disease

- Later age at PD onset
- Longer disease duration
- Greater disease severity
- Advanced age
- Family history of dementia (AD or PDD)
- Exposure to herbicides and pesticides

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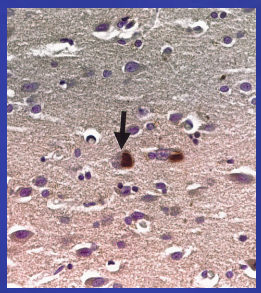
Pathology in NCD due to Parkinson's Disease

- PDD Lewy bodies are primarily in the *basal ganglia*
- DAT scans may differentiate LBD from non-LBDs



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NCD DUE TO FRONTOTEMPORAL LOBAR DEGENERATION

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NCD due to Frontotemporal Lobar Degeneration

- Insidious onset and gradual progression
- Relative sparing of learning, memory and perceptual-motor function
- Must meet criteria for either behavioral or language variant

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NCD due to Frontotemporal Lobar Degeneration

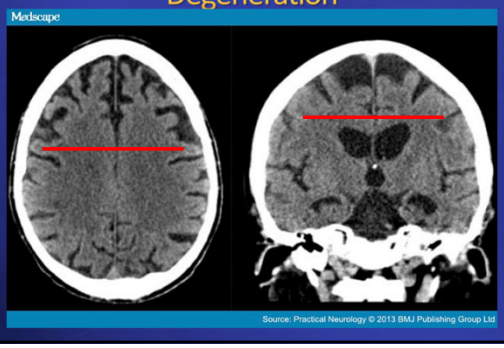
- Behavioral variant: prominent decline in social cognition and/or executive abilities plus (3 or more)
  - Behavioral disinhibition
  - Apathy or inertia
  - Loss of sympathy or empathy
  - Perseverative, stereotyped or compulsive/ritualistic behavior
  - Hyperorality or dietary changes
- Language variant (PPA): prominent decline in language ability (speech production, word finding, object naming, grammar, word comprehension)

Subtypes

  - Semantic (Fluent)
  - Agrammatic (Nonfluent)
  - Logopenic

60

Findings in Frontotemporal Lobar Degeneration



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Findings in NCD due to Frontotemporal Lobar Degeneration

Prominent

- Lack of planning and organization
- Distractibility
- Poor judgment
- Executive dysfunction (impaired mental flexibility, abstract reasoning, response inhibition)
- Apathy
- Disinhibition

Possible

- Extrapyramidal symptoms
- Motor neuron disease features present (e.g., muscle atrophy, weakness)
- Visual hallucinations

Less prominent

- Cognitive decline
- Learning and memory
- Visuospatial deficits
- Perceptual motor abilities

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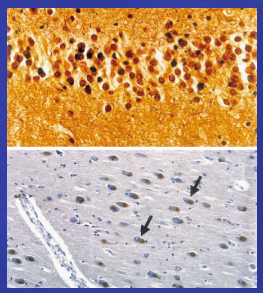
Pick Bodies

- Found in the neocortex and hippocampus
- Intraneuronal build up of tau protein
- May have depigmentation of substantia nigra
- Proteins in brain tissue: tau, ubiquitin, and TDP-43



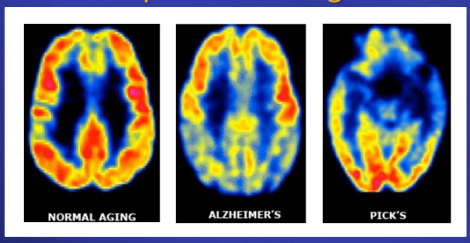
63

Atrophy in NCD due to Frontotemporal Lobar Degeneration

- Behavioral variant
  - Frontal lobes (especially medial frontal lobes)
  - Anterior temporal lobes
- Semantic language variant
  - Middle, inferior, and anterior temporal lobes with left more atrophic than right
- Non-fluent language variant
  - Left posterior frontal-insular
- Logopenic language variant
  - Left posterior perisylvian or parietal

64

PET Scan in NCD due to Frontotemporal Lobar Degeneration



FDG PET images; Red, high FDG uptake, Blue, low FDG uptake.

http://www.mghradrounds.org

65

Epidemiology of NCD due to Frontotemporal Lobar Degeneration

- ~5% of all cases of dementia
- Typical age of onset: 45-65 (range 20s-80s)
  - *2nd most common dementia in those <65 (AD is 1st)*
- Median survival is 6-11 years after symptom onset and 3-4 years after diagnosis

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Epidemiology of NCD due to Frontotemporal Lobar Degeneration

- Motor neuron disease/ALS may co-occur with FTD
  - 15% of those with FTD have evidence of MND
  - 20% of those with ALS have FTD symptoms
- Men: behavioral variant (high risk for suicide) and semantic language variant more common
- Women: nonfluent aphasia more common

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Genetics of NCD due to Frontotemporal Lobar Degeneration

- Family history in up to 40% of cases
  - 10% show an autosomal dominance inheritance
- Chromosome 17
  - *MAPT* mutations = 10-30% of familial FTD
  - *PGRN* mutations = 10% of familial FTD
  - Rare mutations: *CHMP2B*, *VCP*, C9ORF72, TDP-43 or TARDBP, and FUS

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NCD DUE TO HIV/ HIV ASSOCIATED NEUROCOGNITIVE DISORDER (HAND)

69

NCD due to HIV

- Documented infection with HIV
- Not better explained by non-HIV conditions, including secondary brain disease such as progressive multifocal leukoencephalopathy or cryptococcal meningitis

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NCD due to HIV

- Subcortical pattern
  - Impaired executive function
  - Slowing of processing speed
  - Problems with more demanding attentional tasks
  - Difficulty learning new information
- Psychiatric symptoms
  - Mood lability
  - Aggression
  - Inappropriate affect
  - Apathy
- Advanced NCD
  - Incoordination
  - Ataxia
  - Motor slowing

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Course of NCD due to HIV

- Heterogeneous
- Subcortical pattern predominates but anywhere in brain can be affected
- Resolve, improve, slowly worsen or have a fluctuating course
- Aging, Alzheimer's dementia and vascular disease can further complicate presentation

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Risk for NCD due to HIV

- Severe immunosuppression (very low CD4)
- High viral loads in CSF
- Indicators of advanced HIV disease such as anemia and hypoalbuminemia

73

MRI Findings in NCD due to HIV

- Reduction in total brain volume
- Cortical thinning
- Reduction in white matter volume and patchy areas of abnormal white matter (hyperintensities)

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NCD DUE TO TRAUMATIC BRAIN INJURY

75

NCD due to Traumatic Brain Injury

- Evidence of TBI with one or more-
  - Loss of consciousness
  - Posttraumatic amnesia
  - Disorientation and confusion
  - Neurological signs
- Neurocognitive disorder presents immediately after the occurrence of the TBI or immediately after recovery of consciousness and persists past the acute post-injury period

76

NCD due to Traumatic Brain Injury

- Common areas of impairment
  - Complex attention
  - Executive ability
  - Learning
  - Memory
  - Information processing speed
  - Social cognition
- More severe TBI
  - Aphasia
  - Neglect
  - Constructional dyspraxia
- Psychiatric symptoms
  - Irritability
  - Affect lability
  - Disinhibition
  - Apathy
  - Aggression
  - Suspiciousness

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NCD due to Traumatic Brain Injury

- Severity of TBI does not necessarily correspond to severity of resulting NCD
- Course of recovery from TBI is variable and depends on specifics of injury and
  - Age
  - Prior history of brain damage
  - Substance abuse
  - Apoε4

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NCD DUE TO SUBSTANCE/MEDICATION USE

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NCD due to Substance/Medication Use

- Substance/medication, duration and extent of use are capable of producing the impairment
- Temporal course of deficits is consistent with timing of use and abstinence
- Impairments do not occur exclusively during delirium; persist beyond intoxication and acute withdrawal

80

NCD due to Substance/Medication Use

- Sedative, hypnotic, or anxiolytics
  - Greater disturbances in memory than in other cognitive functions
- Methamphetamines
  - Difficulties with learning and memory
  - Executive dysfunction
  - May also have vascular injury

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NCD due to Substance/Medication Use

- Alcohol
  - Executive dysfunction and impairment in memory and learning
- Alcohol-induced amnestic confabulatory NCD (Korsakoff's)
  - Prominent amnesia
  - Confabulation
  - May occur with thiamine encephalopathy (Wernicke's)

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NCD DUE TO HUNTINGTON'S DISEASE

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NCD due to Huntington's Disease

- Insidious onset and gradual progression
- Clinically established HD or risk for HD based on a family history or genetic testing

84

NCD due to Huntington's Disease

- Visuospatial deficits
- Executive dysfunction
  - Processing speed
  - Organization
  - Planning
  - Impaired recall that improves with cuing
- Retention is relatively normal
- Procedural memory is impaired (evidence in tests of skill and motor learning)

85

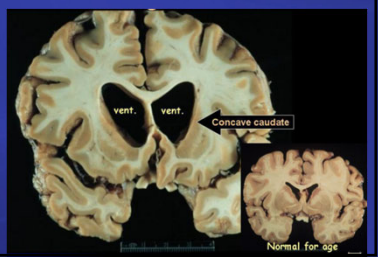
NCD due to Huntington's Disease

- Autosomal dominant
- *CAG trinucleotide expansion on chromosome 4* (exon 1 of HD gene)
  - Codes for glutamine
  - Repeat length of 36 or more
  - Longer repeat lengths are associated with earlier age of onset (*anticipation*)

86

Neuroimaging in Huntington's Disease

- Volume loss in basal ganglia (especially *caudate nucleus and putamen*) → widespread atrophy



https://medpix.nlm.nih.gov

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NCD DUE TO PRION DISEASE

88

NCD due to Prion Disease

- Insidious onset and rapid progression of impairment is common
- Motor features of prion disease, such as myoclonus or ataxia OR biomarker evidence

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Prion Disease

- Annual incidence: 1-2/million
- Any age (median age at death 67 years)
- Transmission
  - Cross-species transmission of prions
  - Corneal transplantation
  - Human growth factor
- Up to 15% of cases may have genetic component (autosomal dominant)

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Pathology in Prion Disease

- Spongiform degeneration- microscopic vacuolization of brain tissue causes tissue to deteriorate and develop into spongy texture
- Scrapie Prion Protein (PrP^{Sc})
  - Abnormal protein
  - Presence allows definite diagnosis
  - Believed to result from change in the conformation of a normal protein (cellular prion protein)

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NCD due to Prion Disease

- Sporadic
  - **Creutzfeldt-Jakob disease= sporadic CJD (sCJD)**
  - Sporadic Familial Insomnia (sFI)
- Familial
  - Familial CJD (fCJD)
  - Fatal Familial Insomnia (FFI)
  - Gerstmann-Straussler-Scheinker syndrome
- Acquired
  - Iatrogenic CJD (iCJD)
  - Variant CJD (vCJD)
  - Kuru

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NCD due to CJD

- Neurocognitive deficits
- Abnormal movements (myoclonus, chorea, dystonia), ataxia, startle reflex
- Rapid progression
- vCJD- may present more psychiatric symptoms (low mood, withdrawal and anxiety)

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NCD due to CJD

- Characteristic biomarker features
  - Multifocal gray matter hyperintensities in subcortical and cortical regions on MRI with DWI
  - *Tau or 14-3-3 protein in CSF (especially for CJD)*
  - *Characteristic periodic sharp, triphasic waves with synchronous discharges at 0.5-2Hz on EEG*
  - Family history or genetic testing for familial forms
- Testing for PrP gene in blood and other tissues
- Confirmed by biopsy or autopsy

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EVALUATION & MANAGEMENT

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Evaluation

- Goals:
  - Rule out reversible causes of symptoms
  - Identify contributing medical issues
  - Obtain information that can support/refute etiology

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Evaluation

- Interview of patient and a reliable informant
  - Comprehensive medical and surgical history
  - Social history
  - Medication history
  - Functional history
  - Review of systems
  - History of recent changes in behavior, including vegetative symptoms

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Evaluation

- Assessment
  - Medical exam
  - Neurological exam
  - Mental status exam
  - Cognitive assessments

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Evaluation

- Labs and studies
  - CBC, BMP, LFTs, TSH, Vitamin B12, RPR, HIV
  - Non-contrast head CT or MRI
- Neuropsychological testing if diagnosis is unclear

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Management

- Multidisciplinary
- Goals:
  - Improve, maintain, or slow decline in function
  - Control troublesome behaviors
  - Ease loss of independence
  - Ease caregiver burden
  - Delay placement in long-term care facility

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Management

- Discontinuation of medications that may exacerbate decline or behavior problems
- Treatment of contributing medical issues
- Pharmacotherapy
- Education for patient and caregiver
- Referral to appropriate community organization
- Respite
- Medical, financial, and legal planning

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Pharmacotherapy

- Lack of unequivocal disease modifying agents
- 2 FDA approved treatment categories
  - Acetylcholinesterase inhibitors (AChEIs)
    - Donepezil
    - Galantamine
    - Rivastigmine (also available as oral solution and patch)
    - [Tacrine]
  - NMDA Antagonist: Memantine

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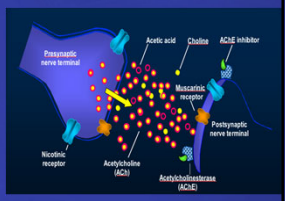
AChE Inhibitors

- Inhibit AChE activity thereby blocking the metabolism of ACh to choline and acetate
- ⇧ ACh in synaptic cleft
- ⇧ ACh availability for postsynaptic and presynaptic nicotinic (and muscarinic) ACh receptors



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103

AChE Inhibitors

- AChE Inhibitors are approved for mild and moderate AD
- Donepezil approved for severe AD
- Improve ADAS-Cog score (rate of decline remains same)
- Reduce caregiver burden
- Delay NH placement

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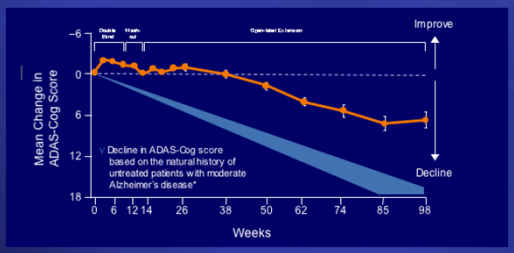
Impact of Donepezil on ADAS-Cog



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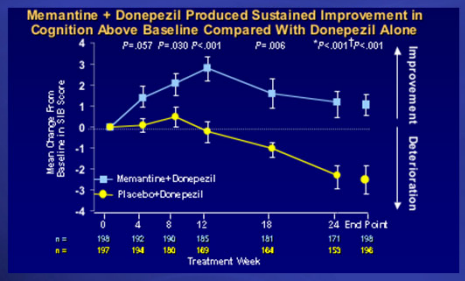
105

Memantine

- Memantine approved for moderate and severe AD
- Low affinity antagonist of NMDA receptors
- Reduces neuronal effects of abnormal glutaminergic neurotransmission
- Developed to be neuroprotective (maintain or improve cognition)
- Modest effect on cognition and global function both as monotherapy and dual therapy with AChEIs

106

Memantine and Donepezil in Moderate-Severe AD



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Pharmacotherapy: NCD due to PD

- Rivastigmine is only approved drug for PDD
  - Modest improvements in attention and executive function and stabilization of ADLs
  - Increasing data to support use of donepezil
  - Galantamine and memantine haven't had enough adequate trials

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Pharmacotherapy: NCD due to FTLD

- AChEIs may worsen irritability
- Management is symptomatic
  - SSRIs for irritability, impulsivity, and compulsions (off label use)
  - Trazodone and atypical antipsychotics for physical agitation (off label use)

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NEUROPSYCHIATRIC BEHAVIORS ASSOCIATED WITH DEMENTIA

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Neuropsychiatric Behaviors

- Mood
- Anxiety
- Irritability
- Impulsivity
- Apathy
- Disinhibition
- Wandering
- Pacing
- Pseudobulbar affect
- Obsessive/repetitive mannerisms
- Hallucinations
  - Visual
- Delusions
  - Persecution
  - Misidentification

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Neuropsychiatric Behaviors

- Agitation
  - Verbal
  - Physical, non-aggressive
  - Physical, aggressive

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Theories

- Direct impact of dementia

Region	Cardinal Signs
Orbitofrontal system	Disinhibition
Mesial frontal system	Apathy

- Unmet needs
  - Unable to recognize needs
  - Unable to address/communicate needs

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Assessment

- Identify specific behavior
- Define events surrounding behavior
- Why now?
- What was outcome?
- Pain, hunger, thirst, fatigue, etc?
- Change in environment?
- Known change in medical status?
- Change in medications?

114

Evaluation

- Work-up for delirium
- Premorbid psychiatric conditions
  - Trauma
  - Depression
  - Anxiety
  - Substance use
  - Personality

115

Non-Pharmacologic Management

- Caregivers
  - Education
  - Redirection
  - Distraction
- Environmental
  - Physical activity
  - Sensory stimulation
  - Designed appropriately

116

Pharmacologic Management

- Treatment often ends up targeting symptoms and not underlying cause
- No medications FDA approved for treatment of neuropsychiatric behaviors of dementia
- Pimavanserin- FDA approved for hallucinations/delusions in PD
- Dextromethorphan-quinidine- FDA approved for PBA in ALS and MS

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Pharmacologic Management

- AChE Inhibitors and Memantine
  - Meta-analyses and guidelines support use of acetylcholinesterase inhibitors to treat/manage neuropsychiatric behaviors that warrant medication
  - Stabilized or improved neuropsychiatric symptoms shown with
    - Galantamine
    - Donepezil and memantine when used together

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Pharmacologic Management: Use of antidepressants

- Conflicting data regarding efficacy treating/managing depression as NPS
- CitAD showed improvement in agitation with citalopram (off label use for agitation)
- Citalopram with some benefit in apathy (off label use)

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Pharmacologic Management: Use of mood stabilizers

- Carbamazepine (black box warning) has most evidence (off label use for agitation)
- Minimal evidence for use of gabapentin, topiramate and lamotrigine (more RCTs needed) (off label use for agitation)
- Essentially no evidence for use of valproate, oxcarbazepine, and lithium (off label use for agitation)

120

Pharmacologic Management: Use of antidepressants

- Black box warning
- Aripiprazole, risperidone and olanzapine have most evidence (off label use for agitation)
- Pimavanserin FDA approved for hallucinations/delusions in PD
- Quetiapine for visual hallucinations in NCD due to LBD or PD (off label use)

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Good Luck!

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Substance Use in Older Adults and Comorbid Psychiatric Conditions

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McLean Hospital

1

DISCLOSURES

- **Olivera Bogunovic, MD** has no financial relationships to disclose relating to the subject matter of this presentation

2

LEARNING OBJECTIVES

- Review prevalence rates of substance abuse among older adults
- Discuss special considerations for older adults
- Explore co-occurring psychiatric disorders in older adults
- Better understand diagnosis of substance use disorders in this population
- Understand implementation of evidence-based treatment

3

TOPICS TO BE COVERED: SUBSTANCE USE DISORDERS IN OLDER ADULTS

- Prevalence of Substance Use Disorders
- Special considerations for older adults
- Alcohol use
- Other illicit drug use
- Comorbid psychiatric conditions
- Treatment and rehabilitation strategies

4

SUBSTANCE USE DISORDERS IN OLDER ADULTS

Prevalence of substance use disorders

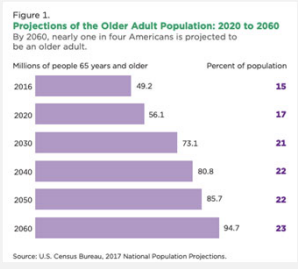
- Special considerations
- Alcohol use
- Other substance use
- Comorbid psychiatric conditions
- Treatment and rehabilitation strategies

5

THE GERIATRIC POPULATION IS GROWING

Baby Boomer Generation[1, 2]

- Years Born: 1944–1964 (78 million births)
- Current Ages: 56–76, first turned age 70 in 2017
- Make up 21% of our current population
- **By 2030,** all will be >65 and **adults 65 years of age or older will account for >20% of the population** (73.1 million people)



1 https://www.prb.org/aging-unitedstates-fact-sheet/
2 https://www.statista.com/statistics/296974/us-population-share-by-generation/

6

THERE IS INCREASED PROPENSITY FOR DRUG ABUSE IN BABY BOOMER GENERATION

- **Increased life expectancy** in the general population and **improved access to healthcare**, harm reduction, and drug treatment is leading to more longevity among drug users[1]
- Historic thinking about SUD in older adults is that people "age out" of drug addiction[2,3]
- **Baby Boomers** (and post-baby-boom cohorts) are **more accepting of drug use** than previous generations, experienced **more drug availability** and had higher rates of illicit drug use during their youth than previous generations[4]
  - **Social upheavals** of the 1960s and 1970s, included a dramatic increase in the use of illicit drugs
  - **Increase in opiate prescriptions** in mid 1990s – early 2000s (pain as a "fifth vital sign")[5]
    - Retail sales of oxycodone and hydrocodone increased by 866% and 280%, respectively, from 1997 through 2007

1 Carew AM, Comiskey C. Treatment for opioid use and outcomes in older adults: a systematic literature review. *Drug Alcohol Depend.* 2018;182:48-57.
2 Snow M. Maturing out of narcotic addiction in New York City. *Int J Addict* 1973;8:921–938.
3 Winnick C. Maturing out of narcotic addiction. *Bull Narc* 1962;14:1–7.
4 Cross HJ, Kleinhesselink RR: The impact of the 1960s on adolescence. *Journal of Early Adolescence* 5:517-538, 1985.
5 Chisholm-Burns MA, Spivey CA, Sherwin E, Wheeler J, Hohmeier K. The opioid crisis: Origins, trends, policies, and the roles of pharmacists. Am J Health Syst Pharm. 2019 Mar 19;76(7):424-435.

7

IT IS DIFFICULT TO QUANTIFY THE IMPACT OF ADDICTIVE SUBSTANCE ON THE ELDERLY

- Nicotine — 4% - 22%[1]
- Alcohol — Binge: 9% (in past month)[2]; Dependence: 2.1% - 67%
- Marijuana — 2.9% – 3.9%
- Opiates — <1% - 21%;
- Benzodiazepines — 1.7% - 11.4%

True incidence/prevalence is not known due to variable diagnostic / screening tools, definition of abuse, dependence, misuse

1 Yarnell, S., Li, L., MacGrory, B., Trevisan, L., & Kirwin, P. (2020). Substance Use Disorders in Later Life: A Review and Synthesis of the Literature of an Emerging Public Health Concern. *The American Journal of Geriatric Psychiatry, 28*(2), 226–236.
2 Han, B. H., Moore, A. A., Sherman, S. E., & Palamar, J. J. (2018). Prevalence and correlates of binge drinking among older adults with multimorbidity. *Drug & Alcohol Dependence, 187*, 48–54.

8

ADMISSIONS OF ADULTS 65+ FOR SUBSTANCE USE ABUSE IS GROWING

According to the 2017 TEDS, adults age >65 represented **1.3% (26,110) of all admissions to substance abuse treatment,** increase from 0.7% (15,116) of admissions in 2007

	Percent of Admissions of adults 65+
Alcohol (including alcohol only and alcohol + 2nd drug)	**52%**
Opiates	**25%**
Cocaine	5%
Sedatives	3%

Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 11.21.18.

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SUBSTANCE USE DISORDERS IN OLDER ADULTS

- Prevalence of substance use disorders

Special considerations

- Alcohol use
- Other substance use
- Comorbid psychiatric conditions
- Treatment and rehabilitation strategies

10

THERE ARE MULTIPLE RISK FACTORS FOR SUBSTANCE USE IN LATER LIFE

General Risk Factors for SUD

- Age of first exposure to substances
- Adverse childhood experiences
- History of trauma
- Psychiatric co-morbidities
- Family hx of substance use disorder

Older adults

- **Disability**
- **Loss of a partner**
- **Chronic physical illness or pain**
- **Loneliness or social isolation**
- **Being a caregiver**
- **Change in living situation or career**

Aging is NOT protective against SUDs, a significant number of people initiate substance use later in life

Yarnell, S., Li, L., MacGrory, B., Trevisan, L., & Kirwin, P. (2020). Substance Use Disorders in Later Life: A Review and Synthesis of the Literature of an Emerging Public Health Concern. *The American Journal of Geriatric Psychiatry*, *28*(2), 226–236.

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OLDER ADULTS ARE AT HIGHER RISK FOR COMPLICATIONS FROM SUBSTANCE MISUSE/ ABUSE

- **Decrease in hepatic metabolism** affects pharmacokinetics of alcohol and other drugs, leading to increase susceptibility to harmful effects
- Older adults are more likely than younger adults to have chronic health conditions and to **take more prescription medications** that can interact with alcohol and other illicit substances
- **Co-existing medical conditions** can complicate the diagnosis of SUD in older adults
- Usual **social indictors of impaired function can be less relevant** for older adults (difficulty at work, problems with driving, legal charges)
- The likelihood that a PCP will have a conversation about alcohol declines as the patient ages

Lehmann SW, Fingerhood M. Substance-Use Disorders in Later Life. *N Engl J Med*. 2018;379(24):2351-2360.

12

OLDER ADULTS WHO MISUSE SUBSTANCES CAN BE CLASSIFIED AS EARLY ONSET VS LATE ONSET

Early onset

- Approx 2/3rd
- Men > women
- Prior history of AUD
- Psychiatric co-morbidities common

Late onset (>55)

- Approx 1/3rd
- Women > men
- Appear psychologically / physically healthier
- Escalating use often in setting of **major life changes** (retirement, death of a spouse)
- More amenable to treatment

Han BH, Moore AA. Prevention and Screening of Unhealthy Substance Use by Older Adults. *Clin Geriatr Med.* 2018;34(1):117-129. doi:10.1016/j.cger.2017.08.005

13

SCREENING & ASSESSMENT IS DIFFICULT IN THE GERIATRIC POPULATION

Where are most older adults screened for AUD?

- Primary care setting (87% of patients see PCP)
- Mental health settings
- Other potential sources: Friends, meal delivery personnel, staff members at senior citizen centers, health fairs, nursing homes

What is involved in an assessment?

- Skillful interviewing
- Psychiatric evaluation
- Evaluation of motivational stage of change
- Neurological evaluation
- Functional evaluation
- Social evaluation

Especially important in geriatric population

Ross, S. Alcohol Use Disorders in the Elderly. Primary Psychiatry. 2005;12(1):32-40.

14

DSM-5 SUBSTANCE USE DISORDER

A problematic pattern of use leading to **clinically significant impairment or distress** is manifested **by two or more of the following** within a 12-month period:

1. Often taken in larger amounts or over a longer period than was intended.
2. A persistent desire or unsuccessful efforts to cut down or control use.
3. A great deal of time is spent in activities necessary to obtain, use, or recover from the substance's effects.
4. Craving or a strong desire or urge to use the substance.
5. Recurrent use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by its effects.
7. Important social, occupational, or recreational activities are given up or reduced because of use.
8. Recurrent use in situations in which it is physically hazardous.
9. Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance
10. Tolerance.
11. Withdrawal.

Mild: 2 – 3

Moderate: 4 – 5

Severe: 6+

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DSM-5 MAY NOT CAPTURE PROBLEMATIC DRINKING IN OLDER ADULTS

Partial DSM –V Criteria for SUD	Considerations for Older Adults
A substance is often taken in larger amounts or over a longer period than was intended.	**Cognitive impairment** can prevent adequate self-monitoring. Substances may more greatly impair cognition among older adults than younger adults.
There is craving or a strong desire to use the substance.	Older adults with **entrenched habits** may not recognize cravings.
There is recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or at home.	**Role obligations** may not exist for older adults in the same way as for younger adults because of life-stage transitions (retirement)
Important social, occupational, or recreational activities are given up or reduced because of substance use.	Older adults may engage **in fewer activities** regardless of substance use
Tolerance - a need for markedly increased amounts of the substance to achieve intoxication or the desired effect OR a markedly diminished effect with continued use of the same amount of the substance	Because of the **increased sensitivity** to substances as they age, older adults will seem to have lowered rather than increase in tolerance.
Withdrawal - characteristic withdrawal symptoms or the needs to medication to relieve or avoid withdrawal symptoms	Withdrawal **symptoms can be more subtle**, late-onset substance users may not develop physiologic dependence

Han, B. H., & Moore, A. A. (2018). Prevention and Screening of Unhealthy Substance Use by Older Adults. *Clinics in geriatric medicine*, *34*(1), 117–129.

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SUBSTANCE USE DISORDERS IN OLDER ADULTS

- Prevalence of substance use disorders
- Special considerations
- **Alcohol use**
- Other substance use
- Comorbid psychiatric conditions
- Treatment and rehabilitation strategies

17

IT IS RECOMMENDED THAT OLDER ADULTS LIMIT ALCOHOL INTAKE

- The National Institute on **Alcohol Abuse and Alcoholism (NIAAA)** and the **Center for Substance Abuse Treatment (CSAT)** recommend people age ≥ 65 consume:
  - **No more than one standard drink / day or seven standard drinks / week**
  - **No more than two standard drinks on any drinking day** or occasion (e.g.l, wedding, New Year's Eve, etc.)
- Women age 65 or older should consume slightly lower amounts than those listed above as they get older.

A standard drink is 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of distilled spirits ("hard" alcohol). These recommendations also fit into the current research information about the health benefits for some older adults of a small amount of alcohol (one drink per day).

https://www.aagponline.org/index.php?src=gendocs&ref=substanceabuse&category=Foundation

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THERE IS WIDE SPAN OF ALCOHOL MISUSE AMONG OLDER ADULTS

- Abstinence
- Low-risk use
- **At risk drinking** – more than 1 drink / day (maximum of 2 drinks on any "drinking occasion")
- **Hazardous Drinking** – pattern of consumption that carries a risk of consequences
  - Binge drinking
  - Drinking with medications
  - Drinking with co-morbid medical d/o
- **Harmful Drinking** – drinking causing physical or mental harm
- **Dependence**

Alcohol mis-use

14.5% of older drinkers consume alcohol at a level **above the limit** recommended by the Ntl Inst on Alcohol Abuse and Alcoholism

When coexisting medical conditions (e.g., HTN, DM) are factored in, **53.3%** of drinkers 65 years or older have **potentially harmful levels of consumption**

Culberson JW (2006). Alcohol use in the elderly: beyond the CAGE: part 1 of 2: prevalence and patterns of problem drinking. *Geriatrics, 61*(10), 23–27.
Lehmann SW, Fingerhood M. Substance-Use Disorders in Later Life. *N Engl J Med*. 2018;379(24):2351-2360. doi:10.1056/NEJMra1805981

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THERE IS A HIGH PREVALENCE OF GERIATRIC ALCOHOL USE IN THE MEDICAL ENVIRONMENT

- 10 – 15% Primary Care Patients with "problem drinking" (drinking that has resulted in adverse medical, physiological, social consequences or increases likelihood of these problems)
- 30% of all older patients hospitalized in general medicine units with alcohol use disorder
- 50% of all older patients hospitalized in psychiatric units

Bommersbach, T. J., Lapid, M. I., Rummans, T. A., & Morse, R. M. (2015). Geriatric Alcohol Use Disorder: A Review for Primary Care Physicians. *Mayo Clinic Proceedings, 90*(5), 659–666.

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THERE IS AN INCREASE RISK OF ADVERSE EFFECTS FOR GERIATRIC PATIENTS WHO USE ALCOHOL

- **Increased Blood Alcohol Concentration** because
  - Decreased lean body mass
  - Decreased total body water
  - Decreased gastric alcohol dehydrogenase

Older adults can have a higher blood alcohol level and demonstrate less awareness of impairment

- Alcohol and drugs **more intoxicating** in geriatric patients
  - Increased blood-brain barrier permeability
  - Increased sensitivity to sedative effects of alcohol – increased risk of falls

Many older adults with multiple medications that can adversely interact with alcohol

Yarnell, S., Li, L., MacGrory, B., Trevisan, L., & Kirwin, P. (2020). Substance Use Disorders in Later Life: A Review and Synthesis of the Literature of an Emerging Public Health Concern. *The American Journal of Geriatric Psychiatry, 28*(2), 226–236.

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MEDICAL COMPLICATIONS OF ALCOHOL IN GERIATRIC PATIENTS

- **Cirrhosis:** 60% 1-year death rate > age 60 vs 7% in younger population
- **Cardiac problems** (coronary artery disease – exacerbating HTN and HLD, masking angina pectoris; atrial fibrillation)
- **Cancers** (upper GI, liver, renal)
- **Thrombocytopenia**
- Potential for **drug-interactions**
- **Osteomalacia** (alcohol inhibitory effect of hydroxylation of vitamin D)

Bommersbach, T. J., Lapid, M. I., Rummans, T. A., & Morse, R. M. (2015). Geriatric Alcohol Use Disorder: A Review for Primary Care Physicians. *Mayo Clinic Proceedings*, 90(5), 659–666.
Thygesen LC, Mikkelsen P, Andersen TV, Tønnesen H, Juel K, Becker U, & Grønbaek M. (2009). Cancer incidence among patients with alcohol use disorders--long-term follow-up. *Alcohol & Alcoholism*, *44*(4), 387–391.

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NEUROLOGIC COMPLICATIONS OF ALCOHOL IN GERIATRIC PATIENTS

- Increased risk for **stroke** (ischemic / hemorrhagic)
- **Wernicke encephalopathy** – thiamine deficiency → ophthalmoplegia, gait ataxia, confusion
  - Poor diet, impaired absorption and altered metabolism of thiamine
  - 17% mortality
- **Korsakoff syndrome** – retrograde and anterograde amnesia, confabulation
  - Will developed in 80 – 90% of people with WE if untreated
- **Alcohol-Induced Major / Mild Neurocognitive Disorder** – neurotoxic effects of ethyl alcohol (thiamine deficiency, vascular injury, immune-related injury can also play a role)
  - Reduction in white matter density in frontal cortex
  - Memory and executive functions
  - Prefrontal and frontal on neuroimaging studies both at micro- and macrostructural level
  - Older adults with AUD are twice as likely to develop severe memory impairment

Bommersbach, T. J., Lapid, M. I., Rummans, T. A., & Morse, R. M. (2015). Geriatric Alcohol Use Disorder: A Review for Primary Care Physicians. *Mayo Clinic Proceedings*, 90(5), 659–666.
Thygesen LC, Mikkelsen P, Andersen TV, Tønnesen H, Juel K, Becker U, & Grønbaek M. (2009). Cancer incidence among patients with alcohol use disorders--long-term follow-up. *Alcohol & Alcoholism*, *44*(4), 387–391. Topiwala A, Ebmeier KP. Effects of drinking on late-life brain and cognition. *Evid Based Ment Health*. 2018;21(1):12-15.

23

ALCOHOL USE HAS BEEN ASSOCIATED WITH RISK OF DEVELOPING DEMENTIA

- Some studies have shown a statistically significant association between **light to moderate** alcohol use and a **lower risk of being diagnosed with cognitive impairment** and different types of dementia, however, **these results have not been consistently reported** and recent examination of the literature finds this evidence to be only moderate
- **Chronic heavy alcohol use was associated with an increased risk** of being diagnosed with either cognitive impairment or dementia
  - A 2-year follow-up study of 2632 participants found that excessive drinking had a 45% increased risk of dementia
- An association was also found between engaging in **irregular heavy drinking** and the risk of being diagnosed with either cognitive impairment or dementia

Deng J, et al. *Clin Neurol Neurosurg*. 2006;108(4):378-383. Crews FT, et al. *Alcohol Clin Exp Res*. 2005;29(8):1504-1513.
Rehm J, Hasan OSM, Black SE, Shield KD, Schwarzinger M. Alcohol use and dementia: a systematic scoping review. Alzheimers Res Ther. 2019 Jan 5;11(1):1.

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ALCOHOL WITHDRAWAL IN OLDER ADULTS

- **Confusion,** rather than tremor and tachycardia, is often the predominant clinical sign
- **Severity** of withdrawal symptoms may increase with age and for adults 50+ there is a dose-dependent relationship between withdrawal and time required for detox
- There are no specific guidelines for management of alcohol withdrawal for older patients
  - Benzodiazepines used in a symptom-triggered approach (CIWA)

Lehmann SW, Fingerhood M. Substance-Use Disorders in Later Life. *N Engl J Med.* 2018;379(24):2351-2360.

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SIGNS OF POSSIBLE PROBLEMATIC SUBSTANCE USE IN OLDER ADULTS

Psychiatric Symptoms	Sleep disturbances, frequent mood swings, persistent irritability, anxiety, depression
Physical Symptoms	Nausea, vomiting, poor coordination, tremors
Physical Signs	Unexplained injuries, falls or bruises, malnutrition, evidence of self-neglect (e.g., poor hygiene)
Cognitive changes	Confusion and disorientation, memory impairment, daytime drowsiness, impaired reaction time

Lehmann SW, Fingerhood M. Substance-Use Disorders in Later Life. *N Engl J Med.* 2018;379(24):2351-2360.

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SCREENING METHODS AND INSTRUMENTS

- **Questions about quantity and frequency**
  - How many days does the individual drink
  - Number of drinks consumed
  - Maximum number of drinks on any given occasion

What might make the typical screening instruments less helpful in the geriatric population?

- **Traditional instruments**
- **CAGE** questionnaire / CAGE-AID
- **AUDIT** (Alcohol Use Disorders Identification Test)
- **ASSIST** (Alcohol, Smoking, and Substance Involvement Screening Test)
- **MAST** (Michigan Alcoholism Screening) / Short-MAST / Drug-AST

Geriatric-specific instruments

- **MAST-G** (Michigan Alcoholism Screening) / Short-MAST –G
- **ARPS** (alcohol related problems survey)
- **DPI** (Drinking Problem Index)

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HOW IS THE SMAST-G DIFFERENT?

- **Removes** questions asking **about legal consequences and employment or family role obligations**
- Reframes questions around **normative drinking habits and interaction with medical personnel**
- Includes additional questions asking about **physical and medical consequences** of drinking
- Further explores **underlying mental health and emotional triggers** for alcohol use

1. When **talking with others, do you underestimate** how much you really drink?
2. After a few drinks, **have you eaten or have been able to skip a meal** because you didn't feel hungry?
3. Does having a few drinks help **decrease your shakiness or tremors**?
4. Does alcohol sometimes make it **hard for you to remember parts of the day or night**?
5. Do you usually take a drink to **relax or calm your nerves**?
6. Do you drink to **take your mind off your problems**?
7. Have you increased your drinking after **experiencing a loss in your life**?
8. Has a **doctor or nurse** ever said they were worried or concerned about your drinking?
9. Have you **ever made rules to manage** your drinking?
10. When **you feel lonely**, does drinking help?

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SUBSTANCE USE DISORDERS IN OLDER ADULTS

- Prevalence of substance use disorders
- Special considerations
- Alcohol use
- **Other substance use**
  - **Benzodiazepines**
  - Marijuana
  - Cocaine
  - Opiates
- Comorbid psychiatric conditions
- Treatment and rehabilitation strategies

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BENZODIAZEPINES ARE WIDELY PRESCRIBED FOR OLDER ADULTS

- There is a consensus among medical and psychiatric associations, including the American Geriatrics Society**, that benzodiazepines should be avoided in patients > 65** (Beers Criteria)
- Benzodiazepine **prevalence among adults ≥65 is 8.6%** (vs 5% of the U.S. adult population)[1]
- Approximately one-third of older adults between 65 and 80 received benzodiazepines for longer than 120 days in a year[2]
- PCPs prescribe the largest absolute number of long-term benzodiazepines due to seeing the greatest number of elderly patients, however, **PCPs prescribe benzodiazepines at a similar rate as psychiatrists**[2]
- The proportion of visits for long-term continuation of benzodiazepine prescriptions increases with age, even among persons who are 80 years of age or older

1 Maust DT, Lin LA, Blow FC. Benzodiazepine Use and Misuse Among Adults in the United States. *Psychiatr Serv*. 2019;70(2):97-106.
2 Markota M, Rummans TA, Bostwick JM, Lapid MI. Benzodiazepine Use in Older Adults: Dangers, Management, and Alternative Therapies. *Mayo Clin Proc*. 2016;91(11):1632-1639.
Maree RD, Marcum ZA, Saghafi E,Weiner DK, Karp JF.A Systematic Review of Opioid and Benzodiazepine Misuse in Older Adults. *Am J Geriatr Psychiatry*. 2016;24(11):949-963.

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BENZODIAZEPINE MISUSE IS LIKELY UNDERRECOGNIZED IN OLDER ADULTS

- Although prevalence of benzodiazepines use among older adults is similar to younger adults, **the diagnosis of benzodiazepine use disorder is much lower**
  - 0.6% for adults >65 vs up to 5.2% for adults18–25
  - Other datasets have predicted 12-month prevalence of diagnosed sedative, hypnotic, or anxiolytic use disorder is as low as 0.04%
- Compared to younger adults, **more likely to endorse misuse to help with sleep** rather than misuse to get high
- Although alprazolam is the most commonly mis-used benzodiazepine overall, older **adults are more likely to misuse lorazepam and diazepam** than younger adults

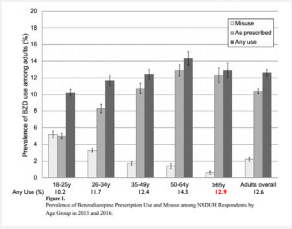

Figure 1.
Prevalence of Benzodiazepine Prescription Use and Misuse among NSDUH Respondents by Age Group in 2015 and 2016.

Maust DT, Lin LA, Blow FC. Benzodiazepine Use and Misuse Among Adults in the United States. *Psychiatr Serv*. 2019;70(2):97-106. doi:10.1176/appi.ps.201800321

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BENZODIAZEPINES ARE PARTICULARLY DANGEROUS FOR OLDER ADULTS

Older adults have **increased sensitivity of benzodiazepine receptors** as well as a increased fat : muscle ratio, which leads to a **longer half-life for fat soluble benzodiazepines**[1]

Benzodiazepines in the elderly will increase risk of….

- **… falls and fractures** due to increased reaction time, disrupted balance and gait, sedation, and impaired vision
  - Patients prescribed benzos are 50% more likely to fall (this is dose dependent, with a 20% increased fall risk with daily average prescribed dose)
  - Specifically associated with **hip fractures**, up to 1/3rd of elderly patients with a hip fracture will die within 1 year
  - Falls often result in fear of future falls which can limit daily activities
  - … **respiratory distress,** especially in setting of COPD
    - Elderly BZD users with COPD have increased risk for PNA and respiratory exacerbations
- … **delirium**
- … **cognitive impairment**
  - Short term and possibly long-term **cognitive deficits** (memory, learning, attention, and visuospatial ability)
    - 60 – 80% increased risk of car accidents
  - Associated with long-term development of dementia (unclear if causal)
- **…all-cause mortality**, with exposed patients dying at a 1.2- to 3.7-times higher rate per year (unclear if causal)

Airagnes G, Pelissolo A, Lavallée M, Flament M, Limosin F. Benzodiazepine Misuse in the Elderly: Risk Factors, Consequences, and Management. *Curr Psychiatry Rep*. 2016;18(10):89.
Markota M, Rummans TA, Bostwick JM, Lapid MI. Benzodiazepine Use in Older Adults: Dangers, Management, and Alternative Therapies. *Mayo Clin Proc*. 2016;91(11):1632-1639.
Maust DT, Lin LA, Blow FC. Benzodiazepine Use and Misuse Among Adults in the United States. *Psychiatr Serv*. 2019;70(2):97-106.

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RISK FACTORS FOR BENZODIAZEPINE ABUSE AND MISUSE

- Female gender
- Multiple prescribers and polypharmacy
- Chronic pain, physical disabilities or reduced mobility
- Cognitive impairment
- Social withdrawal
- Suicidal ideation
- Prolonged duration of treatment
- Sleep disorders

Airagnes G, Pelissolo A, Lavallée M, Flament M, Limosin F. Benzodiazepine Misuse in the Elderly: Risk Factors, Consequences, and Management. *Curr Psychiatry Rep*. 2016;18(10):89.

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SUBSTANCE USE DISORDERS IN OLDER ADULTS

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- Special considerations
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MORE OLDER ADULTS ARE INCREASING MARIJUANA USE

- Changing attitudes towards marijuana, increasing use for medical reasons and legalization for recreational use in several states has increased prevalence nationwide
- National prevalence of past-year marijuana use in 2012/2013 of 4.8% among older adults
  - 57.8% relative increase from 2006/2007 among adults aged 50–64
  - 250% relative increase among adults ≥65

Han, B. H., & Moore, A. A. (2018). Prevention and Screening of Unhealthy Substance Use by Older Adults. *Clinics in geriatric medicine*, *34*(1), 117–129.
Image: https://www.mdlinx.com/article/how-to-prescribe-medical-marijuana-for-the-right-patients/lfc-2548

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MARIJUANA USE CAN BE DANGEROUS FOR OLDER ADULTS

- Increased injury (falls, MV accidents)
- Increased mental health problems (depression, schizophrenia, other SUD)
- Cardiovascular disease (4x increase of cardiac events in first 4 hours of use; increased HR, increased BP)
- Respiratory problems
- Metabolic syndrome / unhealthy diet
- Cancer (head and neck, lung)

Lloyd, S. L., & Striley, C. W. (2018). Marijuana Use Among Adults 50 Years or Older in the 21st Century. *Gerontology & geriatric medicine*, *4*, 2333721418781668.

36

THE EFFECTS OF MARIJUANA ON COGNITION IN THE ELDERLY IS NOT CLEAR

Most studies have been done in younger patients

- **Short term effects include impairments in:**
  - Attention
  - Memory - encoding, consolidation & retrieval of memories
  - Verbal learning
  - Executive function - more dysfunction seen in older patients than adolescents
  - Psychomotor function affects reaction time in dose dependent manner
- **Long term effects are not clear:**
  - Acute and chronic exposure associated with dose-related cognitive impairment
  - Magnitude of neuropsychological impairment depends on the **frequency and duration of use**, length of abstinence and age at onset of use
- Might have protective effects against neuropathological hallmarks of AD
  - Protective effects against Aβ peptide and tau phosphorylation (neuropathological hallmarks of AD)

Volkow ND et al. JAMA Psychiatry 2016; 73(4):292-297
Ranganathan M et al. Psychopharmacology (Berl) 2006; 188(4):425-444
Solowij, N et al. Curr Drug Abuse Rev 2008;1:81-98
Bolla KI. Neurology 2002;59:1337-1343
Ahmed AIA et al. Clinical Pharmacol & Therapeutics 2015;97(6)597-606
Cao C et al. J Alzheimer's Dis 2014;42:973-984

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COCAINE

- Overall the percentage of older cocaine users is low
  - In 2005/2006, 0.41% of adults 50 and older reported past year use of cocaine
  - Studies done in urban hospital settings show a substantially higher prevalence ranging from 2%–2.3%
  - In a study looking at drug overdose deaths among New Yorkers from 2000-2016, **cocaine was involved in 51% of all drug overdose deaths** for adults aged 65+[1]

1 Han BH, Tuazon E, Kunins HV, Mantha S, Paone D. Unintentional drug overdose deaths involving cocaine among middle-aged and older adults in New York City. *Drug Alcohol Depend.* 2019;198:121-125.
Eric W, Daniel W, Lisa D *et al.* Geriatric patients on a substance consultation service. *Am J Geriatr Psychiatry* 2002;10:337–342.
Kim, S.T., & Park, T. (2019). Acute and Chronic Effects of Cocaine on Cardiovascular Health. *International journal of molecular sciences*, *20*(3), 584

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COCAINE USE CARRIES A HIGH RISK FOR MEDICAL PROBLEMS

- Medical risks of cocaine use are **more dangerous in older adults** due to increase risk for **medical complexity** and **underlying atherosclerotic disease**

Acute Risks	Chronic Risks
• Cardiac arrhythmias • Myocardial and cerebrovascular ischemia • Vascular vasospasm	• Accelerated atherosclerosis • Hematological abnormalities • Cardiomyopathy • CAD

Cocaine users of all ages are **more likely also to smoke tobacco and drink alcohol** than those who do not use cocaine. The combination of cocaine, tobacco, and alcohol can further and synergistically exacerbate underlying medical conditions.

Han BH, Tuazon E, Kunins HV, Mantha S, Paone D. Unintentional drug overdose deaths involving cocaine among middle-aged and older adults in New York City. *Drug Alcohol Depend.* 2019;198:121-125.
Eric W, Daniel W, Lisa D *et al.* Geriatric patients on a substance consultation service. *Am J Geriatr Psychiatry* 2002;10:337–342.
Kim, S. T., & Park, T. (2019). Acute and Chronic Effects of Cocaine on Cardiovascular Health. *International journal of molecular sciences*, *20*(3), 584.

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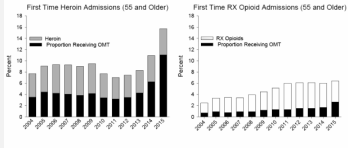
OLDER ADULTS ARE AT HIGH RISK FOR BEING PRESCRIBED OPIATES

- Older adults have a **higher rate of prescription opioid exposure** than any other age group (4-9% of adults 65+)
  - Make **more clinic visits**
  - M**ore likely to be seen for pain** than younger patients
- Office visits where opiates are prescribed increased from 0.55% of visits (1995 – 1998) to 2.51% of visits (2007 – 2010)[2]
- Of adults 50 and older who misused prescription opioids, **40 – 50% obtained those medications through physicians**
- ED visits for opiate misuse doubled in metropolitan areas in Unites States from 2004 to 2008[3]



The proportion of older adults seeking treatment for OUD is rising

Steady rise between 2004-2013 (41.2% increase)

Rapidly rise between 2013-2015 (53.5% increase)

Huhn AS, Strain EC, Tompkins DA, Dunn KE. A hidden aspect of the U.S. opioid crisis: Rise in first-time treatment admissions for older adults with opioid use disorder. Drug Alcohol Depend. 2018 Dec 1;193:142-147.
Olfson M, Wang S, Iza M, Crystal S, Blanco C. National trends in the office-based prescription of schedule II opioids. J Clin Psychiatry. 2013 Sep;74(9):932-9.
Schieber LZ, Guy GP Jr, Seth P, Losby JL. Variation in Adult Outpatient Opioid Prescription Dispensing by Age and Sex - United States, 2008-2018. MMWR Morb Mortal Wkly Rep. 2020 Mar 20;69(11):298-302.
Morse RD, Marcum ZA, Saghafi E, Weiner DK, Karp JF. A Systematic Review of Opioid and Benzodiazepine Misuse in Older Adults. *Am J Geriatr Psychiatry.* 2016;24(11):949-963.

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WOMEN ARE DISPROPORTIONATELY AFFECTED BY OPIATES

- More likely to have chronic pain and be prescribed prescription pain killers; higher doses and use them longer than men
- Prescription pain reliever OD deaths among women of all ages **increased more than 400% from 1999 to 2010** compared to 265% among men
- Heroin overdose deaths among women have tripled from 2010 through 2013[3]

Centers for Disease Control and Prevention:Vital signs: overdoses of prescription opioid pain relievers and other drugs among women—United States, 1999–2010. Morb Mortal Wkly Rep 2013; 62:537–542.

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SUBSTANCE USE DISORDERS IN OLDER ADULTS

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- **Comorbid psychiatric conditions**
- Treatment and rehabilitation strategies

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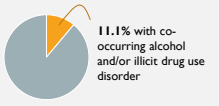
SUBSTANCE USE DISORDERS OFTEN OCCUR WITH PSYCHIATRIC COMORBIDITY

- There is limited research on psychiatric comorbidity with SUD among older adults, but evidence suggests there is a **high correlation between substance use, specifically alcohol use, and depression and other affective disorders**
- Analysis of the 2015–2018 National Survey of Drug Use and Health, which includes community dwelling adults (excluding people in treatment centers or other institutions)

Aged 50 + with any mental disorder



11.1% with co-occurring alcohol and/or illicit drug use disorder

Aged 50+ with alcohol and/or illicit drug use disorder

38.2% with co-occurring mental disorder

Choi, N. G., & DiNitto, D. M. (2020). Characteristics of Mental Health and Substance Use Service Facilities for Older Adults: Findings from U.S. National Surveys. *Clinical Gerontologist*, 1–13.

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DEPRESSION AND SUBSTANCE USE

Older adults with depression ….

- **…** are more likely to engage in **unhealthy drinking and binge drinking**
  - *~13% of older adults with a lifetime diagnosis of depression also met criteria for alcohol abuse*
- …. are more likely to have **used MJ and cocaine** in the last year

Older adults with alcohol dependence…

- … are **three times more likely to have depression** than those without
  - *A study comparing "high-risk" alcohol users to "low-risk" users,* ***found a higher prevalence of major depression*** *(24.9% vs 3.2%) among "high-risk" users*

Older adults with co-morbid depression and SUD….

- … are more likely to have a **poor response to treatment**
- … are **less likely to receive care**
  - *Co-occurring SUD was associated with an 8% decreased likelihood of receiving past-year depression care (looking at 25,500 adults over 2008 – 2014), and a 13% decreased likelihood when looking exclusively at men*

Wu LT, Blazer DG. Substance use disorders and psychiatric comorbidity in mid and later life: a review. *Int J Epidemiol*. 2014;43(2):304-317.
Han B, Olfson M, Mojtabai R. Depression care among depressed adults with and without comorbid substance use disorders in the United States. Depress Anxiety. 2017 Mar;34(3):291-300.

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SUBSTANCE USE AND SUICIDE AMONG OLDER ADULTS

Older adults and suicide

- Older adults have **higher suicide rates than the general adult population**
  - ***15.3*** *vs. 10.7 completed suicides / 100,000*
- Older adult suicide completers are **less likely to have attempted suicide previously** and **more likely to be "successful"** (1 in 4 vs. 1 in 25 among all ages) due to more **lethal methods** (72.9% of elderly suicide involved firearms in 2000), increased **social isolation and poor physical health**

Older adults, suicide, and substance use

- SUDs are the **2nd most common type of psychiatric disorder associated with completed older adult suicide** (after depression)
  - *3 to 44% of elderly suicide completers had a substance use disorder*

Alcohol

- Medical examiner toxicology reports on older suicide completers found that **14.8% of 64- to 73-year-olds and 5.8% of those aged 74 and older** had alcohol present in the blood stream
- A study of elder suicide attempts, **24.5% of patients aged 60 to 69 and 13% of those patients aged 70 to 79** had consumed alcohol before the attempt

Benzos

- Older adults using benzodiazepines have an increased risk of **suicidal thoughts, plans and suicide attempts,** even more dangerous in elderly who have the highest risk of completed suicide[3]

Opiates

- Study analyzing 184,136 cases involving intentional misuse of prescription opioid medications (from 2006 – 2013) showed a significant **linear increase in rates of opioid misuse with suicidal intent in adults over 60**

Blow FC, Brockmann LM, Barry KL. Role of alcohol in late-life suicide. Alcohol Clin Exp Res. 2004 May;28(5 Suppl):48S-56S..
Airagnes G, Pelissolo A, Lavallée M, Flament M, Limosin F. Benzodiazepine Misuse in the Elderly: Risk Factors, Consequences, and Management. *Curr Psychiatry Rep*. 2016;18(10):89.

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ANXIETY AND SUBSTANCE USE DISORDER

- **The co-occurrence of anxiety and substance use disorders among older adults is well established**
  - A study looking at 4646 current alcohol users aged 60+ found **8.8% of high-risk drinkers had co-morbid anxiety** (vs 1.4-2.3% for low and moderate risk drinkers)
  - A study following **older adults with AUD found that 2% developed GAD** over the course of 3 years
- **Anxiety itself increases risk for harmful substance use**
  - Anxiety and insomnia are the most common reasons for physicians to prescribe benzodiazepines to older adults despite **no studies showing efficacy for these indications in older adults,** and well documented **dangers and complications from use**
  - Mild cognitive impairment, **major depression and <u>anxiety disorders</u> are** associated with increased odds of benzodiazepine dependence

Markota M, Rummans TA, Bostwick JM, Lapid MI. Benzodiazepine Use in Older Adults: Dangers, Management, and Alternative Therapies. Mayo Clin Proc. 2016 Nov;91(11):1632-1639.
Wu LT, Blazer DG. Substance use disorders and psychiatric comorbidity in mid and later life: a review. *Int J Epidemiol*. 2014;43(2):304-317.

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COVID-19, MENTAL HEALTH, AND SUBSTANCE USE AMONG OLDER ADULTS

Increased risk of infection	• **Increased mortality among older adults** following infection with SARS-CoV-2 • Older adults with SUD are at increased risk for pulmonary infection and complications from pulmonary infection due to **substance abuse related medical concerns**, including cardio-pulmonary morbidities, a dysfunctional immune system and vitamin deficiencies
More limited support	• Older adults are **vulnerable to the detrimental effects of isolation**, exacerbated with social distancing • Older adults in recovery from substance use disorders have **limited options for in-person resources**, support has shifted to online treatment and self-help resources
Continued access	• Previous research has demonstrated **increased benzodiazepine use associated with disaster situations** • Authorities deemed alcohol to be an "essential commodity," there was **a reported surge in the sale of alcohol throughout the lockdown** period

Satre DD, Hirschtritt ME, Silverberg MJ, Sterling SA. Addressing Problems With Alcohol and Other Substances Among Older Adults During the COVID-19 Pandemic. Am J Geriatr Psychiatry. 2020 Jul;28(7):780-783.

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SUBSTANCE USE DISORDERS IN OLDER ADULTS

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- Special considerations
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- Other substance use
- Comorbid psychiatric conditions

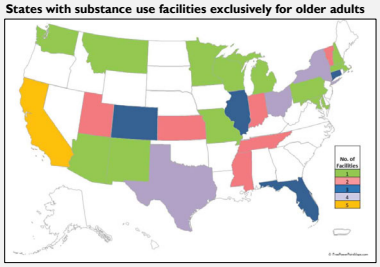
Treatment and rehabilitation strategies

50

THERE HAS BEEN AN INCREASE IN SUBSTANCE USE DISORDER CARE TAILORED FOR OLDER ADULTS

- In 2012 6.7% (952 facilities) of reporting substance use service facilities offered a program dedicated/tailored for older adults, this increased to 23.2% (3,701 facilities) by 2019
- There are currently 53 substance use service facilities in 26 states dedicated exclusively to older adults

States with substance use facilities exclusively for older adults



Choi, N. G., & DiNitto, D. M. (2020). Characteristics of Mental Health and Substance Use Service Facilities for Older Adults: Findings from U.S. National Surveys. *Clinical Gerontologist*, 1–13.

51

DESPITE INCREASED ACCESS, OLDER ADULTS ARE LESS LIKELY TO SEEK CARE

- Despite increased availability for care, compared to younger age-groups, **adults 65+ are less likely to received treatment for SUD.** Older adults entering SUD treatment are more likely to be….
  - Male
  - White
  - High school educated
  - Widowed or divorced
  - Retired,
  - Disabled

Choi NG, DiNitto DM, Marti CN. Treatment use, perceived need, and barriers to seeking treatment for substance abuse and mental health problems among older adults compared to younger adults. Drug Alcohol Depend. 2014 Dec 1;145:113-20.

52

WHAT DOES TREATMENT LOOK LIKE FOR OLDER ADULTS?

A study examining almost 60,000 first time substance abuse treatment admissions in Iowa 2010 – 2013 found

- By age 75, the **majority of participants lived alone**
- The percentage of participants with operating while intoxicated (OWI) charges was greater in each age group until aged 75, with **OWI accounted for 26.6% of referrals for aged 70 to 74** (vs. 6.9% aged 30 to 49)
- Older adults had **significantly more hospitalizations for substance use at** 22% vs 11% in the youngest group (aged 30 – 34)
- Excluding the oldest group (aged 75 – 96), **older age was associated with greater successful completion of programs**

Choi NG, DiNitto DM, Marti CN. Treatment use, perceived need, and barriers to seeking treatment for substance abuse and mental health problems among older adults compared to younger adults. Drug Alcohol Depend. 2014 Dec 1;145:113-20.

53

THE HEALTHCARE SETTING PLAYS AN INCREASINGLY IMPORTANT IN ACCESS TO CARE

- Most referrals for older adults are through **health care settings**
  - Increasing percentage of older adults widowed / living alone
- There is evidence that individuals 65- 74 are more likely to complete treatment successfully than younger or older individuals

Sahker E, Schultz SK, Arndt S. Treatment of Substance Use Disorders in Older Adults: Implications for Care Delivery. J Am Geriatr Soc. 2015 Nov;63(11):2317-23.

54

BENEFITS OF AGE-SPECIFIC TREATMENT PROGRAMS

- **Changing social roles** (less concern with employment, family formation)
- **Unique challenges** in social roles (widowhood, shrinkage of friendship networks, lack of means for increasing income, cognitive and physical decline)
- Increased **comfort** disclosing and discussing problems with **same-age peers**

Rothrauff TC, Abraham AJ, Bride BE, Roman PM. Substance abuse treatment for older adults in private centers. Subst Abus. 2011 Jan;32(1):7-15.

55

TREATMENT APPROACHES

Suggested Treatment Approaches

- Engaging in **non-confrontational** treatment
- Focusing on (re)building **self-esteem**
- Teaching **skills** to cope with depression, loneliness, loss
- Focusing on (re)building **social networks**
- Tailoring **content & pace** toward older adults
- Hiring staff interested/experienced working with older adults
- Providing linkages with medical services and community-based services

Treatment including

- Cognitive-behavioral treatment
- Group-based treatment
- Individual counseling
- Medical/psychiatric treatment
- Marital/family involvement/therapy
- Case management/community linked services

Rothrauff TC, Abraham AJ, Bride BE, Roman PM. Substance abuse treatment for older adults in private centers. Subst Abus. 2011 Jan;32(1):7-15.

56

BRIEF INTERVENTIONS HAVE BEEN STUDIED WITH ALCOHOL MIS USE WITH GOOD EFFECTS

- **Screening, Brief Intervention, and Referral to Treatment (SBIRT)** delivers early intervention and treatment to people with substance use disorders and those at risk of developing these disorders, includes universal screening, brief interventions, and referral to treatment for those needing more extensive treatment
- Applied specifically older adults with the **Florida Brief Intervention and Treatment for Elders (BRITE) project, pilot program 2004 - 2007**
  - Screening ~3,500 older adults for alcohol, medications, and illicit substance misuse problems and for depression and suicide risk identified, 10% received intervention
  - Engaged in brief intervention (1 to 5 sessions) or brief treatment (16 sessions) depending on need
  - Depression and alcohol severity scores decreased and medication misuse improved, more than 80% of participants who has a positive SMAST-G screen at baseline continued to have a positive score after the interventions
- Due to the success of the pilot program, BRITE was implemented for another 5 years (2006 – 2011) in Florida, completing over 85,000 screenings and identifying ~8,000 people at high / medium risk

Schonfeld L, Hazlett RW, Hedgecock DK, Duchene DM, Burns LV, Gum AM. Screening, Brief Intervention, and Referral to Treatment for Older Adults With Substance Misuse. Am J Public Health. 2015 Jan;105(1):205-211.

57

ENGAGING AND RETAINING THE OLDER ADULT

- **Integrating** substance abuse, health, mental health, and aging services to provide comprehensive, holistic care tailored to the needs of the older consumer who presents with co-occurring, multiple needs
- Specific, simple goals/objectives
- Offering **services in home and community-based** settings where older adults congregate
- Outreach services
- Extended stay treatment

Steinhagen KA, et al. Substance Abuse and Misuse in Older Adults. *Aging Well*. 2008;1:20. www.todaysgeriatricmedicine.com/archive/071708p20.shtml. Accessed June 18, 2020

58

SPECIAL TREATMENT NEEDS

- Elderly are more likely to present with
  - Multiple medical conditions
  - Cognitive problems
  - Mobility problems
- Sensory deficits - hearing/vision
- Treatment for older adult requires more medical management than standard
  - Detoxification can take up to 28 days
  - Patients are likely taking multiple prescription medications

Doweiko HE. *Concepts of Chemical Dependency*. Ninth Edition. Cengage Learning; 2014

59

OPIOID TREATMENT AMONG OLDER ADULTS

- The number of **older adults receiving methadone treatment is growing** as this population ages and more adults present for the first time aged 50–70 years
- **Older methadone patients do significantly better in treatment.** In a Study comparing treatment outcomes at nine months post-treatment admission
  - 61% of adults aged 55+ had no positive urine-drug-screens compared to 35% the younger group
  - Older adults (aged 55 years and older) were more likely to have longer treatment durations
- Abstinence was greatest among **women aged 55–77 years** (81% for women aged 55–77 vs 44% for women aged <40 years)
- Women aged 55–77 years remained in treatment longer than men in the same age group (20.7 weeks versus 9.5 weeks)

Carew AM, Comiskey C. Treatment for opioid use and outcomes in older adults: a systematic literature review. *Drug Alcohol Depend*. 2018;182:48-57.

60

SUMMARY

- Although it can be difficult to quantify the impact of substances on the elderly, the **population of older adults misusing and abusing substance has been growing** and is projected to continue to grow
- There are **unique risk factors** for misusing substances among this population (loss of a partner, chronic illness, low of day structure), aging is NOT a protective factor
- Older adults **increased risk for the consequences** of substance misuse given a physiologic considerations (decrease in hepatic metabolism, decreased lean body mass and total body water, and co-existing medical conditions)
- Older adults are often **under-diagnosed and mis-diagnosed** due to a decreased likelihood of providers to screen for substances (ageism) and decreased sensitivity of standard screening tools for this population
- **Alcohol is the most widely mis-used substance** by older adults, but use of other substances, including marijuana, benzodiazepines and opiates, is on the rise
- There is evidence that **treatment programs specific for older adults may have better outcomes**, the availability of these programs has been growing

61

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62

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Electroconvulsive Therapy and TMS in the Elderly

Adriana Hermida, MD
Professor, Department of Psychiatry
Director, Geriatric Psychiatry Fellowship
Emory University School of Medicine

1

Disclosure:
Adriana P. Hermida, MD
AAGP Review Course 2022

With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company in the past 24 months which could be considered a conflict of interest.

Off label use of medications will be discussed

2

3

Mechanism of Action

Anticonvulsant Hypothesis
GABA has been postulated as a key mediator of the ECT anticonvulsant effect.

Neurotransmitter Hypothesis
ECT is known to enhance serotoninergic function and activate the mesocorticolimbic dopamine system.

Neuroendocrine Hypothesis
ECT affects the HPA axis normalizing the dexamethasone suppression test.

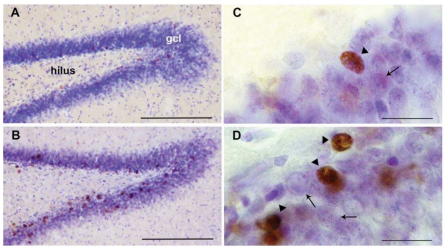
Neurotrophic Hypothesis
Animal studies have shown increase in neurotophic factors and cell proliferation.

4

Hyppocampal Neurogenesis in rodents treated with Electroconvulsive Stimulation (ECS)

Control (A and C)

ECS-treated rats (B and D)

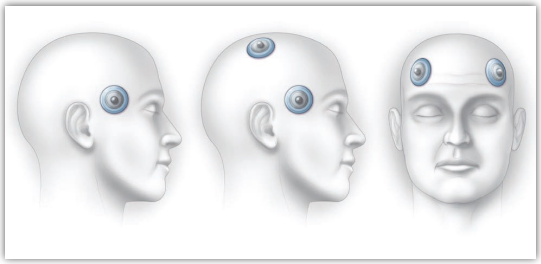


Newly formed hippocampal neurons survived up to 12 months.

HIPPOCAMPUS 27:52–60 (2017)

5

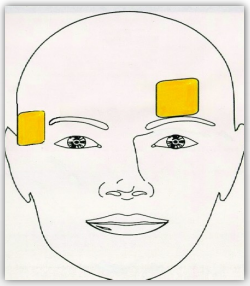
BITEMPORAL **RIGHT UNILATERAL** **BIFRONTAL**



Source: Sarah H. Lisanby, MD Electroconvulsive Therapy for Depression New England Journal of Medicine 2007; 357: 1939 – 1945

6

LART (Left Anterior, Right Temporal)



Schwartz CM 2005

7

Electrode Placement

RUL less cognitive SE. According to PRIDE study: RUL-UBP ECT may be a particular good type of ECT for geriatric Patients. (Should be dosed at supra-sz threshold)

BF/BT for more severe patients, schizoaffective disorder, schizophrenia, past response to BL treatments, failure to UL. (dosed close to seizure threshold)

8

Work up

1. Detailed medical history, PE, neuro, dental eval, psych assessment
2. Baseline cognitive assessment
3. Medication history
4. EKG
5. Brain CT Scan
6. Comprehensive Metabolic Panel
7. Anesthesia w/u (every 6 months for M-ECT)
8. Consent (pre-ECT, when starting C-ECT, every 6 m for M-ECT)

9

Treatment Course

- Average 6 to 12
  Avoid pre-determined number of treatments
- Acute course: 2 to 4 weeks
- RUL three per week or two per week for geriatric pts
- BF/BT two per week

10

What happens after the 6-12 treatments?

- Patients should continue pharmacotherapy.
- DC
- Taper
- Continuation/ M-ECT

11

Relapse after ECT

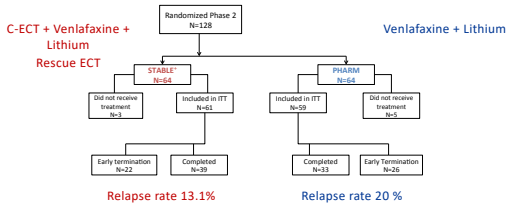
- It is a major issue
- > 50% relapse within first 6 months
- Avoid medications that were not effective pre-ECT
- Taper ECT 3xw ➔1xw ➔10 days ➔2 weeks
- Aggressive pharmacotherapy with combination & augmentation

  ✓ *CORE data about NT & Li or VN & Li*
  ✓ *MAOi*
  ✓ *Continue antipsychotics*
  ✓ *Use therapeutic dosages*

12

A Novel Strategy for Continuation ECT in Geriatric Depression: Phase 2 of the PRIDE Study

PRIDE Phase II Consort Chart



Relapse rate 13.1%

Relapse rate 20 %

UB RUL was effective and well tolerated in geriatric pts

Kellner Am J Psychiatry 2016; 173:1110–1118

13

Indications

- Major Depression
- Bipolar Disorder
- Schizophrenia Catatonic specifier
- Schizoaffective Disorder
- Catatonia
- Neuroleptic Malignant Syndrome

Other Illness

- Catatonia from medical reasons like Lupus
- Depression in Parkinson's Disease
- Status epilepticus. (Raises the seizure threshold)
- Intractable seizures
- Post-stroke depression

14

14

ECT in Dementia

Safety and Efficacy of Electroconvulsive Therapy for the Treatment of Agitation and Aggression in Patients With Dementia

Manjola Ujkaj, M.D., Ph.D., Donald A. Davidoff, Ph.D., Stephen J. Sewer, M.D., James M. Ellison, M.D., M.P.H., David G. Harper, Ph.D., Brent P. Forester, M.D.

The American Journal of Geriatric Psychiatry; Jan 2012

Electroconvulsive therapy (ECT) for treating agitation in dementia (major neurocognitive disorder) – a promising option

Oliver M. Glass,[1] Brent P. Forester[2] and Adriana P. Hermida[3]

Hermida AP, Tang YL, Glass O, Janjua AU, McDonald WM. Efficacy and Safety of ECT for Behavioral and Psychological Symptoms of Dementia (BPSD): A Retrospective Chart Review. Am J Geriatr Psychiatry. 2020

15

Major Depression

- ECT is an effective treatment in 60- 80% of patients with treatment resistant unipolar or bipolar major depression.
- ECT is more effective than antidepressant pharmacotherapy.

16

16

Major Depression

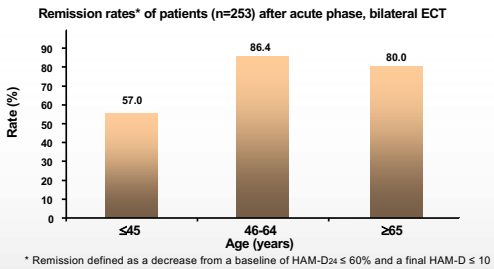
- STAR*D trial (a) (Sequenced Treatment Alternatives to Relieve Depression)
  - Response rate was 47%
  - Remission rate was 28%

  After 14 weeks of a SSRI (citalopram)

17 Trivedi, Rush, Wisniewski, et al: Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: Implications for clinical practice. Am J Psychiatry 2006; 163:28-40.

17

The "Gold Standard"
remission rates with ECT

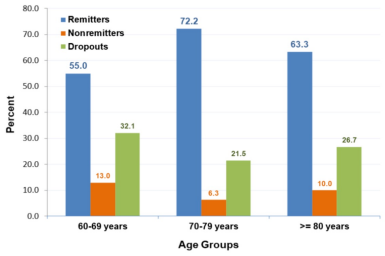


* Remission defined as a decrease from a baseline of HAM-D$_{24}$ ≤ 60% and a final HAM-D ≤ 10

O'Connor et al. *Am J Geriatr Psychiatry* 2001; 9: 382-390

18

PRIDE Phase 1 Outcome by Age Category (n=240)



Kellner Am J Psychiatry 2016; 173:1110–1118

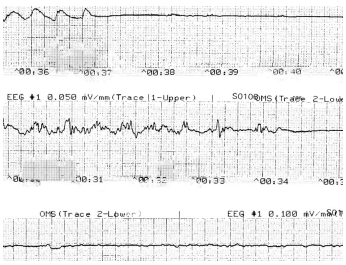
19

Clinical predictors of good response

- Older age (O'Connor et al.)
- Presence of psychosis (Petrides et al 2001)
- Catatonic symptoms (Buchan et al. 1992)
- Response by session 3 of ECT may predict long-term efficacy
- Post-ictal suppression
- History of good response to ECT in the past

20

Post-ictal suppression



Nobler et al. 1993

21

Negative predictors

- Failure to several antidepressant trials.
- Personality disorders -especially borderline (Rasmussen 2015)
- Longer current episode of depression. (Dombrovski et al. 2005)
- Periventricular hyperintensities in MRI (Oudega et al. 2011)
- Substance abuse

22

Contraindications

- No absolute contraindications to ECT
- Recent myocardial infarction or unstable cardiac conditions
- Any illness that increases intracranial pressure
- Recent cerebral infarction, particularly hemorrhagic infarction
- Aneurysm or vascular malformation
- American Society of Anesthesiology (ASA) physical status classification of level 4 or 5
- Severe pulmonary disease
- Cochlear implant

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Contraindications

- Retinal detachment
- Active substance use
- Pheochromocytoma
- Pregnancy is not a contraindication
- Dementia is not a contraindication
- VNS, Pacemaker and defibrillators are not a contraindication.

24

Complications

- PIA (Post-ictal agitation)
- Delirium
- CV side effects
- Cognitive side effects

25

25

Postictal agitation (PIA)

- Can be a cause of injury for an elderly patient
- PIA may be associated with increased lactate level form motor activity

Table 1 RICHMOND AGITATION-SEDATION SCALE

SCORE	TERM	DESCRIPTION
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitated	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff
+2	Agitated	Frequent nonpurposeful movement or patient–ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	
-1	Drowsy	Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice
-2	Light sedation	Briefly (less than 10 seconds) awakens with eye contact to voice
-3	Moderate sedation	Any movement (but no eye contact) to voice
-4	Deep sedation	No response to voice, but any movement to physical stimulation
-5	Unarousable	No response to voice or physical stimulation

Hermida AP, Janjua AU, Tang Y, et al: Use of orally disintegrating olanzapine during electroconvulsive therapy for prevention of postictal agitation. J Psychiatr Pract 2016

26

Postictal agitation (PIA)

- Strategies:
  - Midazolam or Lorazepam or propofol after the treatment
  - Increasing succinylcholine to decrease muscle activity and decrease serum lactate.
  - Dissolvable olanzapine (ie, Zydis) given immediately before the seizure is both safe and effective in preventing PIA after subsequent ECT treatments
  - Propofol after central Sz ends and before the patient wakes up

Sterina E.; Gregory N.; **Hermida AP.** Acute and Prophylactic Management of Post-ictal Agitation in Electroconvulsive Therapy. Journal of ECT 2022

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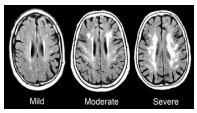
Delirium



- Increase incidence with advancing age.
- Risk factors: Parkinson's, Alzheimer's, one or more CV risk factors, structural changes in caudate nucleus.
- Strategies: If identified treatments should be held, administered less frequently, lower electrical charge.

28

Cardiovascular complications

- Rare but can be serious in the elderly
  - Arrhythmia
  - Transient hypertension
- Most of the complications are caused by known preexisting conditions
- Strategies:
  - Patients should take their prescribed cardiac medications on the morning before ECT
  - Most cardiac pacemakers can be used safely during ECT. Special precautions are needed in patients with implantable cardioverter defibrillators
  - Cardiology consult

Hermida AP, Mohsin M, Pinheiro AM, McCord E, Lisko JC, Head L. The Cardiovascular Side Effects of EC and their management J ECT. 2022

29

Memory side effects in ECT

- The severity and duration of cognitive side effects have been shown to be related to:
  - ✓ *Retrograde and anterograde memory deficits*
  - ✓ *Position of the electrodes.*
  - ✓ *Dose of electricity relative to a patient's seizure threshold*
  - ✓ *Frequency of administration*
  - ✓ *Pulse width (Brief vs ultrabrief)*
  - ✓ *Total number of treatments*

Flint AJ, Gagnon N. Effective use of electroconvulsive therapy in late-life depression. Can J Psychiatry. 2002 Oct;47(8):734-41. Review. PMID: 12420651

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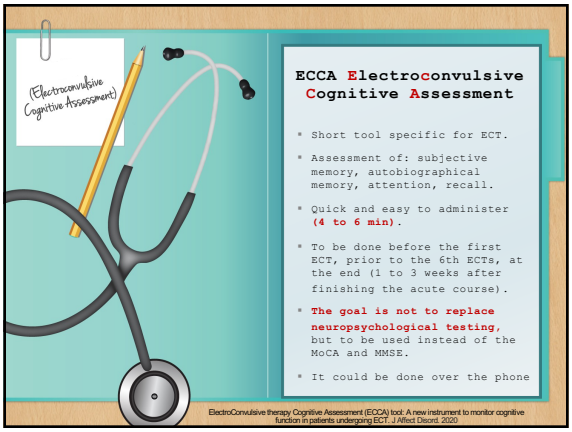

31

Minor complications

- Headache: 45% develop headache cause unclear possible a vascular process. Acetaminophen , NSAIDs. Sumatriptan pre-ECT.
- Nausea approx. 25%. Prochlorperazine, Metoclopramide and Ondansetron.

32

The ECT experience

- Patients who received ECT were satisfied with their treatments and had more favorable attitudes about ECT than patients who have not had ECT.
- 85% pts who have received ECT would agree to a second course of ECT if needed.

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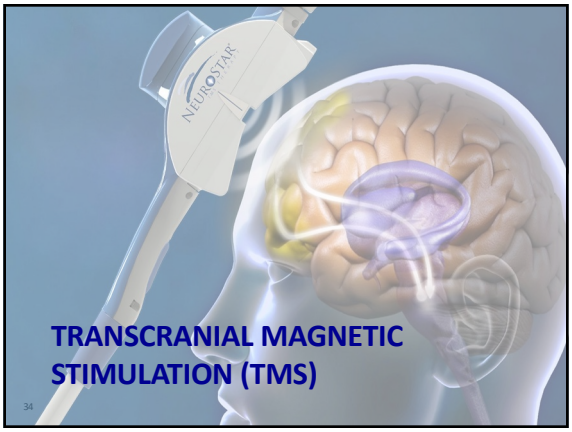

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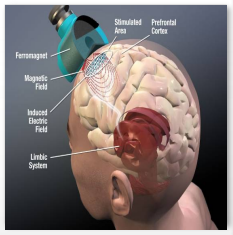
TMS

- Approved in 2008
- Focused Sub-convulsive stimulus
  - 10 Hz at 120% MT intensity
  - Total pulse count of 90,000 pulses
  - 4–6 weeks (20–30 sessions)
  - Intermittent theta-burst stimulation (iTBS) -- Brainsway Deep TMS FDA cleared for 3 min Theta Burst (April 2021)
- Typically Left pre-frontal cortex. Also R r-TMS and B-TMS
- It does not require anesthesia
- Not associated with cognitive side effects, no driving restrictions



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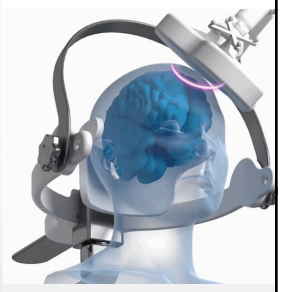
TMS

- The TMS coil creates a magnetic field that crosses the scalp and skull, depolarizes cortical neurons, and triggers action potentials.
- The depth of the penetration is only about 1–2 cm and therefore the stimulus only affects cortical neurons directly.
- With repeated stimulation and longer stimulus trains, the effect of the TMS stimulation has been shown to persist beyond the duration of stimulation through a process termed *long-term potentiation*.

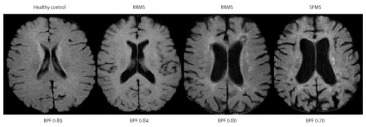


Cappon D, den Boer T, Jordan C, Yu W, Metzger E, Pascual-Leone A. Transcranial magnetic stimulation (TMS) for geriatric depression. Ageing Res Rev. 2022

36

TMS

- TMS may not be able to effectively stimulate cortical areas on patients with cortical atrophy

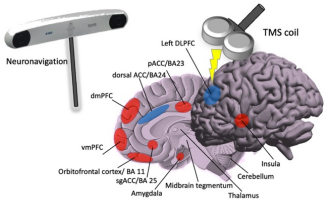


- The efficacy of TMS in geriatric patients may be dependent upon intact neuroanatomic circuits to reach these structures.

McDonald WM. Neuromodulation Treatments for Geriatric Mood and Cognitive Disorders. Am J Geriatr Psychiatry 24:12, December 2016

37

TMS & Brain Networks in Geriatric Depression



Brain Networks in Geriatric Depression

Cognitive Control Network (CCN)	DLPFC dorsal ACC	Hypoactivity	Executive Dysfunction
Default Mode Network (DMN)	dmPFC pACC	Hyperactivity	Self-referential thinking, rumination
Salience Network (SN)	Amygdala Insula	Hyperactivity	Apathy, negative thinking, negative bias

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Cappon et al Transcranial magnetic stimulation (TMS) for geriatric depression Ageing Research Reviews 74 (2022) 101531

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TMS in Geriatric Depression

- 14 studies evaluated the efficacy of rTMS for GD (controlled and uncontrolled studies)
  - 7 RCT which with a total of 260 patients (148 in the active and 112 in the sham groups). Considerable variability in response and remission
    - -Response ranging from 6.7% to 54.3%
    - -Remission ranging from 8.2% to 40%
- Remission rates are significantly lower than the remission rates in ECT
- TMS in GD –safe and well tolerated. Need optimization strategies and individualized targeting in GD
- Not indicated in patients with comorbid psychosis, suicidal intent, and those in need of acute treatment

Cappon et al Transcranial magnetic stimulation (TMS) for geriatric depression Ageing Research Reviews 74 (2022)

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Conclusions

ECT

- ECT is not a treatment of "last resort"
- It is the treatment of choice for psychotic and suicidal patients.

ECT

- It is the most effective treatment in TRD
- Different modalities have different efficacy rates and different SE profile

ECT predictor

- Older age is a positive predictor

TMS

- TMS has a place in clinical practice, for less severe and less refractory cases

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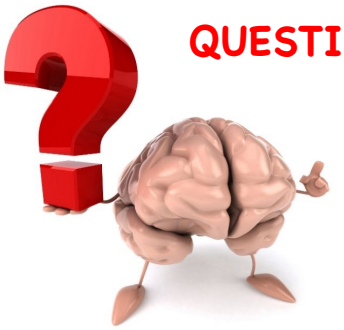

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Anxiety Disorders in Geriatric Psychiatry

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Associate Director for Clinical Programs
VISN 16 Geriatric Research Education and Clinical Center (GRECC)

2022 AAGP Review Course, San Antonio, TX

1

Disclosure of Conflict

- Research funding by NIH, the Department of Veterans Affairs, the Alzheimer's Association, Neuronetics (supplies only)
- Off label use of medications will be discussed

2

Question 1

- As part of the routine medical workup in the ER, emergent functional magnetic imaging is performed in a patient with panic disorder. Hyperactivity in which region of the brain is most likely to be found?

A. Amygdala
B. Anterior cingulate cortex
C. Hippocampus
D. Medial prefrontal cortex
E. Pituitary

3

Question 2

- The neurotransmitter most directly implicated in the psychological and physical sensations of anxiety is

A. Serotonin
B. Dopamine
C. Norepinephrine
D. Acetylcholine
E. GABA

4

Question 3

- The nucleus in the pons that produces norepinephrine, the neurotransmitter most associated with these anxiety symptoms, is the

A. Raphe Nuclei
B. Substantia nigra
C. Nucleus basalis
D. Locus Coeruleus
E. Changus Jasonis

5

Question 4

- What medical disorder would be in the differential diagnosis of the presenting symptoms of a patient in a panic attack?

A. Hyperglycemia
B. Hypertension
C. Hyperlipidemia
D. Hyperthyroidism
E. Hyperkalemia

6

Anxiety

- Expected, Normal and transient response to stress
- Fear = anxious arousal
  - Sudden onset, short duration
  - Amygdala/Insula
- Worry = anxious apprehension
  - Sustained, long-lasting
  - Prefrontal cognitive/affective regions (DLPFC, OFC)
- Pathological anxiety:
  - Autonomous: no trigger
  - Intensity
  - Duration
  - Impairs coping

7

Manifestations of Anxiety

- Physical — autonomic symptoms
- Affective — edginess to loss of control
- Behavior — avoidance or compulsions
- Cognition — worry, obsessions

8

Neurophysiology

- Central Noradrenergic system
  - Stimulation of Locus coeruleus generates panic attacks
- GABA neurons
  - Limbic system mediate generalized anxiety, worry and vigilance
- Serotonergic system
  - Important modulators of the above two

9

Anxiety Disorders: DSMIV to DSM5

- Separation of DSM-IV Anxiety Disorders chapter into four distinct chapters
  - Fear-based anxiety disorders (e.g., phobias)
  - Disorders of obsessions or compulsions (e.g., OCD)
  - Trauma-related anxiety disorders (e.g., PTSD)
  - Dissociative disorders
- Hoarding disorder has been added
- No need for insight that anxiety is "excessive or unreasonable"

10

Anxiety Disorders (Red=changed/moved to new section)

DSM-IV	DSM-V
• Panic Disorder Without Agoraphobia and Panic Disorder With Agoraphobia	• Separation Anxiety Disorder
• Agoraphobia Without History of Panic Disorder	• Selective Mutism
• Specific Phobia	• Specific Phobia
• Social Phobia	• Social Anxiety Disorder
• Obsessive Compulsive Disorder	• Panic Disorder
• Posttraumatic Stress Disorder	• Agoraphobia (now separated from Panic Disorder)
• Acute Stress Disorder	• Generalized Anxiety Disorder
• Generalized Anxiety Disorder	• Substance/Medication Induced Anxiety Disorder
• Anxiety Disorder Due to GMC	• Anxiety Disorder Due to Another Medical Condition
• Substance Induced Anxiety Disorder	• Other Specified Anxiety Disorder
• Anxiety Disorder NOS	• Unspecified Anxiety Disorder

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Geriatric rephrasing

- Anxiety ---- "Cautious", "careful". May think of this as normal or age appropriate
- Urges ----- "need to save", "cannot part with", "might need it in the future"
- Excessive and unreasonable ---- "I have always worried"
- Difficulties in assessing avoidance due to the life-long pattern

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Epidemiology

- GAD is as common as in adults: 2-4%
  - LASA >10% of had anxiety disorders including GAD, phobic disorder, panic disorder, OCD
  - NCS-R: Much lower rates of all anxiety disorders in those 65 years or older
  - GAD is much more common in those with chronic breathing disorders: 19% (Kunik)
- The most common anxiety disorders in later life are:
  - phobias 3-4% (specific phobia & agoraphobia > social phobia)
- The least common anxiety disorders in later life are:

panic disorder (0.1-1%) & OCD (0.1-0.8%)

- OCD and PTSD are rarer

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Demographic considerations

- Anxiety in older adults is much more common in women (Wolitzky-Taylor K)
- Non-Hispanic white and Latinos have the highest rates of anxiety disorders (Jimenez DE)
- High rates in AA women but low rates in AA men

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Age-related risk and protective factors for anxiety

Risk

- Female gender
- Living alone
- Recent adverse life events
- Cognitive decline
- Role transitions
- chronic disability
  - Self
  - Spouse

Protective

- Better coping and emotional regulation
- Survivorship
- Biological changes such as less autonomic arousal
- Less negative affect

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Subsyndromal Anxiety is Common

- May not meet the number and/or intensity of symptoms
- Qualitative differences from disorder criteria
  - generalized anxiety vs. GAD
  - 'panicky' vs. panic attacks
  - Fear vs. phobia
- Lack of clear cut dysfunction

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Significance

- GAD linked to stroke, cardiovascular events, mortality
- Poor quality of life
- Risk of conversion from MCI to AD (likely bidirectional)
- Increased health service use
- Effect on mobility and function
- Benzodiazepine use (45-60% of older adults with anxiety)
- Increased risk of suicide in anxious depression

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Assessment scales

- Geriatric Anxiety Inventory (Pachana *et al.*, 2007)
- Geriatric Anxiety Scale (Segal *et al.*, 2010)
- Hospital Anxiety and Depression Scale
- Beck Anxiety Inventory
- Penn State Worry Questionnaire
- State-Trait Inventory for Cognitive and Somatic Anxiety

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Generalized Anxiety Disorder

- Excessive, multiple, uncontrollable worries
- <20% of patients with GAD have anxious mood as *primary* complaint
- Majority of GAD is seen in primary care
- Older adults less likely to believe worry is excessive
- Frequent doctor visits with unexplained physical symptoms (fatigue, aches and pains, GI symptoms, insomnia)

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Generalized Anxiety Disorder

- Frequent association with depression
  - comorbid GAD 3x more prevalent than 'pure' GAD
  - Common symptoms
  - Bidirectional risk: LASA: 48% of elderly with MDD had a comorbid anxiety disorder, 25% of those with anxiety disorders had MDD
  - Shared underlying neurocircuitry
- Comorbidity with depression
  - Marker for poorer prognosis, treatment resistance
  - Higher risk of suicide

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Phobias

- May be difficult to detect in elderly particularly if the phobia has been lifelong
- Specific phobias are common
- Social phobia is less common
  - Still fairly common in old age
  - Qualitatively similar to young adults (Cairney et al 2007)

21

Fear of Falling

- 7-14% in community-dwelling older adults
- Higher rates among fallers (92%) (Bower 2015)
- 30% of people aged ≥ 65 fall each year
- 50% curtail activities because of fear
- Fear of falling can develop in the absence of falls

- In DSM-5 :
  - Agoraphobia
  - Specific phobia (Specific fear of injury or ambulation

22

Fear of falling

- Individuals don't feel that their fear is excessive and unreasonable
  - Only 1 of 48 subjects with moderate to severe fear of falling considered their fear to be unreasonable (Gagnon 2005)
- DSM V: fear that is "out of proportion to actual danger posed"
  - Severe levels of fear and avoidance in individual who are at low objective fall risk could be diagnosed as phobia

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Agoraphobia

- A Anxiety about being in places or situations from which escape might be difficult
- B Situations are avoided or else are endured with marked distress or with anxiety about having a panic attack or require a companion
- C Not accounted by GMC/ Social or specific phobia

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Agoraphobia

- Persistent (>6mo) fear of 2/5 situations
- Avoid (or requires a companion)
- Thoughts that escape might be difficult in the event of developing panic-like symptoms or other incapacitating or embarrassing symptoms (e.g., fear of falling in the elderly; fear of incontinence)
- Fear out of proportion

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Agoraphobia in Late Life

- History of panic disorder rare
- Physical illness/traumatic events important antecedents
- Comorbid depression often 2º to phobia
- Moderately severe social impairment
- Rarely comes to psychiatric attention

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Panic Attack

- Discrete period of intense fear or discomfort
- Peak within 10 minutes, and last up to 30 minutes
- At least 4 of the following:
  - Palpitations
  - Sweating
  - Trembling
  - SOB
  - Choking
  - Chest pain
  - Nausea
  - Dizzy
  - Derealization
  - Parasthesias
  - Fear of Dying
  - Chills
  - Fear of losing control

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Panic Disorder: Facts

- 2:1 female/male ratio
- Many affected individuals recall a significant life event the year before the onset
- Most studies have found a low prevalence
- Less severe or less frequent panic attacks
- Panic disorder can still be highly disabling in the elderly
- Late-onset panic disorder appears to be rare and may be a prodrome of a medical or neurological problem

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Anxiety and Cognitive Impairment

- Anxiety associated with accelerated cognitive decline
- Bidirectionality
- Psychological and Biological (Neurodegenerative, Inflammatory, Genetic)
- PTSD associated with double risk of dementia
- Executive dysfunction is prominent in hoarding disorder
- Elevated cortisol in late life GAD decreases with pharmacological treatment and is associated with improved memory

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Anxiety Associated with Dementia

- Common neuropsychiatric symptom of dementia
- 20-40% of patients with dementia have symptoms of anxiety
- Anxiety frequently associated with depression
- Anxiety hastens the dementia process and increases caregiver burden

30

Anxiety Associated with Physical Conditions

- Normal or pathological response to physical illness
- Commonly associated with: Movement disorders,
- COPD, Stroke, Cancer, Heart disease, Pain disorders
- Associated with more functional impairment, morbidity & mortality
- Anxiety about disability, consequences of illness
- Physical pathology (e.g. ↑thyroid,↑calcium, hypoxia, temporal lobe lesion) create anxiety-related sensations
- Risk of misattribution of anxiety to physical disease

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Hoarding Disorder

(Obsessive-Compulsive and Related Disorders)

- Newly added to DSM-5 (now a separate dx from OCD)
  - Rationale: Clinically significant hoarding is prevalent and can have direct and indirect consequences on the health and safety of patients as well as that of others (e.g., dependents, neighbors). Inclusion will increase the chances of these individuals receiving treatment.

32

Hoarding Disorder

Diagnostic Criteria **300.3 (F42)**

A. Persistent difficulty discarding or parting with possessions, regardless of their actual value.

B. This difficulty is due to a perceived need to save the items and to distress associated with discarding them.

C. The difficulty discarding possessions results in the accumulation of possessions that congest and clutter active living areas and substantially compromises their intended use. If living areas are uncluttered, it is only because of the interventions of third parties (e.g., family members, cleaners, authorities).

D. The hoarding causes clinically significant distress or impairment in social, occupational, or other important areas of functioning (including maintaining a safe environment for self and others).

E. The hoarding is not attributable to another medical condition (e.g., brain injury, cerebrovascular disease, Prader-Willi syndrome).

F. The hoarding is not better explained by the symptoms of another mental disorder (e.g., obsessions in obsessive-compulsive disorder, decreased energy in major depressive disorder, delusions in schizophrenia or another psychotic disorder, cognitive deficits in major neurocognitive disorder, restricted interests in autism spectrum disorder).

Specify if:

With excessive acquisition: If difficulty discarding possessions is accompanied by excessive acquisition of items that are not needed or for which there is no available space.

Specify if:

With good or fair insight: The individual recognizes that hoarding-related beliefs and behaviors (pertaining to difficulty discarding items, clutter, or excessive acquisition) are problematic.

With poor insight: The individual is mostly convinced that hoarding-related beliefs and behaviors (pertaining to difficulty discarding items, clutter, or excessive acquisition) are not problematic despite evidence to the contrary.

With absent insight/delusional beliefs: The individual is completely convinced that hoarding-related beliefs and behaviors (pertaining to difficulty discarding items, clutter, or excessive acquisition) are not problematic despite evidence to the contrary.

33

Psychological Treatment of Anxiety in Older Persons

- Controlled trials mostly for GAD
- Small to moderate effect sizes in meta-analyses
- CBT less efficacious for GAD in older vs. younger adults
- Two recent meta-analyses also support the use of CBT for a wide range of late-life anxiety disorders, including GAD, panic disorder, mixed anxiety disorders (Thorp SR)
- Medication > CBT for late-life anxiety *(Pinquart & Duberstein, 2007, Schuurmans 2006)*
- Recent evidence for Mindfulness Based Stress Reduction *(Weatherall et al, J Clin Psychiatry 2017)*

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Cognitive Behavioral Therapy

- Relaxation training – most effective component for late-life worry
- Cognitive restructuring, Guided self-help
- Other components: exposure, problem-solving, sleep hygiene, behavioral activation
- Adaptations for older adults: Repetition and review, less abstract cognitive focus, more behavioral focus, written summaries, check-in phone calls

Mohlman et al, 2003, Am J Geri Psychiatry; Thorp et al, 2009, Am J Geri Psychiatry

35

Pharmacologic Treatment of Anxiety Disorders

SSRIs and SNRIs are first line treatment
RCTs primarily for GAD

- SSRIs: Citalopram (Celexa), Escitalopram (Lexapro), Sertraline† (Zoloft)
- SNRIs: Duloxetine (Cymbalta), Venlafaxine ER (Effexor ER)

[retrospective analyses of pooled RCT data]

- Benzodiazepines: Oxazepam (Serax)
- Buspirone (Buspar)
- Pregabalin (Lyrica)† (Montgomery et al. (2008))
- Quetiapine XR (Seroquel XR)† (Mezhebovsky et al. (2013)
- A small study of risperidone ([Moríñigo et al. 2005]) showed it to be efficacious as an augmentation strategy. †

† Off-label

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Side effects of SSRIs to watch out for in the elderly

- Weight loss
- Gait abnormalities and falls
- SIADH
- GI bleeding

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Benzodiazepines in Older Adults

- Still most commonly used medication for anxiety in the elderly
- Lorazepam, oxazepam, or temazepam preferred
  - shorter half-life
  - no active metabolites
  - clearance not affected by age (conjugation)
- Define duration of treatment
- Gradual discontinuation
- Structured discontinuation interventions have good evidence in primary care

(Vincens et al, Br J Gen Pract 2016; 66 (643): e85-e9)

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Benzodiazepines: Side Effects

- Cognitive impairment
- Psychomotor impairment
- Falls
- Sedation
- Depressed respiration
- Potentiation of other CNS depressants
- Tolerance, dependence, withdrawal

39

Recommendations of the Anxiety Disorders Advisory Committee

- Specific phobia
  - Fear of falling, may not think that the fear or avoidance behavior is excessive
- Social anxiety disorder
  - Related to sensory impairment, memory
- Panic disorder
  - Full blown panic attacks uncommon
- GAD
  - Probe health and finances
- PTSD
  - Subthreshold (partial) PTSD more common
  - PTSD symptoms may persist over 50 years and cognitive decline and social isolation may exacerbate

40

Conclusions

- Anxiety disorders are common and often difficult to diagnose
- Late-life anxiety is often symptomatic of other conditions, especially depression
- Treat the underlying condition(s)
- Make use of relatively simple and effective interventions such as psychoeducation, relaxation therapy
- CBT is effective for GAD
- SSRIs and SNRIs are first line treatments

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Ethical and Legal Issues In Geriatric Psychiatry

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2022 AAGP Review Course

1

Disclosure of Conflict

- None

2

Goals and Objectives

By the end of the conference audience will learn:

- Outline the principles of medical ethics
- Discuss the process of performing competency evaluations with particular emphasis on driving in dementia
- Discuss various medico-legal issues pertinent to older patients with mental illness
- Overview of legal issues related to driving in dementia
- Review basics of malpractice law

3

Which of the following statements about older drivers is true:

A. Cessation of driving rarely leads to depression and social isolation
B. Deteriorating driving performance in the elderly is not correlated with progression of dementia
C. Common neuropsychological tests (e.g., MMSE) are not good predictors of driving ability
D. Older drivers have a decreased crash rate per mile driven
E. Older drivers have a disproportionately lower percentage of fatalities

4

4

The correct order for guardianship cases is:

A. Adjudication, hearing, guardian, termination
B. Appointment, notice, hearing, monitoring
C. Hearing, appointment, notice, monitoring
D. Petition, hearing, adjudication, appointment
E. None of the above

5

5

Competency to make decisions involves:

A. Ability to appreciate the situation and its likely consequences
B. Ability to communicate a choice
C. Ability to manipulate information rationally and relevantly
D. Ability to understand relevant information
E. All of the above

6

6

True or False

- Competency and capacity to consent mean the same
- If a patient refuses treatment that in the opinion of the surgeon is necessary but not lifesaving but the patient is refusing the procedure, they should be deemed to lack capacity to consent for the procedure

7

7

For Board review

- Only Federal Case law
  - No need to learn or memorize state-specific laws

8

8

Principles of medical ethics

- **Autonomy** (allow me to decide)
- **Beneficence** (decide what is best for me)
- **Non-malfeasance** (don't hurt me)
- **Justice** (do for me what you do for others)

9

9

Ethical dilemmas arise when two (or more) of these principles come into conflict

- Autonomy vs beneficence is the most common conflict in medicine.
  - Paternalism
  - Leads to discussions of capacity/competence, as well as surrogate decision-making
- NOTE: Ethics and law are different

10

10

Medico-legal and ethical issues pertinent to geriatric psychiatry

- Decision making capacity
  - Informed consent
  - Financial management
  - Participation in clinical research
  - Driving
- Guardianship
- Elder abuse
- Malpractice

11

11

Informed consent: Three Elements

- Voluntariness
  - Willingness to participate
- Information:
  - Sufficient information on which to base a decision
- Capacity:
  - Capacity to weigh information and provide consent

12

Voluntariness

- Consent must be freely given
- There must be no coercion, and physician must be alert for "undue influence"
- Refusal cannot lead to termination of treatment

13

13

Information:
The Patient Should Be Informed of..

- ...diagnosis
- ...nature of recommended treatment
- ...risks and consequences
- ...benefits
- ...alternatives
- ...likely outcome if nothing is done
- ...the right to ask questions & seek a second opinion
- ...the limits of confidentiality

14

14

Capacity:
The Patient Should Demonstrate...

- ... factual understanding of the relevant information
- ... appreciation of the situation and its consequences
- ... ability to rationally manipulate the information
- ... ability to communicate the choice

15

15

Competency vs Capacity

- Incompetence is a legal determination by a court
  - Uniform Probate Court Standard of Competency
  - May be specific or general
- Incapacity indicates a functional inability as determined by a clinician (Mishkin 1989).

*ALL PATIENTS ARE CONSIDERED COMPETENT AND ASSUMED TO HAVE CAPACITY UNLESS SPECIFICALLY DECIDED OTHERWISE

16

Different types of competency

- **General**: Global ability to handle affairs
- **Specific**
  - Testamentary
  - Fiduciary
  - To consent to medical treatment
  - To participate in research
  - To enter contracts
  - To drive a motor vehicle

17

17

Standardized tools are available

- UBACC for research participation (UCSD Brief Assessment of Capacity to Consent)
- MMSE/SLUMS/MOCA
- HCAI: Hopemont Capacity Assessment Inventory
- MacCAT-T (MacArthur)

18

18

Ways to improve capacity

- Address sensory impairment
- Bite size bits of information
- Memory aids
- Include trusted others in the process
- Translators
- Addressing emotional issues
- Addressing capacity issues over time

19

19

Patient Confidentiality

- Ethical considerations
  - Confidentiality is right of all patients
- Legal considerations
  - Health Insurance Portability and Accountability Act (HIPAA), 2003
    - Health information may not be released without patient's consent, except to those people for whom it is necessary in order to implement the treatment plan
- Exceptions
  - Duty to Warn and Protect Third Parties
    - *Tarasoff v. Regents of University of California* (1974) ruled that psychotherapist has duty to warn patient's potential victim of potential harm
  - Most states have similar laws regarding duty to warn third parties of potential life threats

20

Surrogate Decision Making

- The advance directive standard ends as a riddle: The competent patient can decide but can't know the circumstances of the decision; the incompetent patient experiences these circumstances intimately but can no longer decide"
  - Fellows (1998)

21

21

Patient Self Determination Act 1991

- All persons entering a health care facility must be asked if they have an advanced directive and that should be entered into record
- Does not cover outpatient
- A competent person may make an advance health care directive
- Presumption that person 16 or older is competent
- May contain
  - Instructions
  - Appointment (durable power of attorney: immediate or springing)
- Formal requirements
  - Written
  - Signed by maker
  - Two witnesses

22

22

Advance directives

- Only 10-30% of older adults have AD
  - Slightly higher percentage in nursing home residents
- Living will
  - A guide to preferences: not legally binding!
- Power of attorney
  - A contract between patient and designated individual
  - Patient must be competent when it is signed
  - Must be DURABLE to be valid when the patient lacks capacity. A non-durable POA is useless for medical decision-making

23

23

Guardianship Process:

- Petition
- Physician's statement
- Notice to the respondent and interested parties
- Court hearing
- Adjudication
- Appointment of guardian
  - Conservator
  - General guardianship
- Monitoring

24

24

Models of Proxy Decision-Making

- **Substituted judgment**
  - Attempt to recreate patient's decisions, reflecting their attitudes towards health care, suffering, and quality of life
  - Closer to autonomy or self-determination
  - Generally recognized as more ethical
  - Can help families make difficult decisions
- **Best interest determination**
  - Subjective- based on principle of beneficence
  - Prevent suffering
  - Can involve values and biases of the proxy decision-maker
  - A more paternalistic model

25

25

End of Life Care

- It is not unethical to withdraw care
- Decision to end life should be made considering:
  - Patient's values/wishes
  - The medical situation (suffering, futility, resources)
  - Assessment of quality of life
  - Community values and standards
- Consider hospice when appropriate
  - Usually when <6 months estimated life
  - In dementia can be:
    - Poor PO intake/ food refusal
    - Repeated infections
    - Chronic illness requiring significant intervention

26

26

Elder Abuse

- May be **physical**, **sexual**, **financial/exploitative**, or **neglect**
- Very low percentage of elder abuse cases are ever reported
- Majority of the abusers are related to the victims
- In most cases the victim is totally dependent on the abuser
- Risk factors of abusers:
  - Prior history of domestic abuse
  - Substance use
  - Financial dependence on the elder

27

27

Warning signs of elder abuse

- Cuts, black eyes, bruises or burns, especially when the caregiver cannot adequately explain how they occurred
- Signs of malnutrition or dehydration
- Signs of poor hygiene, including infestations
- A fear by the elderly person of being left alone with a caregiver
- Unexplained withdrawal from regular activities.
- Bedsores
- Difficulty sitting or walking
- Physical signs of a sexually transmitted disease or injury to the genital areas.

28

28

Child and Elder Abuse Reporting Statutes

- All states have enacted child abuse reporting statutes
  - Many states specifically require nurses to report suspected abuse
- Numerous states have also enacted elder abuse reporting statutes
  - Agencies receiving federal funding (i.e., Medicare/Medicaid) must follow strict guidelines for reporting abuse of older adults

29

29

Driving

- Aging increase crash rates per miles driven
- Increases the likelihood of death with crash
- Safety to the patient
  - Impact on self-esteem
  - Rural areas
- Protecting society
- Driving evaluations
- Mandatory reporting

30

30

Driving Safety: It is Not Age but Disability

- Medical conditions and medications are the primary cause of decline in driver safety.
  - Can make even the best of drivers unsafe to drive.
  - Can affect drivers of any age: Increasingly likely as age ↑s
- The safety concern is not the presence of diseases/disabilities but the severity and/or instability of conditions (including medication changes.)

31

How good is the MMSE in predicting driving capacity?

- There is questionable correlation between driving safety and the MMSE.
- Functional abilities Instrumental Activities of Daily Living (IADLs) are better correlated.
- Consider a formal driving examination (usually conducted by Occupational Therapy)

32

Trails A + B

Trails A and B are tests of memory, visuospatial, attention and executive function. More than 1 error or scoring below the 10th percentile in the time (in seconds) taken raises concerns about driving safety (50th percentile is given for comparison).

Norms for Trails A and B by age (in seconds) and education				
Age	Percentiles	Trails A* (education – no change)	Trails B ≤Grade 12	Trails B >Grade 12*
65-69	50	37	86	68
	10	**53**	**137**	**77**
70-74	50	38	101	84
	10	**61**	**172**	**112**
75-79	50	46	120	81
	10	**70**	**189**	**178**
80-84	50	52	140	128
	10	**93**	**158**	**223**
85+	50	54	143	121
	10	**120**	**319**	**240**

***Generally time over 3 minutes or > 1 error is a failure. Observations may also help**

- **hesitancy**
- **self corrections**
- **poor focus**

***Passing Trails A+B does not necessarily mean that the patient is safe to drive+**

TN Tombaugh *Arch clin neuropsychol* 2004;19.pg 203-14

33

Trails B

Timing/Errors

1. <2 min/<2 errors = GOOD
2. 2-3 min/≤ 2 errors = OK dependent on other observations
3. >3 minutes/2 errors = LIKELY UNSAFE

Observations

- Slowness
- Hesitancy
- Self-corrections
- Poor focus

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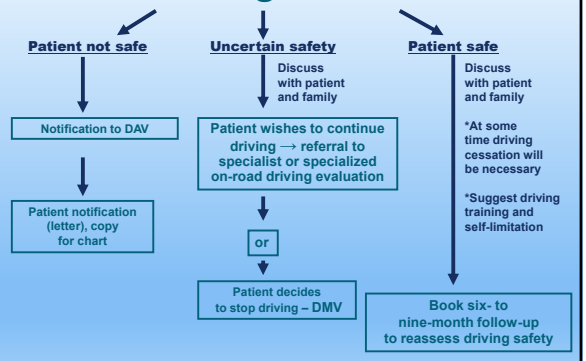
After Driving Assessment



35

Enlisting Family help if you suspect the patient won't comply with stopping driving

- Put notification letter from physician or MOT in obvious location and refer to it to remind patient they can't drive.
- Hide keys
- Substitute a door key for the ignition key
- Disable the car – i.e. simplest way is to remove the battery
- Remove the car – i.e. have a family member borrow it and never bring it back; or, have a tow truck tow it in for repairs and never return it. (LePore, 2000)
- Buy a new alarm for the car to inform you if they attempt to drive
- Keep tabs on driving – i.e. jot down mileage of odometer

36

Malpractice: General Concepts

- **Tort**: Civil wrong
- Intentional tort
  - Assault (attempt to inflict bodily injury)
  - Battery (touching without consent)
- Negligent tort
  - 4 Ds
- Strict liability
  - No need for proof of lack of due care

37

Malpractice

- Duty
- Dereliction
- Direct cause
- Damage

38

Duty

- Is there a doctor-patient relationship?
- Established when patient seeks treatment and it is provided
- Duty can be established by treatment recommendations:
  - Over the telephone
  - Even without patient's consent
  - When the patient is not competent to consent
- Physicians may have a duty to 3rd parties at risk for:
  - Communicable diseases
  - Harm from dangerous patients

39

Deriliction

- Most difficult component to establish
- Refer to the community Standard of Care
- My be via Commission or Omission
- Res ipsa loquitur

40

Avoiding Liability

- Respond to the patient
- Educate the patient
- Know and comply with the standard of care
- Supervise care
- Adhere to the mandated processes
- Document carefully & thoroughly
- Follow up and evaluate
- Maintain a good interpersonal relationship with client and family

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Stay safe (and ethical) out there!!!

Thanks!

Questions/coments to: LPKRAIN@UAMS.EDU

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AAGP 2022 Geriatric Psychiatry Review
Sleep Disorders

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Assistant Clinical Professor of Psychiatry
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1

AAGP 2022 Geriatric Psychiatry Review
Sleep Disorders

Disclosures

Nery A. Diaz, D.O., FAPA, FAAGP

- I have no relevant financial relationships to disclose
- I will discuss off-label medication use for education purposes

2

EEG Wave morphology

- Wake: Alpha Waves, 8-14 Hz
- NREM 1: Theta waves, 4-7 Hz
- NREM 2: Theta waves, 4-7 Hz; sleep spindles (12-14 Hz ≥0.5 sec); K-Complexes (triphasic waves)
- NREM 3: Delta waves, 0.5-2 Hz
- REM: relatively low-voltage mixed-frequency (triphasic) waves.

3

Terminology

Sleep Latency is the time it takes to fall asleep after going go bed at night, usually within 10-20 minutes.

REM Latency is the time from sleep onset until the beginning of the first REM period, usually 90-100 min.

Sleep Efficiency is a ratio of total sleep time to time in bed.

4

EEG sleep changes frequently observed in older adults

1. Increased sleep latency
2. Reduced NREM 3 and NREM 4
3. Increased REM latency
4. Reduced total REM amount
5. Increased awakenings
6. Decreased sleep efficiency

5

The Mammalian Pacemaker is the Suprachiasmatic Nucleus

- An internal biological clock
- located in the hypothalamus
- Sets the daily (circadian) sleep-wake cycle at 24.5-25 hours
- Also sets the circadian hormone and metabolic rhythms

6

Melatonin

- Synthesized in the pineal gland.
- Promotes sleepiness and advances the sleep phase
- Daylight suppresses melatonin synthesis and secretion
- Night has an opposite effect

- Synthesis: Tryptophan→ Serotonin→ N-acetyl-serotonin→ melatonin
- SSRIs increase melatonin plasma concentrations

7

Neurobiology of sleep

- Remains elusive.
- Sleep is promoted by cells in the ventrolateral preoptic (VLPO) area of the hypothalamus, containing Galanin and GABA.
- Wakefulness is promoted by
  - Cell groups at the midbrain-pontine junction that project to the thalamus and cortex.
    - These cell groups contain acetylcholine, noradrenaline, serotonin, dopamine, and histamine.
  - Cells in the lateral hypothalamus contain the peptide, orexin, and project to the cortex.

8

Treatment for Insomnia

Q: What is the first-line treatment for insomnia?

A. Temazepam
B. Melatonin
C. Doxepin
D. CBT-I
E. Diphenhydramine

9

CBT-I

non-pharmacological interventions should be attempted prior to pharmacological treatments.

Below are some of the major core features of CBT-I.

Q: What component of CBT-I attempts to reduce cognitive and physiological arousal in bed and promote the association of bed and sleep?

A. Sleep Restriction
B. Stimulus control
C. Relaxation therapy
D. Cognitive therapy
E. Sleep hygiene

10

Stimulus Control

What component of CBT-I attempts to reduce cognitive and physiological arousal in bed and promote the association of bed and sleep?

A. Sleep Restriction
B. Stimulus control
C. Relaxation therapy
D. Cognitive therapy
E. Sleep hygiene

CBT-I is most helpful for reducing time awake at night, and not for extending total sleep time.

11

Sleep Restriction

- Aims to increase the sleep drive and stabilize circadian rhythm
- Contraindicated in patients diagnosed with epilepsy and BPAD, or any other condition where sleep depravation is contraindicated.

Directions

- Reduce time in bed to perceived total sleep time (not less than 5-6 hours)
- Increase time in bed gradually as sleep efficiency improves
- Specific hours based on optimal circadian timing for specific patient

12

Agents for the treatment of Insomnia

- The choice of agent is based on clinical factors as these pertain to the needs of the patient and the agent's pharmacological profile.
- QUESTION: Current guidelines form the American Academy of sleep medicine suggest starting treatment with the following:
  - A. Short or intermediate-acting benzodiazepine receptor agonists
  - B. Ramelteon
  - C. Melatonin
  - D. All of the above

13

Ramelteon

Current guidelines from the American Academy of sleep medicine suggest starting treatment with the following:

- A. Short or intermediate-acting benzodiazepine receptor agonists
- B. Ramelteon
- C. Melatonin
- D. All of the above

Ramelteon

- Targets sleep-onset insomnia
- A melatonin receptor agonist
- Recommended dose: 8 mg

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Agents for the treatment of Insomnia

Antihistamines

- There is limited evidence for the benefit of using antihistamines for insomnia
- Antihistamines have the potential for substantial side effects in older adults
- Listed on the Beer's Criteria, potentially inappropriate for older adults

Doxepin

- A TCA that is approved by the FDA for the treatment of insomnia
- Listed on the Beer's Criteria, potentially inappropriate for older adults
  - Sedation, urinary retention, incontinence, constipation, arrythmias, falls.

15

Z-drugs

	Dosing Range (mg)	Hours to Peak Plasma Concentration	Half-Life
Zaleplon/Sonata	5-20	1	1
Zolpidem/Ambien	2.5-10	1.6	2.5
Eszopiclone/Lunesta	1-3	1	5-6

Question: Which one of the above agents are on the Beers List for side effects including drowsiness, amnesia, and complex sleep-related behaviors?

A. Zaleplon
B. Zolpidem
C. Eszopiclone
D. All of the above
E. None of the above

16

Benzodiazepine Receptor Agonists

A 72-year-old woman presents to your clinic complaining of a metallic taste in her mouth. She wonders if this could be a side effect of a medication that was initiated for sleep by her PCP. Which one of the following commonly used medications for the treatment of insomnia is known to cause and unpleasant taste?

A. Zaleplon
B. Eszopiclone
C. Doxepin
D. Suvorexant
E. None of the above

17

Benzodiazepine Receptor Agonists

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A. Zaleplon
B. Eszopiclone→ drowsiness, amnesia, complex sleep-related behaviors, unpleasant taste.
C. Zolpidem
D. Suvorexant
E. None of the above

18

SUVOREXANT

What is the mechanism of action of suvorexant?

A. Benzodiazepine receptor antagonist
B. Melatonin receptor agonist
C. Orexin receptor antagonist
D. Anticonvulsant
E. None of the above

19

SUVOREXANT

What is the mechanism of action of Suvorexant?

A. Benzodiazepine receptor antagonist
B. Melatonin receptor agonist
C. Orexin receptor antagonist
D. Anticonvulsant
E. None of the above

Suvorexant was effective in controlled trials for all insomnia symptoms and has a low side-effect burden. All that said, there is no sleep aid that has a low side-effect profile for older, frail adults.

20

What is the most common used stimulant worldwide?

A. Vyvanse
B. Methylphenidate
C. Caffeine
D. Dextroamphetamine
E. Amphetamine

21

Caffeine

- Postulated to act as an antagonist to adenosine
- Abrupt discontinuation leads to headache, anxiety, psychological agitation and excessive daytime sleepiness.

22

Caffeine Consumption

At What daily dose does caffeine consumption lead to caffeine toxicity?

A. 100 mg
B. 150 mg
C. 200 mg
D. 250 mg

23

Caffeine toxicity

- Daily consumption of 250 mg of caffeine typically predisposes to caffeine toxicity, intoxication.
- Insomnia
- Restlessness
- Nervousness
- Excitement
- Diuresis
- GI distress
- Tachycardia
- Arrythmias

24

Common Sleep Presentation for Older Adults

- Phase advance
  - Falling asleep shifts to earlier in the day
  - Common finding in older adults
- Phase delay
  - Falling asleep shifts to later in the in the day

25

Common Sleep Disorders that are underdiagnosed in Older Adults

A 63-year-old man presents to clinic accompanied by his wife who complains that her husband sleeps restless and snores loudly. She is resorted to sleeping in the sofa but can still hear him snoring at night in the living room. She complains that during the day, he falls asleep watching TV or while reading the paper. She is worried that he will suffer a motor vehicle accident. What is the next best step in the management of this patient?

A. Initiate treatment with temazepam
B. Initiate treatment with melatonin
C. Order iron studies
D. Order an overnight PSG
E. Educate the wife about sleep hygiene

26

Obstructive Sleep Apnea

A 63-year-old man presents to clinic accompanied by his wife who complaints that her husband sleeps restless and snores loudly. She is resorted to sleeping in the sofa but can still hear him snoring at night in the living room. She complains that during the day, he falls asleep watching TV or while reading the paper. She is worried that he will suffer a motor vehicle accident. What is the next best step in the management of this patient?

A. Initiate treatment with temazepam
B. Initiate treatment with melatonin
C. Order iron studies
D. Order an overnight PSG
E. Educate the wife about sleep hygiene

27

Polysomnogram Results

The results of your patient's PSG demonstrates a drop in blood oxygen concentration that trigger microarousals and multiple episodes of apnea and hypopnea, with an AHI > 10. What is the best treatment for your patient?

A. Provigil
B. Iron supplements
C. CPAP
D. Sleep Hygiene
E. Ramelteon

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Obstructive Sleep Apnea

- An occlusion of the upper airway at the level of the pharynx that results in oxygen desaturation and leads to repetitive arousals during sleep.
- Epidemiology
  - Estimated prevalence 1% to 2% of the adult male population in the USA
  - Increases to 8.5% of men between the ages of 40 and 65 years.
  - Women account for 12% to 35% of OSA patients
- Risk Factors: male gender, age 40-65 years, obesity, retro-or micrognathia, tonsillar hypertrophy and post-menopausal status in women.
- OSA is a risk factor for HTN, MI and stroke.
- Apnea is the cessation of oronasal airflow for greater than 10 seconds as recorded on a polysomnogram.
- Hypopnea is a 50% reduction of oronasal airflow resulting in either an EEG arousal or at least a 3% decrease in oxygen saturation on the pulse oximeter.
- The apnea-hypopnea index (AHI) is the number of apnea and hypopneas per hour of sleep. AHI>5 is abnormal. Treatment is usually initiated at AHI>10.

29

Common Sleep Disorders that are underdiagnosed in Older Adults

A 77-year-old woman with a history of hypertension and atrial fibrillation reports a feeling of "ants crawling, tingling in the legs at night." The sensation is interfering with her ability to sleep at night. Her symptoms are relieved if she gets up and moves around. She takes carvedilol and apixaban daily. Iron studies are normal. What is the most appropriate initial therapy?

A. ferrous sulfate
B. mirtazapine
C. sertraline
D. ropinirole
E. pramipexole

Adapted from NEUROSAE, 14th edition test

30

Dopamine Agonists

- According to the most recent guidelines for the management of RLS in adults, dopamine agonists are recommended as first-line agents, of which ropinirole has the strongest (Class1, Level A) evidence.
- There is insufficient evidence to support the use of pregabalin over ropinirole or pramipexole.

31

Restless Legs Syndrome (RLS)

Medical Comorbidities

- Iron deficiency
- Anemia
- Diabetes
- Uremia
- Third trimester of pregnancy
- Antidepressants

32

Common Sleep Disorders that are underdiagnosed in Older Adults

A 63-year-old man with RLS presents to clinic accompanied by his wife who complaints that she is having trouble sleeping at night because her husband's legs jerk while he is asleep. A PSG confirms the periodic bursts of muscle activity and leg movement during sleep. What is the most likely cause of the patient's leg movements?

A. Akathisia
B. Restless legs syndrome
C. Periodic limb movements
D. Hypnic jerks
E. Parkinson's disease

Kaufman, 2016

33

Periodic Limb Movement Disorder (PLMD)

A. 80% of patients with RLS also have PLMD
B. Occur at regular intervals
C. Appear only during sleep
D. Not associated with an urge to move
E. Not associated with uncomfortable sensations
F. May disrupt the sleep of a bed partner

Kaufman, 2016

34

Hypnic Jerks

- Benign sensation
- Contraction of antigravity muscles during wake-sleep phase
- In response to a sensation of falling
- No further workup is needed
- Patient re-assurance

- Kaufman, 2016

35

Case Study

A 77-year-old man with a history of ALZ disease is brought to clinic by his wife with a chief complaint of difficulty sleeping over the past week. Over the past two weeks, his wife also reports an increase in pacing, restlessness, and unable to stop moving his legs especially at night. Within the past two months, he started taking quetiapine, and the dose has been gradually increased and as of two weeks ago he takes 200 mg nightly. Medical history includes hypertension, hyperlipidemia, that are well controlled on lisinopril and atorvastatin. What is the next best step in management?

A. Order an overnight polysomnogram to rule out OSA
B. Start treatment with ramelteon for insomnia
C. Order a urinalysis to assess for urinary tract infection
D. Decrease the dose of quetiapine
E. Order Iron studies to rule out restless legs syndrome

Adapted from NeuroSAE, 14th edition

36

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D. Decrease the dose of quetiapine
E. Order Iron studies to rule out restless legs syndrome

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Summary of Treatments

- Atypical antipsychotics predispose to risks for death, cardiovascular disease, akathisia and restlessness.
- Problems with sleep can mimic other co-occurring symptoms.
- Consider the side effects of medications, and the consequences of polypharmacy.
- Consider the onset of symptoms coinciding with increases in dosing or the initiation of medications.
- Consider discontinuing offending agents or reducing the dose of agents that may be leading to side effects.
- Always discontinue medications that the patient is no longer taking.

38

Case Study

A 75-year-old man presents accompanied by his wife with a chief complaint of moving and talking while sleeping. Last night, he fell out of bed and sustained some minor injuries. The patient remembers dreaming that he was conducting an orchestra. What finding on polysomnogram would confirm the presumptive diagnosis?

A. REM sleep without atonia
B. Slow flexion of the hip and knee in non-REM sleep
C. Oxygen desaturation and increased respiratory efforts
D. Intrusions of REM sleep into wakefulness.
E. None of the above

Neurosae, 14th edition Test

39

REM sleep behavior disorder

A 75-year-old man presents accompanied by his wife with a chief complaint of moving and talking while sleeping. Last night, he fell out of bed and sustained some minor injuries. The patient remembers dreaming that he was conducting an orchestra. What finding on polysomnogram would confirm the presumptive diagnosis?

A. REM sleep without atonia is the hallmark finding of REM sleep behavior disorder (RBD), a synucleinopathy. REM atonia is a flaccid, areflexic quadriparesis
B. Slow flexion of the hip and knee in non-REM sleep→ PLMD
C. Oxygen desaturation and increased respiratory efforts→ OSA
D. Intrusions of REM sleep into wakefulness→ Narcolepsy
E. None of the above

Neurosae, 14th edition Test

40

REM sleep behavior disorder

A healthy 75-year-old man presents accompanied by his wife with a chief complaint that he moves and talks in bed while sleeping. The patient remembers dreaming that he was conducting an orchestra. The results of PSG confirm REM episodes without muscle atonia. What is best treatment option for this patient?

A. CPAP
B. Doxepin
C. Clonazepam
D. Sertraline

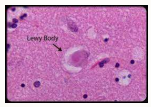
41

Q: Name the a-synucleinopathy

A. Parkinson's disease
B. Dementia with Lewy bodies
C. Multiple systems atrophy
D. All of the above
E. None of the Above

- REM sleep behavior disorder can predate an a-synucleinopathy.

42



43

Fatal Familial Insomnia

- Mutation of prion protein gene (PRNP) leading to the accumulation of abnormal prion protein.
  - Homozygous→ fulminant course
- Average age 50 years
- Refractory insomnia
- Dementia
- Myoclonus
- Autonomic nervous system dysfunction
- Pathology→ spongiform appearance of the cerebral cortex and atrophy of the thalamus.

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Resources

- NeuroSAE Examinations: Neurologist Continuing Certification | AAN
- Diagnostic and Statistical Manual of Mental Disorders: DSM-5. 5th Edition. American Psychiatric Association; 2013.
- Kaufman DM, Geyer H, Milstein MJ. Kaufman's Clinical Neurology for Psychiatrists. Elsevier Inc.; 2016 Dec 13.
- Tampi RR, Tampi DJ, Young J, Hoq R, editors. Absolute Geriatric Psychiatry Review: Essential Questions and Answers. Springer Nature; 2021.

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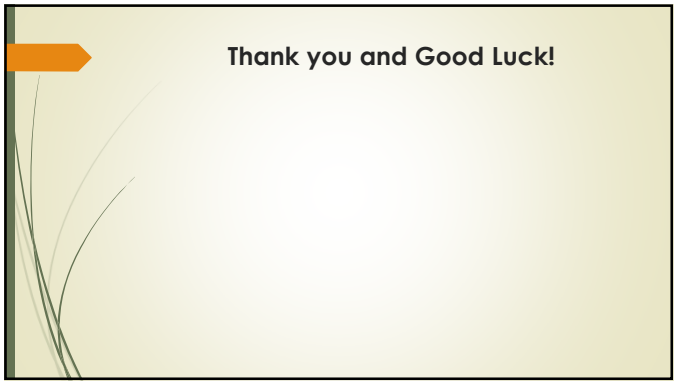

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MAYO CLINIC

PALLIATIVE CARE FOR THE GEROPSYCHIATRIST

AAGP 2022 GERIATRIC PSYCHIATRY REVIEW COURSE

Maria I. Lapid, M.D.
Professor of Psychiatry
Mayo Clinic, Rochester, Minnesota

August 28, 2022

DISCLOSURES

- I receive NIH funding for research
- No relevant financial relationships to disclose
- Will not discuss off-label medication use

LEARNING OBJECTIVES

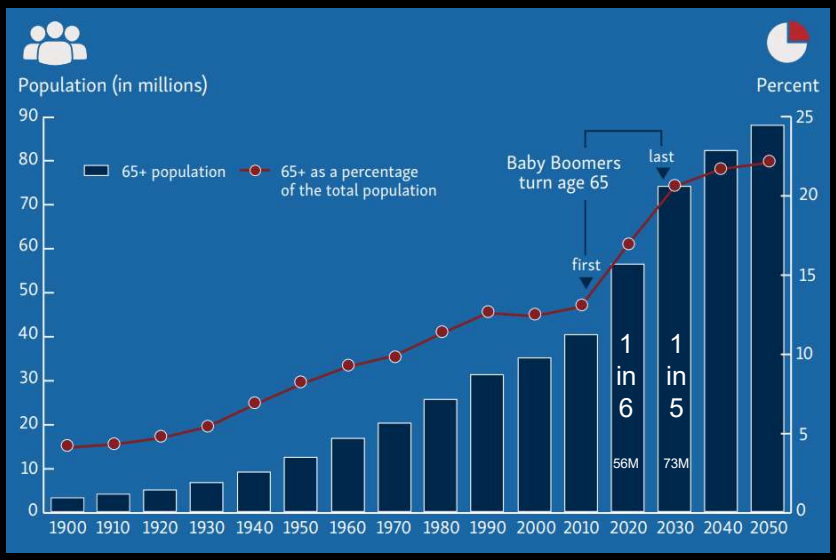
- Describe the principles and key aspects of palliative care
- Define hospice and its benefits

MAYO CLINIC

DEATH AND DYING IN THE UNITED STATES

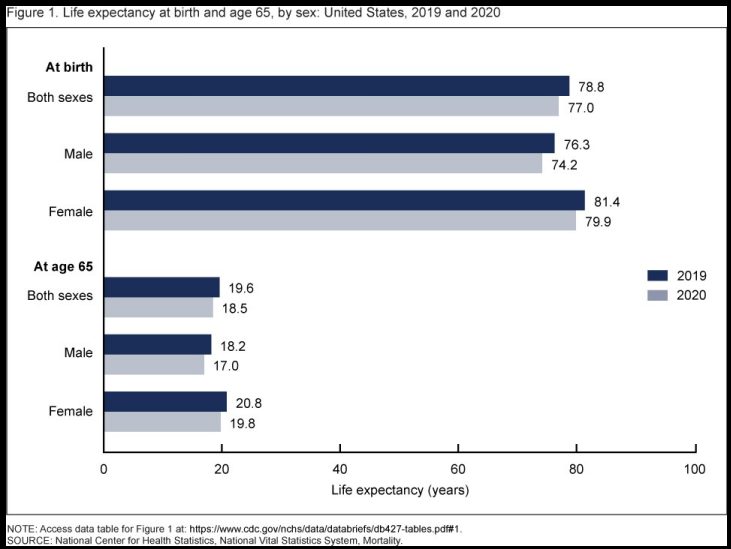
DEMOGRAPHICS OF DEATHS IN THE US

POPULATION AGING IN THE UNITED STATES



https://agingstats.gov/OlderAmericans_AgingPopulation.pdf

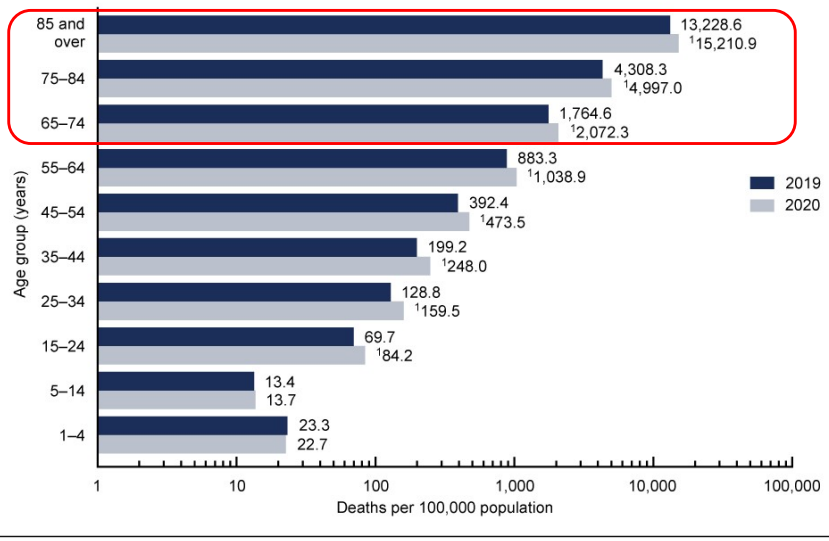
LIFE EXPECTANCY



https://www.cdc.gov/nchs/products/databriefs/db427.htm

DEATH RATES

Figure 3. Death rates for ages 1 year and over: United States, 2019 and 2020

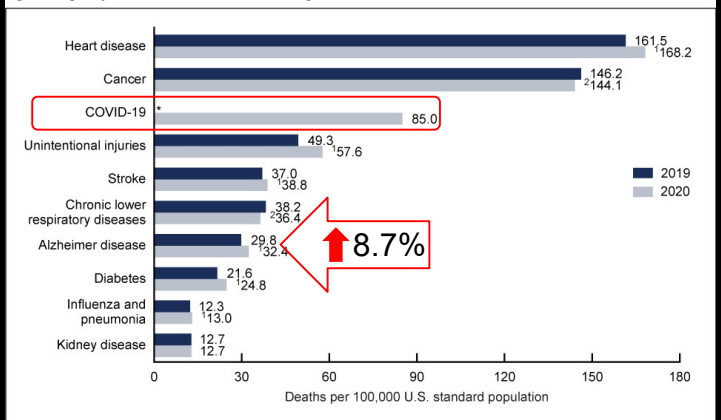


†Statistically significant increase in age-specific death rate from 2019 to 2020 ($p < 0.05$).
NOTES: Rates are plotted on a logarithmic scale. Data table for Figure 3 includes the number of deaths. Access data table for Figure 3 at: https://www.cdc.gov/nchs/data/databriefs/db427-tables.pdf#3.
SOURCE: National Center for Health Statistics, National Vital Statistics System, Mortality.

https://www.cdc.gov/nchs/products/databriefs/db427.htm#Key_finding

LEADING CAUSES OF DEATH – 2019 AND 2020

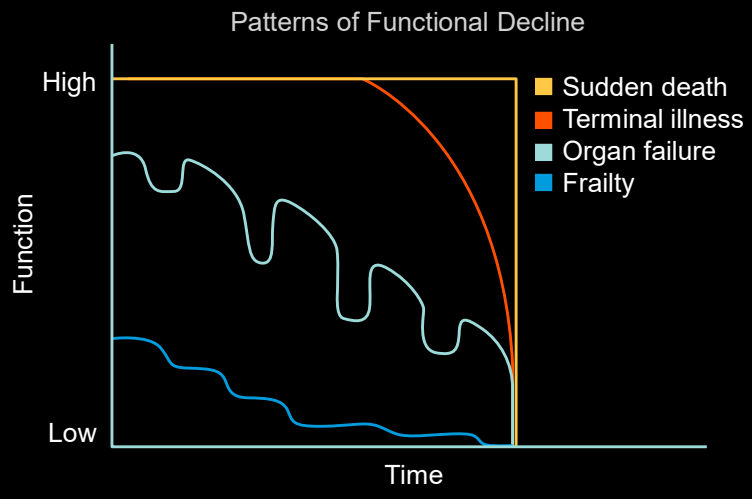
Figure 4. Age-adjusted death rates for the 10 leading causes of death in 2020: United States, 2019 and 2020



* COVID-19 became an official cause of death in 2020; rates for 2019 are not applicable.
†Statistically significant increase in age-adjusted death rate from 2019 to 2020 ($p < 0.05$).
²Statistically significant decrease in age-adjusted death rate from 2019 to 2020 ($p < 0.05$).
NOTES: A total of 3,383,729 resident deaths were registered in the United States in 2020. The 10 leading causes of death accounted for 74.1% of all deaths in the United States in 2020. Causes of death are ranked according to number of deaths. Rankings for 2019 data are not shown. Data table for Figure 4 includes the number of deaths for leading causes and the percentage of total deaths. Access data table for Figure 4 at: https://www.cdc.gov/nchs/data/databriefs/db427-tables.pdf#4.
SOURCE: National Center for Health Statistics, National Vital Statistics System, Mortality.

https://www.cdc.gov/nchs/products/databriefs/db427.htm#section_4

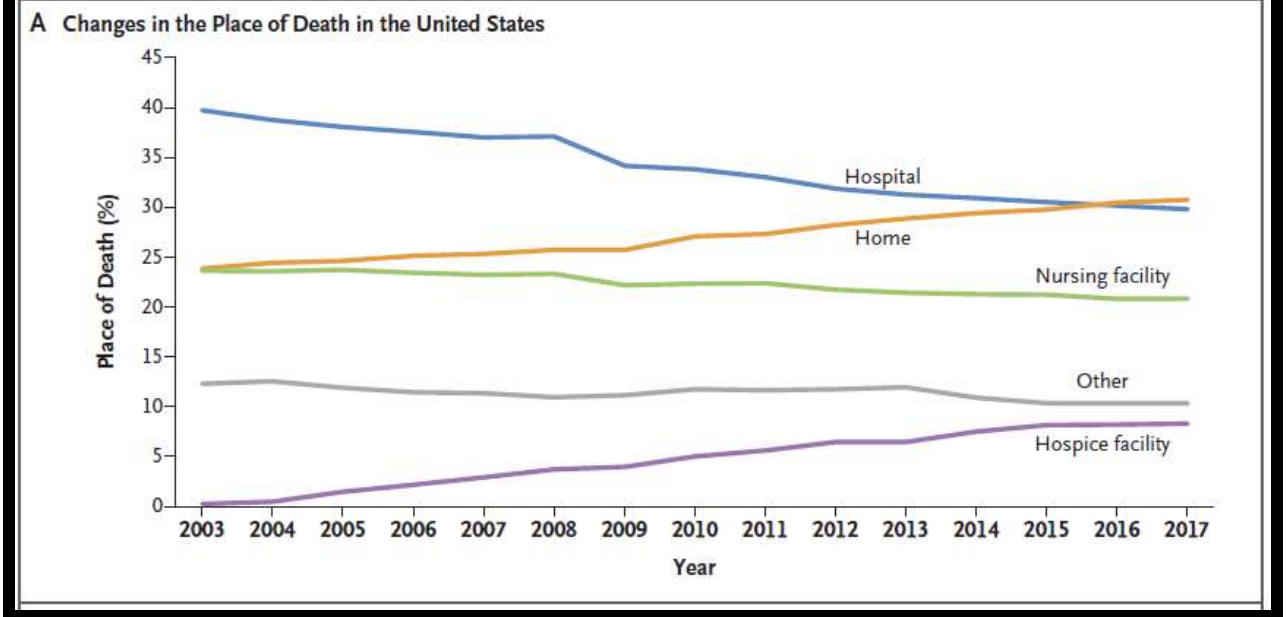
PATTERNS OF FUNCTIONAL DECLINE AT THE END OF LIFE



WHERE DO PATIENTS DIE?

- > 90% adults in the US prefer to die at home.
- However . . .

Gruneir A, Mor V, Weitzen S, Truchil R, Teno J, Roy J. Where people die: A multilevel approach to understanding influences on site of death in America. Med Care Res Rev 64(4):351–78. 2007.



SH Cross, HJ Warraich. N Engl J Med 2019;381:2369-2370.

CASE

GERIATRIC PSYCHIATRY ADMISSION

- Mr. O is a 95 year-old NH resident with advanced dementia, visual hallucinations, behavioral disturbances
- Reason for admission:
  - NH staff report he is "agitated and yelling out very loudly throughout the day and night until he loses his voice and is exhausted"
  - "He also cries frequently, and non pharmacological approaches are very short lived, before he is yelling or crying again."
- Baseline functioning
  - ADLs dependent (dressing, toileting, bathing)
  - Speaks about 1-2 intelligible words/day
  - Unable to ambulate
  - Does not recognize family members

DEFINITION OF PALLIATIVE CARE

The World Health Organization defines palliative care as

" . . . an approach that improves the *quality of life* of *patients* and their *families* facing the problem associated with *life-threatening illness*, through the *prevention and relief of suffering* by means of early identification and impeccable assessment and treatment of *pain* and other problems, *physical*, *psychosocial* and *spiritual*."

http://www.who.int/cancer/palliative/definition/en/

POTENTIALLY LIFE-LIMITING OR LIFE-THREATENING CONDITION

Any disease/disorder/condition

- known to be life-limiting (e.g., dementia, COPD, chronic renal failure, metastatic cancer, cirrhosis, muscular dystrophy, cystic fibrosis), or
- has a high chance of leading to death (e.g., sepsis, multiorgan failure, major trauma, complex congenital heart disease)

- *medical conditions that are serious, but for which recovery to baseline function is routine (e.g., community-acquired pneumonia in an otherwise healthy patient) are not included in this definition

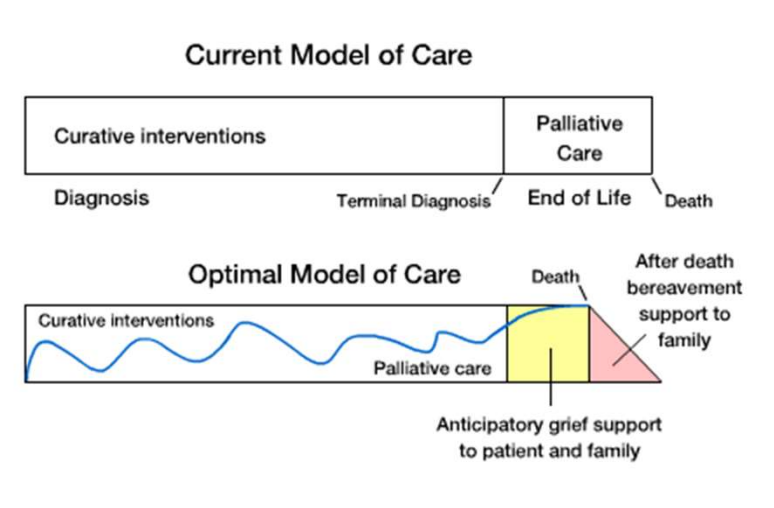
Weissman and Meier. Identifying Patients in Need of a Palliative Care Assessment in the Hospital Setting. Journal of Palliative Medicine. 2011, 14(1): 17-23.

PALLIATIVE CARE PHILOSOPHY:

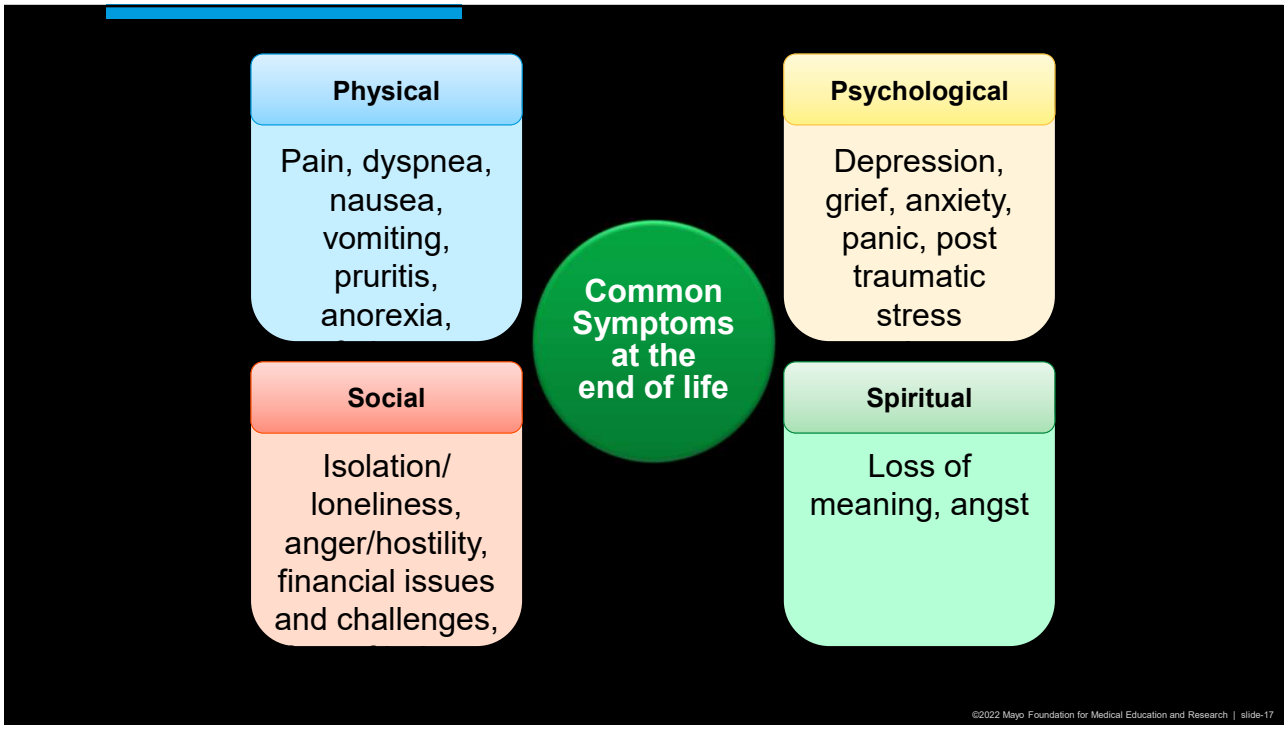
- Provides relief from pain and other distressing symptoms
- Affirms life and regards dying as a normal process
- Neither hastens nor postpones death
- Integrates the psychological and spiritual aspects of patient care
- Offers a support system to help patients live as actively as possible until death
- Offers a support system to help the family cope during the patient's illness
- Offers bereavement support
- Uses a team approach

http://www.who.int/cancer/palliative/definition/en/

MODELS OF CARE



http://endoflife.stanford.edu/M00_overview/model_care.html


Physical
Pain, dyspnea, nausea, vomiting, pruritis, anorexia,
Psychological
Depression, grief, anxiety, panic, post traumatic stress
Common Symptoms at the end of life
Social
Isolation/ loneliness, anger/hostility, financial issues and challenges,
Spiritual
Loss of meaning, angst
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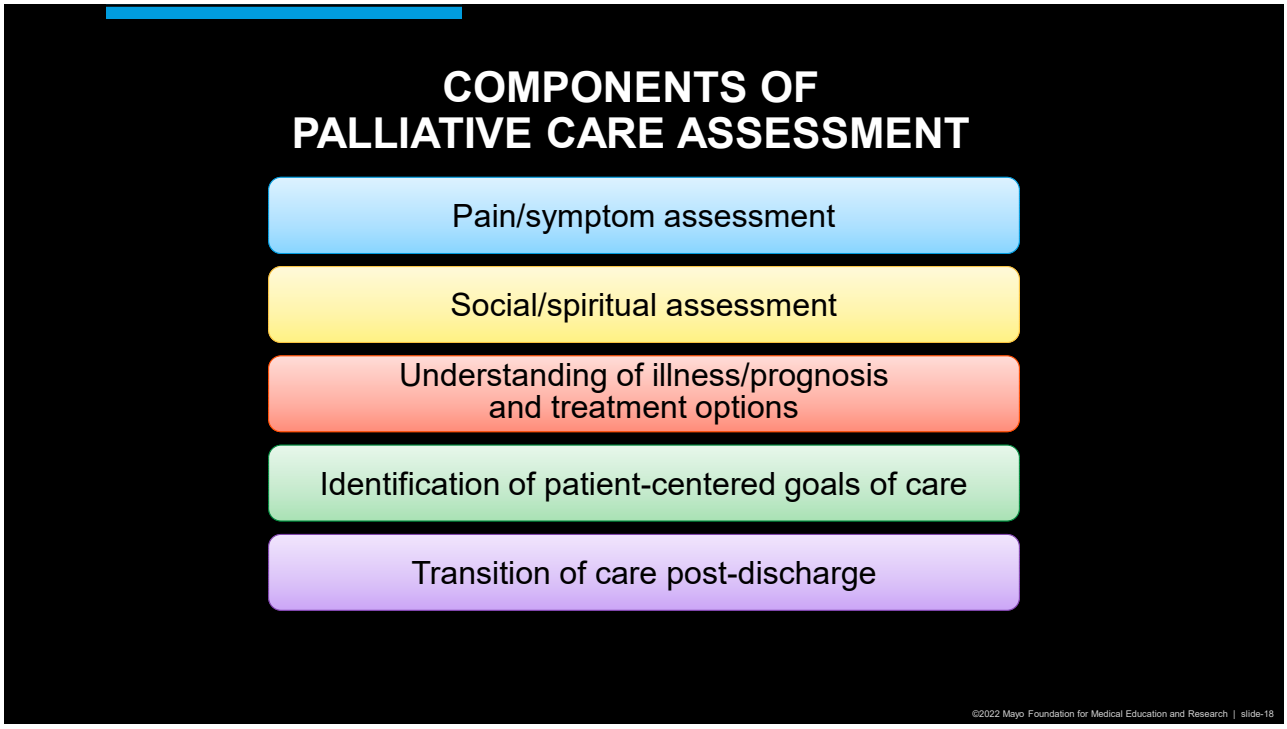
COMPONENTS OF PALLIATIVE CARE ASSESSMENT
Pain/symptom assessment
Social/spiritual assessment
Understanding of illness/prognosis and treatment options
Identification of patient-centered goals of care
Transition of care post-discharge
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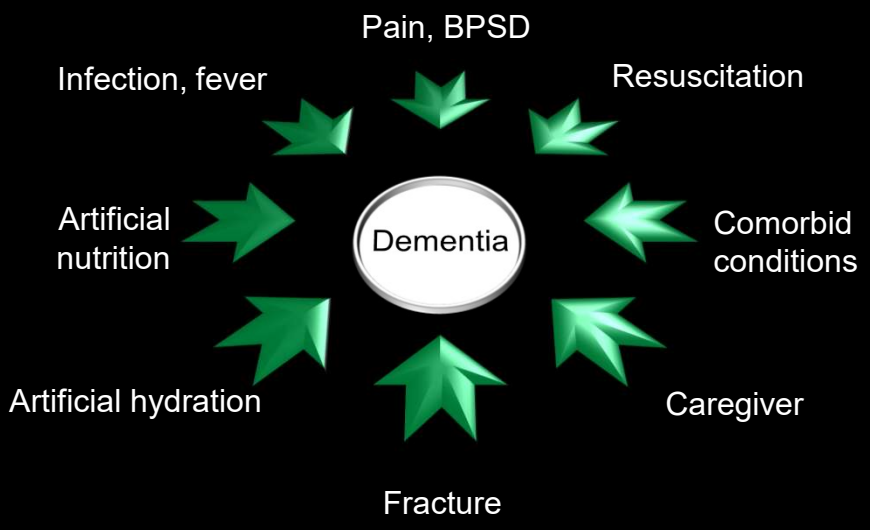
BACK TO MR. O – PALLIATIVE CARE ASSESSMENT

Pain/symptom assessment	Agitated, yelling out, cries frequently
Social/spiritual assessment	Wife/family as caregivers
Understanding of illness/prognosis and treatment options	Family's understanding of stage and end of life issues
Identification of patient-centered goals of care	Discussion of goals of care based on patient preference
Transition of care post-discharge	Discharge planning

MR. O – HOSPITAL COURSE

- In the unit, nursing staff note difficulty with eating, chokes and coughs after swallowing, and expressed concerns about aspiration.
- In having compassionate discussions with family regarding disease trajectory and goal of care discussion, what are the *end-of-life issues in dementia* to include in the discussion?

END OF LIFE ISSUES IN DEMENTIA



MORTALITY IN DEMENTIA

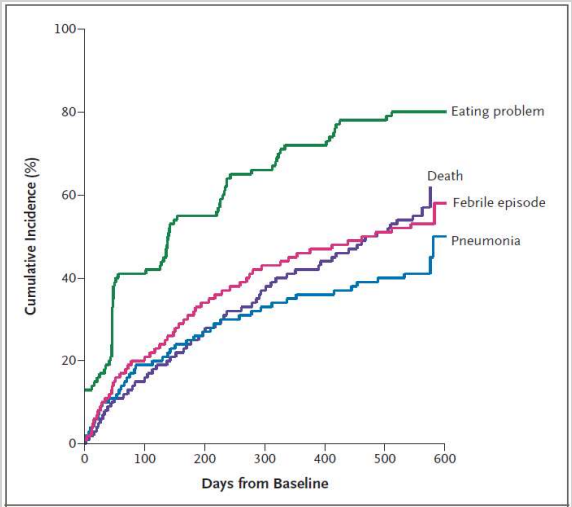


Figure 1. Overall Mortality and the Cumulative Incidences of Pneumonia, Febrile Episodes, and Eating Problems among Nursing Home Residents with Advanced Dementia.

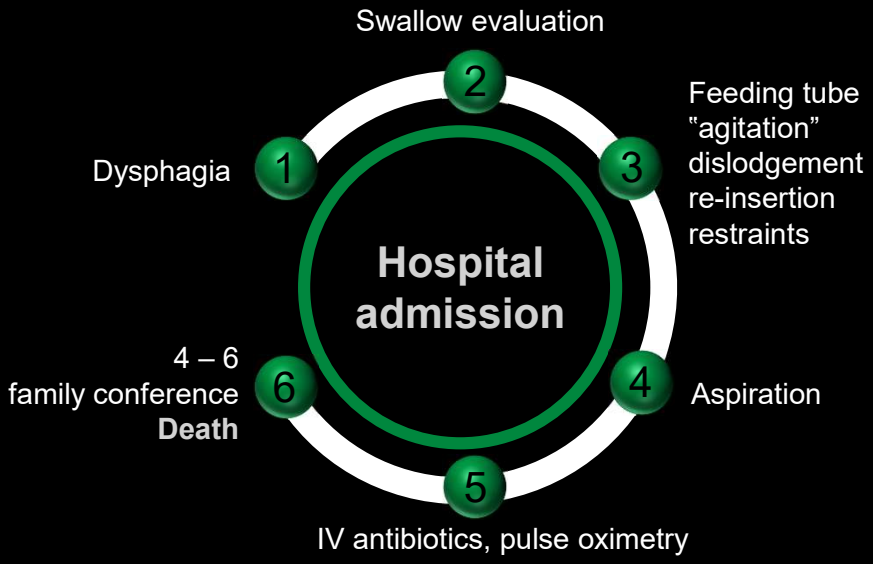
Overall mortality for the nursing home residents during the 18-month course of the study is shown. The residents' median age was 86 years, and the median duration of dementia was 6 years; 85.4% of residents were women.

Mitchell 2009

THE FEEDING TUBE QUESTION

- The family is concerned that Mr. O's aspirations will continue, and would like to know the risks of a feeding tube placement.
- How would you respond?

THE TUBE FEEDING DEATH SPIRAL



WHAT TO DO AS A GERIATRIC PSYCHIATRIST

1. Discuss dying process and end of life goals
2. Know key data on tube feedings
3. Ensure true informed consent
4. Provide clear recommendations
5. If a feeding tube, establish goals/timeline

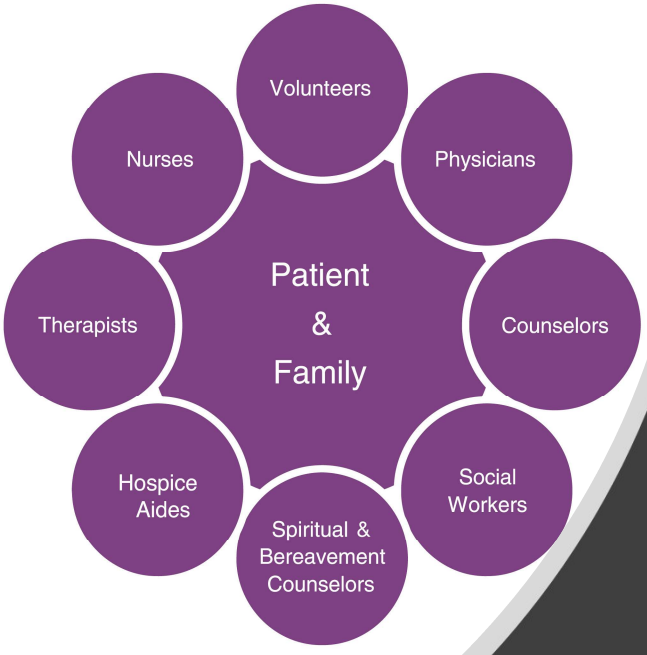
PALLIATIVE CARE IS MORE THAN HOSPICE

Palliative Care

- Recognized by ABMS
- Recognized by CMS
- No limitations to time
- Co manage with primary service
- Life prolonging tx
- Experimental therapies

Hospice

- Medicare rules
- Terminal illness
- 6-month prognosis
  - "Should disease run it's normal course"
- Per diem payment
  - Medications
  - Services
  - Equipment



The Hospice Team

NHPCO
National Hospice and Palliative Care Organization

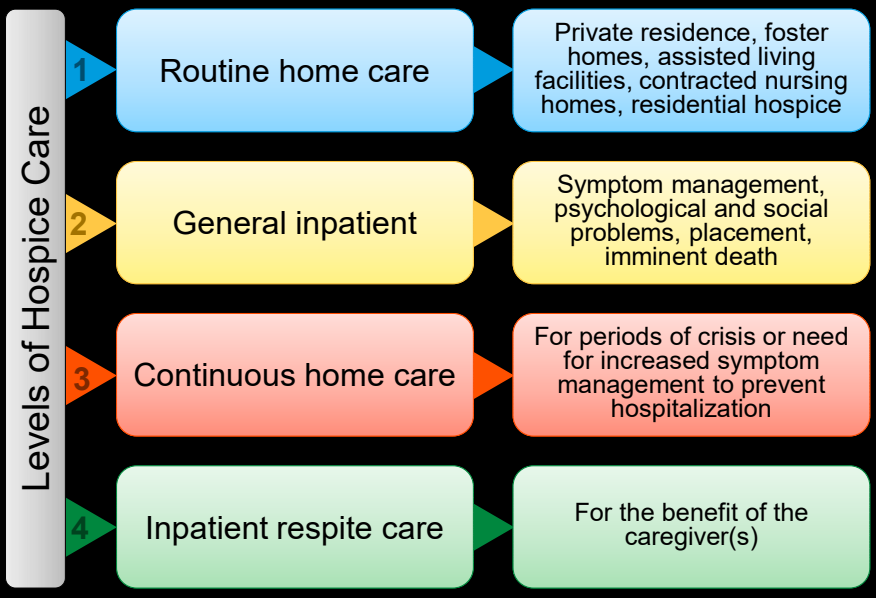
2021 Edition: Hospice Facts and Figures. Alexandria, VA: National Hospice and Palliative Care Organization. www.nhpco.org/factsfigures

WHAT SERVICES ARE PROVIDED?

The interdisciplinary hospice team:

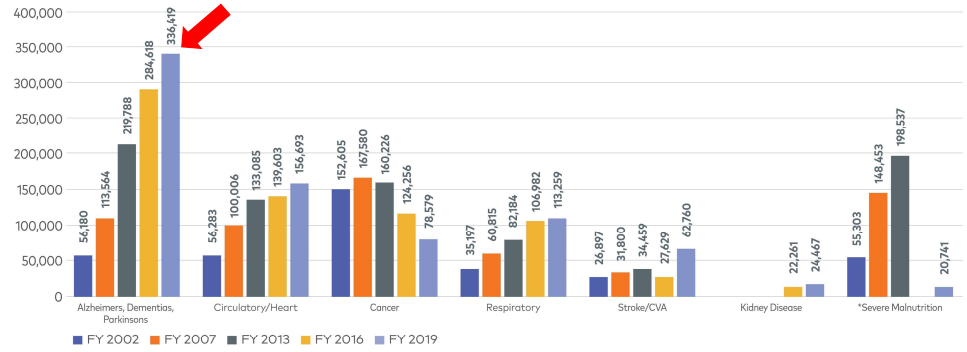
- Manages the patient's pain and other symptoms;
- Assists the patient and family members with the emotional, psychosocial, and spiritual aspects of dying;
- Provides medications and medical equipment;
- Instructs the family on how to care for the patient;
- Provides grief support and counseling;
- Makes short-term inpatient care available when pain or symptoms become too difficult to manage at home, or when the caregiver needs respite time;
- Delivers special services like speech language pathology and physical therapy when needed;
- Provides grief support and counseling to surviving family and friends.

2021 Edition: Hospice Facts and Figures. Alexandria, VA: National Hospice and Palliative Care Organization. www.nhpco.org/factsfigures



Principal hospice diagnosis

Figure 9: Number of Medicare Decedents Using Hospice by Top 15 Diagnoses



** In 2002, 2007 and 2013, severe malnutrition includes debility unspecified and adult failure to thrive. Those diagnoses were disallowed and no longer used in later years.*

Source: CMS-1675-P, FY 2018 Hospice Wage Index and Payment Rate Update and Hospice Quality Reporting Requirements and CMS-1754-P Medicare Program; FY 2022 Hospice Wage Index and Payment Rate Update, Hospice Conditions of Participation Updates, Hospice and Home Health Quality Reporting Program Requirements

NHPCO
National Hospice and Palliative Care Organization

2021 Edition: Hospice Facts and Figures. Alexandria, VA: National Hospice and Palliative Care Organization. www.nhpco.org/factsfigures

FUNCTIONAL ASSESSMENT STAGING (FAST)

1 No difficulties

2 Subjective forgetfulness

3 Decreased job functioning and organizational capacity

4 Difficulty with complex tasks, iADLs

5 Requires supervision with ADLs

6 Impaired ADLs, with incontinence

FAST 7

A. Ability to speak limited to six words
B. Ability to speak limited to single word
C. **Loss of ambulation**
D. Inability to sit
E. Inability to smile
F. Inability to hold head up

HOSPICE ELIGIBILITY FOR DEMENTIA

- National Hospice and Palliative Care Organization (NHPCO) recommends the Functional Assessment Staging (FAST) to determine hospice eligibility
  - FAST 7C or greater (mean survival 3.2 months) or
  - FAST 7A and
    - 1 out of 6 dementia-related co-morbidities (aspiration, upper urinary tract infection, sepsis, multiple stage 3-4 ulcers, persistent fever, weight loss >10% within six months)

https://www.mypcnow.org/fast-facts/

FINAL NOTE ON MR. O

Identified goals of care: comfort, avoid and hospitalization

Enrolled in hospice

Died peacefully in hospice

RECAP

US death and dying demographics

Palliative care principles and assessment

Hospice and benefits

Palliative and hospice care in advanced dementia

RESOURCES

- American Academy of Hospice and Palliative Medicine - aahpm.org
- The National Hospice and Palliative Care Organization - nhpco.org
- Center to Advance Palliative Care (CAPC) - capc.org
- Fast Facts - mypcnow.org
- International Association for Hospice & Palliative Care (IAHPC) - hospicecare.com

THANK YOU!

Q & A

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