

Three “D’s” of
Psychiatric Consultation
in
Hospital Settings:
Delirium,
Decision-Making &
Depression

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Disclosures

- No relevant commercial relationships to disclose



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Educational Objectives

- At the conclusion of this session, participants should be able to:
 - List the Common Elements of Delirium Work-Up and Management
 - Understand the Applebaum Criteria for Decision-Making Capacity
 - Recognize Treatment Options for Depression of the Hospitalized Patient



Delirium



DSM 5 Criteria - Delirium

- Disturbance in attention and awareness
- Develops over short period; fluctuates
- Additional disturbance in cognition
- Not accounted for by other neurocognitive disorders
- Caused by a general medical condition
- Can be multiple etiologies

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Arlington, VA, American Psychiatric Association, 2013.

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- Disturbance in attention and awareness (i.e., reduced ability to direct, focus, sustain and shift attention and reduced orientation to the environment)
- Disturbance develops over a short period of time, is distinctly different from baseline and tends to fluctuate (Fluctuation is hours to a few days)
- Has an additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception)
- Not accounted for by other neurocognitive disorders
- Caused by a general medical condition; can be multiple etiologies (Can be caused by a general medical condition, substance intoxication or withdrawal, toxin exposure or multiple etiologies)
- There is evidence from the history, physical examination or laboratory findings that the disturbance is *a direct* physiological consequence of another medical condition, *substance intoxication or withdrawal (i.e. due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.*

Reference:

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Arlington, VA, American Psychiatric Association, 2013.

Slide 6

A2 I think adding including the full DSM V definition may be helpful- how many of these need to be met
Author, 11/23/2017

DSM 5 Criteria

- Classification of delirium
 - Delirium due to another medical condition
 - Substance intoxication delirium
 - Substance withdrawal delirium
 - Delirium due to multiple etiologies
 - Medication induced delirium



- There is evidence from the H & P and or Lab of a medical condition causing the physiological effects
- Both with substance intoxication and withdrawal, if the symptoms are severe enough to warrant medical attention, then they should be diagnosed with the delirious version, not simply intoxication or withdrawal
- Use multiple etiologies as the diagnosis if the H & P and work up indicate more than one etiology, including a medical condition and substance intoxication
- Medication induced delirium is basically for a side effect from a prescribed medication

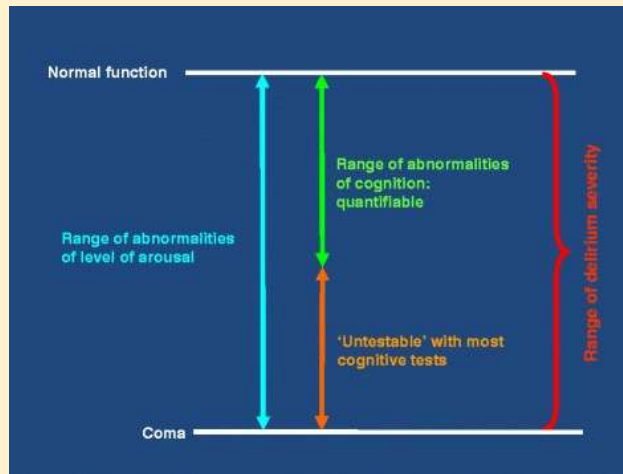
Reference

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Arlington, VA, American Psychiatric Association, 2013

European Delirium Association, American Delirium Society (2014). The DSM-5 criteria, level of arousal and delirium diagnosis: inclusiveness is safer. *BMC medicine*, 12, 141. doi:10.1186/s12916-014-0141-2

DSM 5 Criteria

- Further Specifiers
 - Time
 - Acute : Hours/Days
 - Persistent: Weeks/Months
 - Level of activity
 - Hyperactive
 - Hypoactive
 - Mixed level of activity



Hyperactive: psychomotor activity is elevated in addition to mood lability, agitation, or refusing to cooperate

Hypoactive: psychomotor retardation, sluggishness, lethargy (often misdiagnosed as depression)

Mixed: normal psychomotor activity even with disturbed attention and awareness, or someone whose motor activity fluctuates.

- Picture: Overlap between hypoactive delirium and reduce arousal states (hyperactive delirium not included).

Reference

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Arlington, VA, American Psychiatric Association, 2013

European Delirium Association, American Delirium Society (2014). The DSM-5 criteria, level of arousal and delirium diagnosis: inclusiveness is safer. *BMC medicine*, 12, 141. doi:10.1186/s12916-014-0141-2

Synonyms for Delirium

- Acute confusional state
- Encephalopathy
- Acute brain failure
- ICU psychosis
- Altered mental status
- Acute reversible psychosis
- Reversible dementia
- Acute mental status change
- Organic brain syndrome

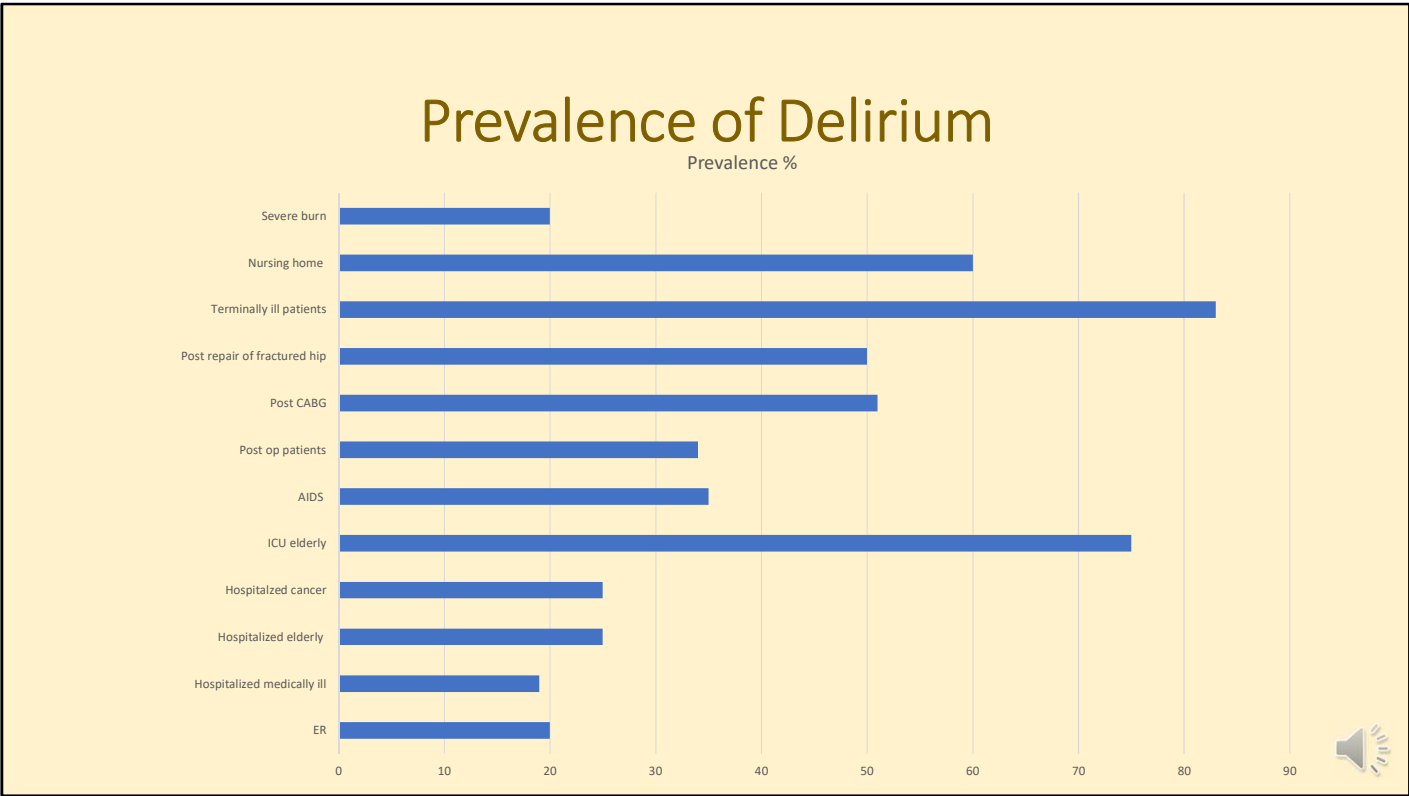


* Only 54% of providers use the term delirium to indicate the disorder of acute change in mental status, inattention, disorganized thinking and altered level of consciousness

* It is important to use the correct terminology and be aware of differences across languages and specialties among clinicians and researchers.

Reference:

Morandi, A., Pandharipande, P., Trabucchi, M. et al. Intensive Care Med (2008) 34: 1907. <https://doi.org/10.1007/s00134-008-1177-6>



- Emergency department patients: 10-30%
- Hospitalized medically ill: 14-24%
- Hospitalized elderly patients: 10-40%
- Intensive care unit elderly patients: 70-87%
- Hospitalized cancer patients: 25%
- AIDS patients: 30-40%
- Post operative patients: 15-53%
 - Post CABG: 51%
 - Post repair of fractured hip: 50%
- Terminally ill patients: 83%

- Nursing home patients: 60%
- Severe burn patients: 20%

Reference

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Arlington, VA, American Psychiatric Association, 2013

Miller, Marcia O. "*Evaluation and Management of Delirium in Hospitalized Older Patients*". American Family Physician, vol. 78, no. 11; pp. 1265-1270, December 1, 2008.

Han J, Wilson A, & Ely E., (2013). Delirium in the Older Emergency Department Patient – A Quiet Epidemic. Emerg Med Clin North Am. doi: [[10.1016/j.emc.2010.03.005](https://doi.org/10.1016/j.emc.2010.03.005)]

Recognition of Delirium

- Delirium is commonly unrecognized
 - ER physicians miss 87-83% of cases (Han, Wilson & Ely, 2013)
 - Hospital admission 14-24% (overall prevalence 1-2%) (Fong, Tulebaev & Inouye, 2011)
 - Nurses recognize delirium more frequently than physicians, 45% v. 20%
- Delirium should always be considered when there is an acute or subacute deterioration in behavior, cognition or function
- 30-40% of delirium cases are preventable (Hshieh, et. Al, 2015)



1. Despite delirium's negative consequences, emergency physicians miss 57% to 83% of cases due to lack of appropriate and routine screening.
2. The overall prevalence of delirium in the community is 1-2% but in the hospital setting, it increases to 14-24%. (Fong, Tulebaev & Inouye, 2011)
3. The incidence of delirium arising during a hospital stay ranges from 6-56% (not including specialized populations such as post-operative, ICU, palliative care etc). (Fong, Tulebaev & Inouye, 2011)
4. At least 30-40% of delirium cases are preventable. There is a strong correlation between delirium and hospital-related falls. Most hospitals do not have delirium prevention protocols or their protocols are inconsistently implemented, with variable adherence. (Hshieh, et. Al, 2015)

Reference:

Fong, T. G., Tulebaev, S. R., Inouye, S. K., (2009). Delirium in elderly adults: diagnosis, prevention and treatment. *Nature Review Neurology* 5, 210-220. doi: [\[10.1038/nrneurol.2009.24\]](https://doi.org/10.1038/nrneurol.2009.24)

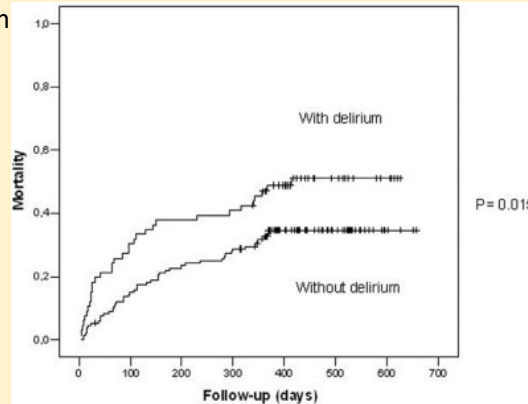
Han J, Wilson A, & Ely E., (2013). Delirium in the Older Emergency Department Patient – A

Quiet Epidemic. *Emerg Med Clin North Am.* doi: [[10.1016/j.emc.2010.03.005](https://doi.org/10.1016/j.emc.2010.03.005)]

Hshieh, T. T., et al. (2015). "Effectiveness of multicomponent nonpharmacological delirium interventions: a meta-analysis." *JAMA Intern Med* 175(4): 512-520

Consequences of Delirium

- Increased Mortality
 - Almost 25% more chances of death with delirium in hospitalized patients (Curyto et al, 2007)
 - Adjusted risk of death – twice as com (1998)
- Increased Morbidity
 - Poor functional recovery
 - Possible future cognitive decline
 - Increased risk of complications
 - Increased nursing home placement
 - Increased costs and LOS
 - Depression, PTSD



- 3-year mortality for hospitalized elderly with index episode of delirium was 75% vs. 51% for non-delirious controls (Curyto et al, 2001)

- No difference in pre-hospital levels of depression, global cognitive performance, physical functioning or medical comorbidity

- Delirious patients experienced an adjusted risk of death of almost 2.0 compared to non-delirious controls (Inouye et al 1998)

- Even after controlling for age, gender, ADL, dementia and APACHE II

References:

Curyto KJ, Johnson J, TenHave T, et al: Survival of hospitalized elderly patients with delirium: a prospective study. *Am J Geriatr Psychiatry* 9:141-147, 2001.

Lima, P. D., Ochiaie, E. M., Lima, B. A., Curiati, J. A., Farfel, M. J., Filho, J. W., (2010). Delirium in Hospitalized Elderly Patients and Post-Discharge Mortality. *Clinics (Sao Paulo)* 65(3), 251-255. doi: [[10.1590/S1807-59322010000300003](https://doi.org/10.1590/S1807-59322010000300003)]

Risk Factors for Delirium (Partial List)

- Elderly
 - Impaired acetylcholine neurotransmission
 - Vascular changes
 - Pharmacokinetic changes
- CNS disorders
 - Major neurocognitive disorders represents one of the greatest risk factors
- Multiple medications (including starting more than 3-5 new meds)
- Burn patients
- Low serum albumin
- Drug and Alcohol Abuse



References:

National Clinical Guideline Centre (UK). Delirium: Diagnosis, Prevention and Management [Internet]. London: Royal College of Physicians (UK); 2010 Jul. (NICE Clinical Guidelines, No. 103.) 7, Risk factors for delirium: non-pharmacological. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK83983/>

Slide 13

A3

ALso, I think a comprehensive list of risk factors may be helpful. Sensory deficits (blindness), previous brain injury, certain surgeries are just a few things that quickly come to mind.

Author, 11/23/2017

Clinical Features

- Diffuse cognitive impairment
 - Attentional deficits
 - Reduced ability to focus, sustain or shift attention
 - “Clouding of consciousness”
 - Memory impairment
 - Long and short term
 - Disorientation
 - Commonly to time and place
 - Rarely to person
 - Executive dysfunction



Reference:

Khan, B. A., Zawahiri, M., Campbell, N. L., Fox, G. C., Weinstein, E. J., Nazir, A., Farber, M. O., Buckley, J. D., Maclulich, A., ... Boustani, M. A. (2012). Delirium in hospitalized patients: implications of current evidence on clinical practice and future avenues for research--a systematic evidence review. *Journal of hospital medicine*, 7(7), 580-9.

Clinical Features

- Thought disturbances
 - Disorganized
- Language disturbances
 - Word finding problems
 - Dysgraphia
 - Dysarthria
 - Dysnomia
- Perceptual disturbances
 - Misperceptions
 - Hallucinations (Visual >> Auditory)



Reference:

Khan, B. A., Zawahiri, M., Campbell, N. L., Fox, G. C., Weinstein, E. J., Nazir, A., Farber, M. O., Buckley, J. D., Maclulich, A., ... Boustani, M. A. (2012). Delirium in hospitalized patients: implications of current evidence on clinical practice and future avenues for research--a systematic evidence review. *Journal of hospital medicine*, 7(7), 580-9.

Clinical Features

- Psychomotor abnormalities
 - Hyper, hypo or mixed
- Sleep-wake cycle disturbance
 - Insomnia
 - Frequent napping or drowsiness during the day
 - Reversal of sleep/wake cycle
- Delusions
 - Usually paranoid and not systematized
- Affective lability
- Neurologic abnormalities



Neurologic abnormalities include:

-Autonomic hyperactivity or instability such as flushing, pallor, sweating, tachycardia, dilated pupils, nausea, vomiting, Fever:

-Myoclonic jerking, cerebellar signs, generalized hyperreflexia

-Nystagmus and ataxia

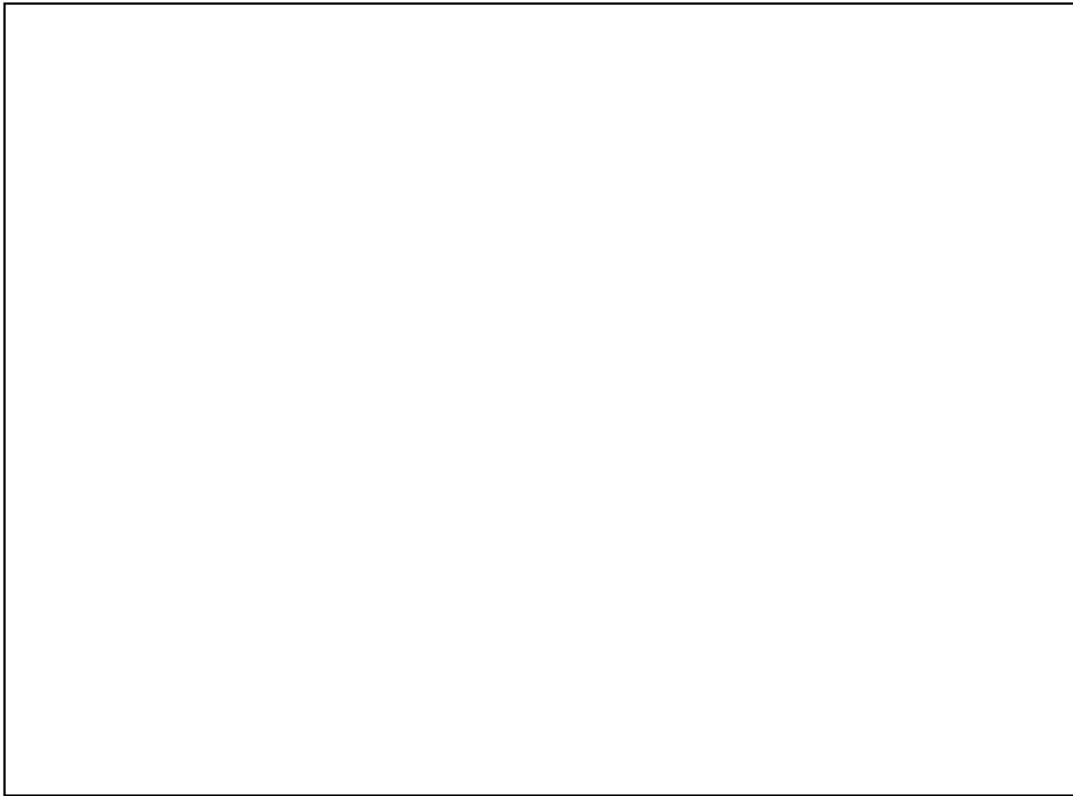
-Tremor

-Asterixis: renal or hepatic insufficiency

References:

Khan, B. A., Zawahiri, M., Campbell, N. L., Fox, G. C., Weinstein, E. J., Nazir, A., Farber, M. O., Buckley, J. D., Maclulich, A., ... Boustani, M. A. (2012). Delirium in hospitalized patients: implications of current evidence on clinical practice and future avenues for research--a systematic evidence review. *Journal of hospital medicine*, 7(7), 580-9.

Caplan JP and Stern TA: Mnemonics in a nutshell: 32 aids to psychiatric diagnosis. *Current Psychiatry* 7(10):27-33, 2008.



References:

Virtual Mentor. 2008. Differentiating among Depression, Delirium, and Dementia in Elderly Patients. 10(6)

Etiology of Delirium

- Intoxication with drugs
 - Many drugs implicated, especially anticholinergic agents, NSAIDs, antiparkinsonism agents, antimicrobials, steroids, opiates, sedative-hypnotics, and illicit drugs
- Withdrawal syndromes
 - Alcohol, sedative-hypnotics, and barbiturates
- Metabolic causes
 - Hepatic, renal or pulmonary insufficiency
 - Endocrinopathies such as hypothyroidism, hyperthyroidism, hypopituitarism or hypoglycemia
 - Disorders of fluid and electrolyte balance



References:

Fong, T. G., Tulebaev, S. R., Inouye, S. K., (2009). Delirium in elderly adults: diagnosis, prevention and treatment. *Nature Review Neurology* 5, 210-220. doi: [\[10.1038/nrneurol.2009.24\]](https://doi.org/10.1038/nrneurol.2009.24)

Etiology of Delirium

- Infections
 - Sepsis, meningitis, pneumonia, syphilis and urinary tract infection
- Head trauma
 - Subdural hematoma, closed head injury/concussion
- Epilepsy
- Neoplastic disease
 - CNS metastasis or limbic encephalopathy
- Vascular disorders
 - Cerebrovascular (stroke)
 - Cardiovascular (acute MI, ACS, Hypertensive Emergency)



References:

Fong, T. G., Tulebaev, S. R., Inouye, S. K., (2009). Delirium in elderly adults: diagnosis, prevention and treatment. *Nature Review Neurology* 5, 210-220. doi: [\[10.1038/nrneurol.2009.24\]](https://doi.org/10.1038/nrneurol.2009.24)

Assessment of Delirium

- Recognition
 - Consider screening tool for ancillary staff (e.g. brief cognitive assessment)
- History
 - Establish course of mental status changes
 - Talk to family or caregivers
 - Recent medication change(s)
 - Symptoms of medical illness
 - Review medical record
 - Review anesthesia record if post-op
 - Onset of delirium is best clue to causality



References:

Fong, T. G., Tulebaev, S. R., Inouye, S. K., (2009). Delirium in elderly adults: diagnosis, prevention and treatment. *Nature Review Neurology* 5, 210-220. doi: [\[10.1038/nrneurol.2009.24\]](https://doi.org/10.1038/nrneurol.2009.24)

A4 including some screening tools may be useful
Author, 11/23/2017

Assessment of Delirium

- Physical and neurologic examination
 - Vitals and focused physical exam
- Mental status
 - Observe for behavioral signs
- Cognitive tests
 - Folstein Mini Mental State Exam
 - Clock drawing task
 - Digit span
 - Months backwards



Reference:

Fong, T. G., Tulebaev, S. R., Inouye, S. K., (2009). Delirium in elderly adults: diagnosis, prevention and treatment. *Nature Review Neurology* 5, 210-220. doi: [\[10.1038/nrneurol.2009.24\]](https://doi.org/10.1038/nrneurol.2009.24)

Assessment of Delirium

- Basic laboratory test
 - Blood chemistries
 - Complete blood count
 - Hepatic function panel
 - TSH
 - B12 and folate
 - RPR
 - ABG
 - Serum drug levels
 - Urinalysis and collection for culture
- Additional tests
 - ECG
 - EEG
 - Cardiac enzymes
 - HIV
 - Chest X-ray
 - ANA, RF, CRP
 - Lumbar puncture
 - Blood cultures
 - Heavy metals
 - CT or MRI



In most cases, the basic laboratory listed above is necessary, especially electrolytes because large shifts can cause osmotic demyelination. Additional tests should be based on history and physical findings. Brain imaging in the absence of focal neurologic deficits is low yield, but still standard of care because in cases where no secondary cause can be found, the imaging reveals the source.

Lumbar puncture is less useful in hospital-acquired delirium, but should be considered in those with delirium who had recent neurosurgery, immunosuppressed patients, or recent TBI patients.

Reference:

Brown, E. G. and V. C. Douglas (2015). "Moving Beyond Metabolic Encephalopathy: An Update on Delirium Prevention, Workup, and Management." *Semin Neurol* 35(6): 646-655.

Assessment of Delirium

- Electroencephalogram
 - Helpful to confirm the diagnosis
 - Usually generalized slowing
 - Low voltage fast activity in alcohol or sedative-hypnotic withdrawal
 - Picture: *Delirium Detection Using EEG*
- Structural Neuroimaging
 - Focal neurologic signs
 - History or concern of head trauma
 - No clear cause of delirium found



EEG:

Despite its frequency and impact, delirium is poorly recognized in postoperative and critically ill patients. EEG is highly sensitive to delirium but, as currently used, it is not diagnostic.

Picture: Most optimal electrode combinations for delirium detection, based on first four rankings of the eyes-closed condition. The thickness of the connecting line corresponds with the rank of the electrode combination: The thickest line represents the highest rank.

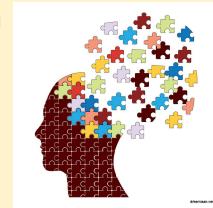
Reference:

Kooi, W. A., Zaal, I., Klijn, F., Koek, L. K., Meijer, C. R., Leijten, F., Slooter, A., (2015). Delirium Detection Using EEG. *Chest* 1 (147) 94-101.

Soiza, R., Sharma, V., Ferguson, K., Shenkin S., Seymour, D., MacLulich, A., (2008). Neuroimaging studies of delirium: A systemic review. *Journal of Psychosomatic Research* 65(3) 239-248.

Treatment of Delirium

- Two important aspects
 - Identify and reverse the reason(s) for the delirium
 - Managing behaviors
 - Sitter
 - Restraints (Not appropriate)
 - Reduce psychiatric or behavioral symptoms of delirium
 - Non pharmacologic treatment
 - Pharmacologic treatment



Managing behaviors:

Sitter:

Allowing a family member or other caregiver to stay with the patient at the bedside may help to manage the patient's behavior. This person can provide reassurance, answer questions, reorient the patient, and notify staff if the person needs assistance. In some cases, the hospital is able to provide a sitter if a family member is unavailable. However, a familiar and trusted family member or friend can provide additional reassurance to the patient.

Restraints:

The use of restraints (to tie a person to their bed or chair) is almost never appropriate, as restraints can increase agitation and create additional problems by preventing the person from moving around as needed. Preventing movement also potentially allows skin sores (called pressure ulcers) to develop from sitting or lying in the same position for long periods. The use of restraints has not been shown to prevent harmful falls among hospitalized patients.

However, in the rare situation where the patient is at high risk for harm and restraints are applied, hospital staff should monitor the patient at least every two hours, untying the restraints and changing the patient's position. The restraints should be removed as soon as possible.

Picture reference:

Kernisan, L., (n.d.). Better Health While Aging. <https://betterhealthwhileaging.net/hospital-delirium-what-to-do/>

Notes from Uptodate: Delirium

Treatment of Delirium

- Non-pharmacologic Interventions
 - Aims
 - Cognitively non-demanding
 - Limit the risk of harm to self and/or others
 - Types
 - Avoid interruption of sleep
 - Room close to nursing station
 - Sitter, feeding assistance and encouragement during meals
 - Clocks and calendar and orientation board
 - Adequate lighting
 - Sensory aids, cleaning of ear wax



Very modest stimulation is important: too much adds to confusion, too little leaves patient locked in own internal disorganized perceptions and thoughts, thus exacerbating the delirium.

Ensure adequate intake of nutrition and fluids, may need assistance with meals.

The staff needs to be educated on the patients' delirium

Assess the patient for safety (such as falls, wandering, inadvertent self-harm)

Educate and support the patient and family

Frequent reorientation (clocks, calendar, radio)

Patients should be oriented to the day-night cycle with open blinds if rooms have windows, or change in lighting; nightlights often help

Familiarity with objects, photos, presence of family members.

Minimize restraints and using a sitter is preferred because the restraints can also agitate the patient.

If patients wear glasses or have hearing aids, make sure family brings them and the patient has access to them.

Reference:

Hshieh, T. T., et al. (2015). "Effectiveness of multicomponent nonpharmacological delirium interventions: a meta-analysis." *JAMA Intern Med* 175(4): 512-520.

Treatment of Delirium

- Major classes of medications utilized
 - Antipsychotics
 - Typical
 - Atypical
 - Cholinesterase inhibitors
 - Benzodiazepines



Medications to control difficult behavior are only to be considered as a last resort, if the patient's agitation is so extreme as to be a potential source of harm. Some classes of drugs, especially sedatives such as lorazepam (Ativan) and diazepam (Valium), can build up in the bloodstream and cause the person to become more confused. Antipsychotic medications, such as haloperidol (Haldol), may be considered, but only in small doses and for short periods of time. If necessary, these medications should be stopped frequently, with direction or approval by the physician, so that the patient can be reevaluated. Antipsychotic medications are not recommended for long-term treatment.

Reference: UptoDate

Treatment of Delirium

- Typical Antipsychotics
 - Low potency
 - Not recommended (anti-cholinergic can worsen)
 - High potency - Haloperidol the “gold standard”
 - Virtually no anticholinergic properties
 - Little risk of hypotension
 - Does not suppress respiration
 - Can be given IV
 - Not FDA approved
 - Note: IV haldol is twice the potency of PO haldol
 - Fast acting



Treatment: Haloperidol Dosing

- Haloperidol starting dose
 - Elderly
 - Mild agitation: 0.5mg
 - Moderate agitation: 1mg
 - Severe agitation: 2mg
 - Young adult
 - Mild agitation: 1-2mg
 - Moderate agitation: 2-5mg
 - Severe agitation: 5-10mg
 - Dose may be repeated at regular intervals until patient is calm
 - Max dose: 10mg/d for elderly & 20mg/d for youth



Haldol can be given orally, IM or IV. Dosing is usually 1-2mg every 2-4 hours to a max of 500mg/24hrs. IV dosing has been shown to reduce EPS and other side effects, but telemetry monitoring needs to occur in this setting. (10mg/hour continuous);

Treatment: Haloperidol Side Effects

- Haloperidol side effects
 - Extrapyramidal reactions (EPS)
 - Very low rate of EPS with IV administration (Tesar GE et al 1985)
 - Co-administration with lorazepam may further lower the incidence (Menza MA et al 1988)
 - Hypotension
 - Usually related to volume depletion



Treatment: Haloperidol Side Effects

- Haloperidol side effects
 - QTc prolongation
 - Rare
 - Recommendations
 - Pretreatment determination of QTc
 - Avoid other medications that may prolong QTc
 - Monitor potassium and magnesium
 - Monitor QTc during treatment
 - Stop haloperidol if QTc > 500 msec or if baseline QTc increases by more than 60 msec



Treatment: Atypical Antipsychotics

- Atypical antipsychotics
 - Increasingly more randomized, prospective studies evaluating efficacy
 - Use partially supported on the basis of clinical experience, case reports and small case studies
 - Theoretical lower risk of extrapyramidal side effects
 - Acute dystonic reactions
 - Drug-induced parkinsonism
 - Akathisia
 - Continued risk of QTc prolongation



Treatment: Atypical Antipsychotics

- Atypical antipsychotics (continued)
 - Quetiapine (Seroquel)
 - Better than placebo in randomized control study
 - Only oral formulation
 - Dosage
 - Starting dose 12.5mg-25mg qhs and titrate to effect
 - Can also use 12.5mg-25mg q6h prn
 - Aripiprazole (Abilify)
 - No randomized prospective studies available
 - Multiple formulations
 - Oral tablet, oral tablet (disintegrating), oral solution, and intramuscular
 - Maybe lower risk of QTc prolongation
 - Dosage
 - ???



Treatment: Atypical Antipsychotics

- Atypical antipsychotic (continued)
 - Risperidone (Risperdal)
 - Has been found in small randomized trials to match Haldol, Olanzapine in efficacy
 - Multiple formulations
 - Oral tablet, oral tablet (disintegrating), oral solution, and long-acting decanoate
 - Dosage
 - Starting dose 0.25mg-0.5mg/day scheduled
 - Can also use 0.25-0.5mg q6h prn agitation
 - Usually no more than 2mg/day required
 - Ziprasidone (Geodon)
 - No randomized prospective studies available
 - Intramuscular route available
 - Dosage
 - 20 mg IM/6 hours but maximum 40mg IM/24 hours



Treatment: Atypical Antipsychotics

- Atypical antipsychotics (continued)
 - Olanzapine (Zyprexa and Zydys)
 - Small prospective, randomized-control studies show efficacy matching Haldol
 - Multiple formulations
 - Oral tablet, oral tablet (disintegrating), oral solution, and intramuscular
 - Dosage
 - Starting dose 2.5mg-5mg qhs
 - Can use 2.5-5mg 6h prn agitation
 - Usually no more than 10mg/day required



Treatment: Other Agents

- Cholinesterase inhibitors
 - Physostigmine
 - Diagnostic tool for anticholinergic toxicity
 - Rarely needed for treatment
 - Usual dose 0.16 mg to 2 mg or 3 mg/hour IV
- Benzodiazepines
 - Most appropriate for alcohol or sedative-hypnotic withdrawal
 - Potential adjunct to high potency antipsychotics
 - Can worsen confusion
- Vitamins
 - B vitamins
 - Nicotinamide



Benzodiazepines (BZDs) are often exacerbators of delirium because they can cause sedation, behavioral disinhibition, amnesia, ataxia, respiratory depression, rebound insomnia, euphoria and withdrawal. They are not as effective as antipsychotics except in combination when assisting with sleep or desire for lower dosing of the antipsychotic. However, BZDs are the drug of choice in BZD or alcohol withdrawal delirium, or when the seizure threshold needs to be raised, or if the side effects of the antipsychotics would be detrimental to the patient's condition. If necessary, the BZDs Lorazepam, Oxazepam, and Temazepam should be used because they are predominantly metabolized by glucuronidation, not oxidation. Also, they have shorter half-lives, which is important in liver failure.

Vitamin replacement, especially B vitamins and nicotinamide, are important in malnutrition from alcohol dependence or any sort of starvation/malabsorption.

Treatment: Other Agents

- Dexmedetomidine (Precedex)
 - Selective alpha-2 agonist
 - Approved for short-term use (<24 hours) in patients initially receiving mechanical ventilation
 - Has been shown to help with ventilator weaning (Ricker et al 2009; Reade et al 2009) and be associated with less incident of delirium as compared with other sedative agents
 - Not well studied as an agent for long-term administration
 - Side effects
 - Bradycardia
 - Hypotension (especially with hypovolemia)
 - Sedation



Decision Making



Purpose and Basis of Informed Consent

- Purpose of informed consent
 - To promote individual autonomy
 - To foster rational decision-making
- Informed consent is founded on two distinct legal principles
 - The right of self-determination
 - The physician's fiduciary responsibility to the patient



Elements of Informed Consent

- 1) Disclosure of information
- 2) Voluntary choice
- 3) Capacity to decide



Important Definitions: Capacity vs. Competency

- Capacity
 - The ability to accept or refuse treatment recommendations
 - Determined by a clinician upon specific elements of a mental status exam
 - Does not have to be psychiatrist or psychologist
 - Treating Physician is often in the best position to do this
- Competency
 - A legal concept formally determined in a court of law
 - Judges often rely on the clinician's recommendations
 - The law presumes competence until proven otherwise



Important Points About Capacity

- Determined on a situation-by-situation basis (Querques et al., 2010)
- Patient can have capacity to make some decisions, but not all
 - Must clarify the specific capacity question
- “Sliding scale” is used to assess capacity (Roth et al., 1977):
 - e.g., patient may have capacity to refuse phlebotomy (risk-to-benefit ratio is low, hence standard to declare patient incapacitated is high)
 - but not capacity to refuse urgent cardiac surgery (risk-to-benefit ratio of refusal is high, hence standard to declare patient incapacitated is low).
 - “Sliding scale” is attempt to honor patients’ autonomy while doing no harm
- Capacity can change over time (e.g., delirious patient may be able to make decision once sensorium clears)
 - Capacity refers to the specific condition or current situation; not an enduring status
 - Reassessment periodically recommended



How to Assess Capacity: Four Abilities Model

Appelbaum, 2007

- **C**ommunicate a (consistent) choice
- **U**nderstand the **R**elevant information
- **A**ppreciate the circumstances and consequences
- **R**ationally **M**anipulate the information

Mnemonic: CRAM

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These 4 elements are considered by many as the standard theoretical framework by which to assess capacity. In considering how stringently to apply these 4 elements, must consider the risk/benefit of the decision to be made; for example, if a patient is refusing a high benefit/low risk intervention (such as antibiotics for sepsis), then a more stringent/stricter capacity assessment should be done; on the other hand, if the patient is refusing a low benefit/high risk intervention (such as palliative chemotherapy for an incurable cancer), then a less stringent standard would be applied- ie, a consistent refusal and a basic understanding of what is being refused might be adequate

Table 1. Legally Relevant Criteria for Decision-Making Capacity and Approaches to Assessment of the Patient.

Criterion	Patient's Task	Physician's Assessment Approach	Questions for Clinical Assessment*	Comments
Communicate a choice	Clearly indicate preferred treatment option	Ask patient to indicate a treatment choice	Have you decided whether to follow your doctor's [or my] recommendation for treatment? Can you tell me what that decision is? [If no decision] What is making it hard for you to decide?	Frequent reversals of choice because of psychiatric or neurologic conditions may indicate lack of capacity
Understand the relevant information	Grasp the fundamental meaning of information communicated by physician	Encourage patient to paraphrase disclosed information regarding medical condition and treatment	Please tell me in your own words what your doctor [or I] told you about: The problem with your health now The recommended treatment The possible benefits and risks (or discomforts) of the treatment Any alternative treatments and their risks and benefits The risks and benefits of no treatment	Information to be understood includes nature of patient's condition, nature and purpose of proposed treatment, possible benefits and risks of that treatment, and alternative approaches (including no treatment) and their benefits and risks
Appreciate the situation and its consequences	Acknowledge medical condition and likely consequences of treatment options	Ask patient to describe views of medical condition, proposed treatment, and likely outcomes	What do you believe is wrong with your health now? Do you believe that you need some kind of treatment? What is treatment likely to do for you? What makes you believe it will have that effect? What do you believe will happen if you are not treated? Why do you think your doctor has [or I have] recommended this treatment?	Courts have recognized that patients who do not acknowledge their illnesses (often referred to as "lack of insight") cannot make valid decisions about treatment Delusions or pathologic levels of distortion or denial are the most common causes of impairment
Reason about treatment options	Engage in a rational process of manipulating the relevant information	Ask patient to compare treatment options and to offer reasons for selection of option	How did you decide to accept or reject the recommended treatment? What makes [chosen option] better than [alternative option]?	This criterion focuses on the process by which a decision is reached, not the outcome of the patient's choice, since patients have the right to make "unreasonable" choices

* Questions are adapted from Grisso and Appelbaum.³¹ Patients' responses to these questions need not be verbal.

Functional Abilities of Capacity: Understanding Appelbaum, 2007

- Ability to understand

- Understanding should be assessed in all cases in which the patient expresses a choice
- Can the patient assimilate the information disclosed regarding the nature of the illness, the treatment options, the prognosis (with and without treatment), and the risks/benefits of treatment?
- Suggested questions to ask:
Tell me in your own words...
 - The nature of your condition
 - The recommended treatment along with possible benefits and risks
 - The possible benefits and risks of alternative treatment or no treatment



Functional Abilities of Capacity (Appreciation) Appelbaum, 2007

- **Ability to Appreciate**
 - Appreciation relates to the patient's ability to apply the information to his/her own situation.
 - The focus is on the patient's beliefs rather than knowledge
 - Belief of illness
 - Belief of treatments
- **Suggested questions:**
 - What do you believe is wrong with you now?
 - Do you think that you need some type of treatment?
 - What do you believe will happen to you if you do not get treated?



Functional Abilities of Capacity (Reasoning)

Appelbaum, 2007

- **Ability to reason**
 - Does the patient use the information disclosed to engage in a rationale process of options?
 - Is there a “reasonable reason” for the patient’s choice?
 - Takes into account the patient’s past preferences and life decisions
 - Suggested questions:
 - Tell me how you reached this decision?
 - How did you weigh the information provided?

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Functional Abilities of Capacity Appelbaum, 2007

- **Summary of functional abilities**
 - **Expressing a choice**
 - Ability to state a preference
 - **Understanding**
 - Ability to comprehend the information provided in the treatment disclosure required for informed consent
 - **Appreciation**
 - The patient's beliefs about the disorder and proposed treatments and to apply it realistically to their own situation
 - **Reasoning**
 - Ability to process information and one's preference in a logical manner

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Make sure to conduct capacity assessment in a way that helps patients bring all strengths to bear/do the best they can

When Should Decision-Making Capacity Be Assessed?

- It is often done at every patient encounter, but unrecognized
- Abrupt changes in mental status
- When patients refuse treatment recommendations, including AMA discharges
- When patients consent to especially risky treatment
- When patients have a risk factor for impaired decision-making



What Types of Conditions Can Diminish Capacity?

- Psychological factors/Cognitive Biases
- Psychiatric diagnoses
- Neurocognitive disorders

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• Cognitive biases/psychologic factors

- Myopic approaches to problem-solving
- Downplaying of risk
- Optimistic framing of problems
- Blindness to the effects of one's decisions on others

• Psychiatric diagnosis:

- Suspicion or presence of incapacity should trigger pursuit of mental illness-based explanations for it (Appelbaum, 1994)

- Would optimally provide recommendations for treating the psychiatric illness in hope of restoring capacity

• Cognitive:

- Clinical assessment of incapacity due to cognitive impairment should be supported by cognitive screening that includes a standardized instrument such as the Montreal Cognitive Assessment (Nasreddine et al., 2005)

Substitute Decision Making

- Once deem patient to lack capacity, need substitute decision maker
- Options for substitute decision making:
 - Advanced directives
 - Decision directives (living will)
 - Documents the patient's choice(s) of treatment under specific circumstances
 - Proxy directives (POA)/Healthcare proxy
 - Patients designate persons they desire to make decisions for them when they are incapacitated
 - Effectiveness depends on patient sharing their choices with the proxy
 - Family/Close friend/Partner
 - If there is no advanced directive, families are usually asked to make decisions
 - Some states have laws which specify which family members have priority



Substitute Decision Making if no Proxy/Family Available

- Courts
 - Decision makers of last resort
 - Many hospitals turn to the courts to adjudicate incompetence and appoint a decision-maker in the absence of an advanced directive
 - Patients can challenge findings of incapacity in court
 - May go to court for treatment order or for guardianship
 - Consider guardianship when:
 - No substitute decision maker
 - Capacity not likely to be restored in near future
 - Ongoing medical decisions will likely need to be made



Depression in Medical Settings



Some Medical Conditions Closely Associated with Depressive Symptoms

- Stroke
- Parkinson's disease
- Multiple sclerosis
- Epilepsy
- Huntington's disease
- Pancreatic and lung cancer
- Diabetes
- Heart disease
- Hypothyroidism
- Hepatitis C
- HIV/AIDS



Difficulties in Diagnosing Depression in the Medically Ill

- Medical symptoms can overlap with depressive symptoms
 - Fatigue/low energy
 - Anorexia and/or weight loss
 - Change in sleep
 - Poor concentration
 - Anhedonia and or apathy
- Difficult to make the attribution to either the psychological or medical conditions
- Medications and interactions can contribute to depressive symptoms



Depression in medical illness

- Coexistence
- Induced by illness or medications
- Causes or exacerbates somatic symptoms



Depression and Heart Disease

- Major depression: 16-23%
- Depressed mood: 37-35%
- Depression associated with:
 - Myocardial infarction
 - Angioplasty
 - Congestive heart failure
 - Coronary bypass graft surgery
 - Coronary artery disease
- Independent risk factor for sudden death and morbidity



Koenig HG, George LK, Peterson BL et al. Depression in medically ill hospitalized older adults: prevalence, characteristics, and course of symptoms according to six diagnostic schemes. *Am J Psychiatry* 1376-1383, 1997.

Depression and Cancer

- Associated more with pancreatic, lung, brain and oropharyngeal cancers
- Prevalence 25% (17-32%) in meta-analysis of 24 studies
- Comorbid with anxiety in half of patients
- Depression is associated with a decrease in treatment compliance
- Can also be side effects of chemotherapy/steroids



Koenig HG, George LK, Peterson BL et al. Depression in medically ill hospitalized older adults: prevalence, characteristics, and course of symptoms according to six diagnostic schemes. *Am J Psychiatry* 1376-1383, 1997.

Depression and Diabetes

- Up to one-third of patients with Type 2 DM has depression
- Depression can lead to poor compliance and poor medical outcomes
- Among patients with Type 2 DM, those with comorbid depression appear to be at greater risk for death from non-cardiovascular, non-cancer causes compared to those without depression



Koenig HG, George LK, Peterson BL et al. Depression in medically ill hospitalized older adults: prevalence, characteristics, and course of symptoms according to six diagnostic schemes. *Am J Psychiatry* 1376-1383, 1997.

Depression in Neurological Diseases

- Parkinson's disease: up to 50%
- Multiple sclerosis: Up to 50%
- Huntington's disease: Up to 32%
- Epilepsy: 10-55%
- Post-stroke depression: 9-13%
- Alzheimer's dementia: 10-32%



Koenig HG, George LK, Peterson BL et al. Depression in medically ill hospitalized older adults: prevalence, characteristics, and course of symptoms according to six diagnostic schemes. *Am J Psychiatry* 1376-1383, 1997.

Medications commonly associated with depressive symptoms

Antiepileptics

* = studies showing mixed/inconclusive results.

Angiotensin-converting enzyme inhibitors* (Boal et al, 2016; Gerstman et al, 1996)

Antihypertensives (especially clonidine, methyldopa, thiazides)

Antimicrobials (amphotericin, ethionamide, metronidazole)

Antineoplastics (procarbazine, vincristine, vinblastine, asparaginase) Benzodiazepines, sedative–hypnotic agents

Beta-blockers* (Boal et al, 2016; Gerstman et al, 1996)

Calcium channel blockers

Corticosteroids

Endocrine modifiers (especially estrogens, leuprolide)

Interferon

Isotretinoin

Metoclopramide

Nonsteroidal anti-inflammatory drugs (especially indomethacin)

Opiates

Statins * (Parsaik et al, 2013)(Thompson et al, 2016)

(Rackley & Bostwick Psych Clin North Am, 2012)



There continues to be mixed studies regarding statins:

-You H, et al, (2013) comment on the possibility of statin use and depression: PMID: 23767773.

-Thompson P, et. al. (2016) Review discusses positive correlation of statin use and depressive symptoms possibly d/t cholesterol role in membrane serotonin receptor function.

-Parsaik A, et al. (2013) review found statin use to be associated with lower risk of depression.

ACE-Inhibitors have also had mixed studies::

-Habra m, et (2010) based on CREATE trial results showed that ACE-I and B-Blockers showed depression had decrease response to antidepressants when on these medications but no comment on association between induction of depressive symptoms.

-Gerstman B, et. al (1996) reviewed incidence of depression with use of ACE-I and B-Blockers and found no increase in depression risk.

-Boal A, et. al (2016) large study suggests that ACE-inhibitors may be associated with decrease risk of mood disorders, and B-Blockers/Calcium channel blockers are associated with increased risk. These were looking at patients that were admitted to hospital for mood disorders.

Treatment of depression in medical setting

- Identifying **possible organic causes**, e.g., thyroid, HIV, medications
- Appropriate management requires first establishing the **most likely diagnosis** that has caused depression (Rackley and Boswick, 2012)



Treatment of depression in medical setting

- Utilize medications, psychotherapies, and psychoeducation
- Be aware of pharmacokinetic (e.g., binding, CYP 450, clearance) and pharmacodynamic (neurotransmitter receptor and transporter effects) factors
- Be mindful of additive sedative, anticholinergic effects from several medications (e.g., pain meds, H2 blockers, antibiotics, antihistamines, steroids, TCAs)



First Line Medication Treatment

Medication	Dose Range	P450 inhibitor	Substrate
Fluoxetine (Prozac)	10mg-40mg	2D6(s), 2C19(s), 3A4(w)	2C9,2C19,2D6
Mirtazapine (Remeron)	15mg-60mg	-----	1A2, 2D6
Bupropion (Wellbutrin)	150mg-450mg	2D6(s)	2B6,
Sertraline (Zoloft)	25mg-200mg	2D6(w), 2C9(w)	2C9,2C19,2D6
Paroxetine (Paxil)	20mg-60mg	2D6(s), 2C9(m), 2C19(w)	2D6
Citalopram (Celexa)	20mg-40mg	2D6(w)	2C19,2D6
Escitalopram (Lexapro)	10mg-40mg	2D6(w)	2C19 ,2D6
Duloxetine (Cymbalta)	20mg-60 mg	2D6(m)	1A2, 2D6
Venlafaxine (Effexor)	75mg-300mg	2D6(w)	2C19,2D6
Trazodone (Desyrel)	50mg-600mg	-----	3A4, 2D6

(s)= strong inhibitor, (m)= moderate inhibitor, (w) weak inhibitor



(s)= strong inhibitor, (m)= moderate inhibitor, (w) weak inhibitor

[Cytochrome P450 Drug Interaction Table](#). Indiana University School of Medicine, 2017.

Cozza KL, Armstrong SC, Oesterheld JR: Concise Guide to Drug Interaction Principles for Medical Practice: Cytochrome P450s, UGTs, P-Glycoproteins, Second Edition. Washington, DC, American Psychiatric Publishing, 2003

Note Substrate: the P450 route(s) the drug is metabolized

Inhibitor: decreases the metabolism and thus functionally increases the levels of medications that use this pathway (Substrates).

Note: high dose bupropion can reduce seizure threshold and cause seizures.

Watch for sustained elevated blood pressures in patients taking venlafaxine and bupropion.

Watch for prostate and urinary symptoms in patients taking paroxetine and venlafaxine.

First line agents are the SSRIs .

Fluoxetine and Paxil do the most inhibition and be careful that beta blockers and other medications may be potentiated.

Sertraline, citalopram, escitalopram and duloxetine tend to have most of their P450 inhibition at higher doses.

Mirtazapine is inert and does NOT effect other medications. It can be affected by others

Clinical Concerns

- 2D6 inhibitors can affect beta-blockers and potentiate fall in blood pressure and pulse (orthostasis)
- Cigarette smokers may need higher doses of mirtazapine through CYP 1A2 induction
- Users of oral contraceptives may have more antidepressant side effects and need lower doses of many medications
- Antidepressants with CYP 2D6 inhibition may decrease effectiveness of Tamoxifen and Codeine (which are pro-drugs)
 - May want to consider alternatives such as venlafaxine and mirtazapine



Many cardiac patients are on beta blocks thus you have to carefully follow pulse and blood pressure so that they don't become too low->may need to **DECREASE** the beta blocker dose.

1. Know the drug interactions of the medications you use most often
2. Look up drug interactions with any and all medicines
3. Be careful of hidden inhibitors or inducers
 - Grapefruit juice
 - Cigarette smoking
 - Oral contraceptive medications
 - Herbal medicines
4. Psychotherapy may help

Clinical Concerns

- Combining serotonergic and/or MAOI medications may cause Serotonin syndrome
 - E.g., SSRI, TCAs, venlafaxine, mirtazapine, triptans, linezolid, tramadol, meperidine
- Citalopram FDA warning (8/23/2011)
 - Citalopram should not be used in doses >40mg qday due to concerns of QT prolongation
 - Citalopram should not be used in doses >20mg qday in patients with hepatic impairment, >60 years of age, 2C19 or 2D6 poor metabolizers



In Chronic Kidney Disease

- SSRI: Sertraline considered to have least dependence on renal function
- Bupropion: decrease dose – authorities advise caution as increased levels may produce seizure
- Mirtazapine: decrease dose - 75% excreted unchanged in urine
- SNRI: Venlafaxine may require dose reduction in renal impairment or dialysis
 - Duloxetine contraindicated in severe renal disease: active metabolite may accumulate and produce confusion



Delirium: Take Home Points

- Delirium is acute alteration in cognitive functioning with fluctuations in attention span and other symptoms
- Delirium is a serious, though under-recognized condition
- Frailty increases risk of delirium
- Management involves maximization of medical condition while minimization of polypharmacy
- Prevention, detection and education are key



Decision Making: Take Home Points

- Capacity can be assessed by any Health Care Provider
- The 4 abilities model is a helpful framework for assessing capacity
- Follow surrogacy guidelines for your state when needing a substitute decision maker



Depression in the Medically Ill: Take Home Points

- Depression in medically ill can be complex and multifactorial, and needs a thorough evaluation
- Check drug-drug interactions for all the patient's medications
 - Computer programs, mobile apps widely available
- Medical conditions and depression affect each others' symptoms and course, and affect the patient's health related quality of life
- Depression may be successfully treated by addressing medical conditions and medical drugs, and utilizing biological, psychological and educational interventions



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Questions?

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