

Graceland: Geriatric Pain Management

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Faculty







- Family of 8 Pharmacists
- Wife, In-Laws, & Cousins
- Family Vineyard in the Marche Region of Italy



Disclosures

- Expert Witness: U.S. Department of Justice, Consumer Protection Branch
- Expert Witness: Cardinal Health

This presentation was not a part of the presenter's official duties at the WVU and does not represent the opinion of WVU

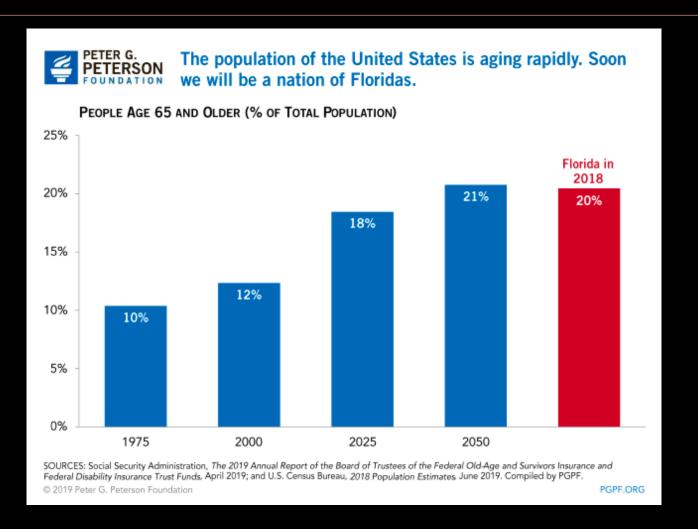


Learning Objectives

- Restate common anatomical and physiological changes alter medication pharmacodynamics and pharmacokinetics in older adults
- Identify pain management medications that are considered to be potentially inappropriate if used in older adults based on the 2019 AGS Beers List
- Recognize Potentially Inappropriate Drug-Drug Interactions That Should Be Avoided In Older Adults based on the 2019 AGS Beers List



Hopefully, We'll All Be Geriatric Patients if Not Already!





How Many Centurions Will Be Alive in 2100?

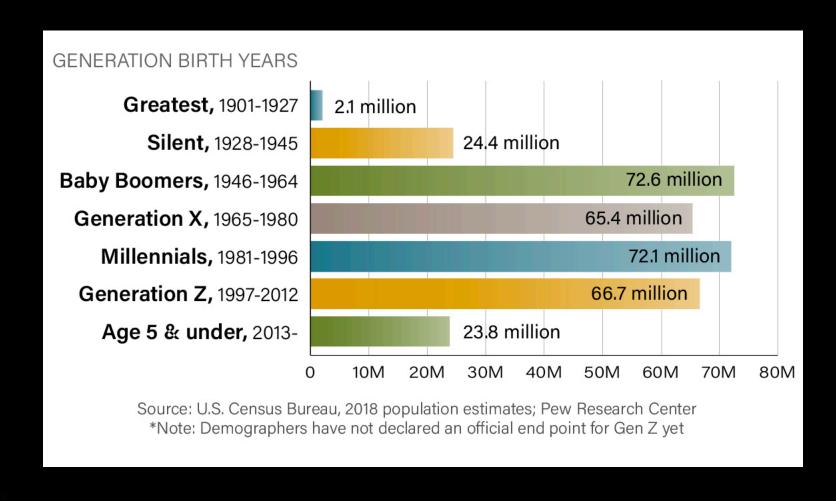
- Roman Centurions
 - -Professional Officers

People living to be 100yo





Generational Differences





Generational Differences

Generation	~Birth Year	Personalities	Preferred Coaching	Descriptions
GI/Silent	1900-1945	Respect, Loyalty, & Order	No news is good news	 Conservative, Clear Gender Roles Like Work, but don't live to work Key Reward: "Satisfaction of a job well done"
Baby Boomers	1946-1964	Optimism Reject Authority	Once a year, needed or not	 Grew up in nuclear families, unlike their own Team Players and workaholics Do NOT want to be continually "connected" Key Rewards are "Money, title, & recognition"
Generation X	1965-1980	Skeptical Don't Value Loyalty	Reject micromanaging "So How am I Doing?"	 Grew up in single parent or dual earner families Independent and question the establishment Key Reward: "Freedom and time"
Millennials (Generation Y)	1981-1995	Respectful Confident	Engaging Immediate Feedback	 "Trophy Kids" with "Helicopter Parents" Do NOT respect chain of commands Key Reward: "Meaningful work"
Generation Z	1996-2011	Empowering	Collaboration	 Raised on the internet Comfortable with social media Now graduating college and entering workforce
Generation Alpha	2012-Present	Inspiring	Co-Creation	 Greek alphabet "alpha" First born entirely in 21st Century Adulthood in 2030's when population is 9 Billion



Aging Anatomy & Physiology

Cardiovascular

- Heart wall thickens
- HR decreases
- Systolic BP increases

<u>Pulmonary</u>

- Chest wall thickens
- Central airways widen
 - Decreased pulmonary Flow

<u>Central Nervous System</u> (CNS)

- Brain size decreases
- Serotonin system changes
- Blood-Brain-Barrier thins





Aging Anatomy & Physiology

Endocrine

- Kidney size decreases
- GFR decreases
- Renin activity decreases
 - Less Na retained
- Hormone receptors decrease
- Glucose tolerance decreases
- Sweat less, thus body overheats easier

Hepatic System

- Liver mass decreases
- CYP3A4 function decreases





Aging Anatomy & Physiology

Immune System

Entire immune system function decreases

Gastrointestinal

- Stomach lining/secretion/gastric emptying frequency decreases
- Stomach pH/gastric emptying time duration increases
- Colon nutritional absorption decreases

Overall Body

- Body water/muscle ratio decreases
- Body fat increases
- Hearing and vision decrease





Geriatric Pharmacokinetics & Pharmacodynamics Pain Management Related

Pharmacodynamics

- -Elderly body has an increased risk of side effects for these medications:
 - Opioids (CNS effects)
 - Antipsychotics (extrapyramidal effects and tardive dyskinesia)
 - Tricyclic antidepressants (orthostatic hypotension)
 - NSAIDs (GI bleeding)

Pharmacokinetics

- -Aging produces reduced CYP450 2D6 & 3A4 Metabolism
- Aging produces reduced first pass metabolism of morphine



Medication Utilization in the Elderly Population

- Elderly women are observed to take more medications than elderly men
- •Medication use is greatest among the frail elderly, hospitalized patients, and nursing home residents
 - —A typical nursing home resident is given 7 to 8 drugs on a regular basis.

Unique Medications	% of Geriatric Population
	90%
5	40%
10	12%



Geriatric Medication Toolbelt

Medication Selection & Utilization Tools for Patients >/= 65yo				
AGS Beers	American Geriatrics Society Beers List			
STOPP	Screening Tool of Older Peoples Prescriptions			
START	Screening Tool to Alert to Right Treatment			
FORTA	Fit fOR The Aged			
MAI	Medication Appropriateness Index			
ADS	Anticholinergic Drug Scale			
ACB	Anticholinergic Cognitive Burden Scale			
ARS	Anticholinergic Risk Scale			



Beers List





Beers List





American Geriatrics Society (AGS) Beers List

CLINICAL INVESTIGATION

American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults

By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel*

From the *American Geriatrics Society, New York, New York.

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See related editorial by Michael Steinman et al.

DOI: 10.1111/jgs.15767





Dr. Mark Beers List

Year	Descriptions
1991	Original guideline of medications to avoid in the elderly
1997	 Clarified medications to avoid, doses/frequencies to avoid, and medications to avoid in patients with specific conditions
2003	 Avoid because of ineffectiveness, or high risk with safer alternative available Further clarified medications to avoid in specific medical conditions
2012	Updated Review Criteria basis: Quality & Strength of evidence
2015	New categories of recommendations including Renal Adjustments & Drug-Drug Interactions
2019	• 13 Experts reviewed 1,400 articles from 2015-2017 for updated clinical information





2019 AGS Beers List (10 Tables)

Table	Descriptions					
I	 Designations Of Quality Of Evidence And Strength Of Recommendations Quality: Low, Moderate, Or High Strength: Weak Or Strong 					
2 (5 Pages)	Potentially Inappropriate Medication Use In Older Adults (PIMs)					
3 (3 Pages)	 Potentially Inappropriate Medication Use In Older Adults (PIMs) Due To Drug-disease Or Drug-syndrome Interactions That May Exacerbate The Disease/Syndrome 					
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Potentially Inappropriate Medications (Pims) for Older Adults Pain Management Related

	Drug Class	Rationale	Recommendation	Quality of Evidence (Low/Moderate/High)	Strength of Recommendation (Strong/Weak)	Alternative(s)
	Ist Generation Antihistamines Diphenhydramine, Doxylamine, Meclizine, Promethazine, etc.	 Anticholinergic Clearance reduced with advanced age Increased risk of confusion, dry mouth, constipation, etc. 	Avoid	Moderate	Strong	2 nd Generation Antihistamines, sleep hygiene, etc.
•	TCAs Amitriptyline, nortriptyline, desipramine, doxepin (>6mg/day), imipramine, clomipramine, etc.	 Anticholinergic Increases risk of sedation, orthostatic hypotension, or bradycardia 	Avoid	High	Strong	SSRI, SNRI, bupropion, melatonin, sleep hygiene, trazodone, topical capsaicin, topical lidocaine



Potentially Inappropriate Medications (PIMs) for Older Adults Pain Management Related

Drug Class	Rationale	Recommendation	Quality of Evidence (Low/Moderate/High)	Strength of Recommendation (Strong/Weak)	Alternative(s)
Benzos • Short, Intermediate, & Long Acting	 Increased benzo sensitivity Slower metabolism of long-acting benzos Increased risk of sedation, falls/fractures, & vehicle crashes 	Avoid	Moderate	Strong	 SSRI, SNRI, bupropion, melatonin, trazodone, sleep hygiene, etc. If absolutely needed, utilize triazolam (short-acting PO)
Z-Hypnotics	 Increased risk of sedation, falls/fractures, ER/hospitalizations, & vehicle crashes Minimal improvement in sleep latency and duration. 	Avoid	Moderate	Strong	 Trazodone, melatonin, sleep hygiene



Potentially Inappropriate Medications (PIMs) for Older Adults Pain Management Related

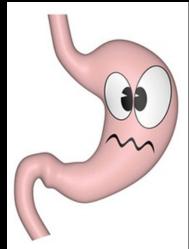
Drug Class	Rationale	Recommendation	Quality of Evidence (Low/Moderate/High)	Strength of Recommendation (Strong/Weak)	Alternative(s)
Meperidine	 Not effective oral analgesic in dosages commonly used Risk of neurotoxicity Exceeds Benefit relative to other opioids 	Avoid	Moderate	Strong	COX-2 Selective NSAIDs, APAP, morphine, hydrocodone, etc.
''Muscle Relaxants'' (Spasmodics)	 Most muscle relaxants poorly tolerated by older adults because of anticholinergic adverse effects, sedation, risk of fracture Effectiveness at dosages tolerated by older adults is questionable 	Assess spasticity versus spasms	Moderate	Strong	 Differentiate spasticity vs. spasms Antispasticity Agents still require monitoring (baclofen & tizanidine)
COX-I Selective NSAIDs	 Increased of GI bleed in high risk groups (>75yo w/ corticosteroid, anticoagulant, or antiplatelet medication) Can increase blood pressure Can increase risk of kidney injury 	Avoid Chronic Use (Unless alternatives fail +/- Miso/PPI to reduce risk)	Moderate	Strong	AcetaminophenTopical lidocaineTopical capsaicinNon-Pharm



COX-1 & COX-2

COX-1 Selective





COX-2 Selective









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Elderly PIMs Due to Drug-Disease/Syndrome Interactions Pain Management Related

Disease Or Syndrome	Drug Class	Rationale	Recommendation	Quality of Evidence (Low/Moderate/High)	Strength of Recommendation (Strong/Weak)
Heart Failure	COX-2 Selective NSAIDs	Potential to promote fluid retention and/or exacerbate HF	 Avoid in patients with symptomatic HF Use with caution for Asymptomatic HF 	Moderate	Strong
Syncope	Tertiary TCAs • Amitriptyline, doxepin, imipramine, clomipramine, & trimipramine	Increased risk of orthostatic hypotension or bradycardia	 Avoid If TCA must be utilize, prefer Secondary Nortriptyline or desipramine 	High	Strong



Elderly PIMs Due to Drug-Disease/Syndrome Interactions Pain Management Related

Disease Or Syndrome	Drug Class	Rationale	Recommendation	Quality of Evidence (Low/Moderate/High)	Strength of Recommendation (Strong/Weak)
Delirium	Anticholinergics, Antipsychotics, Benzos, Z-Hypnotics, Corticosteroids, H2 Blockers, & meperidine	Potential to induce/worsen delirium	Avoid	Moderate (H2 Blockers, Low)	Strong
Dementia or Cognitive Impairment	Anticholinergics, Benzos, & Z-Hypnotics	CNS Side Effects	Avoid	Moderate	Strong
Falls/Fractures History	Benzos, AEDs, Antipsychotics, Z-Hypnotics, TCAs, SNRIs, SSRIs, & Opioids	 May cause ataxia, syncope, & falls Shorter acting benzos not safer than long acting 	 Avoid unless safer alternatives are not available Opioids only for severe acute pain Antidepressants mixed data, but none shown to cause less falls relatively 	Moderate	Strong



Elderly PIMs Due to Drug-Disease/Syndrome Interactions Pain Management Related

Disease Or Syndrome	Drug Class	Rationale	Recommendation	Quality of Evidence (Low/Moderate/High)	Strength of Recommendation (Strong/Weak)
Gl Ulcer History	 Aspirin doses > 325mg/day COX-I Selective NSAID 	May exacerbate current ulcers or precipitate new ulcers	Avoid unless other alternatives are not effective & patient is able to utilize PPI/miso	Moderate	Strong
Chronic Kidney Disease Stage >/= 4 (CrCl < 30mL/min)	All NSAIDs	May increase risk of acute kidney injury and further decline of renal function	• Avoid	Moderate	Strong



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Medications to Be Used With Caution With Older Adults Pain Management Related

Drug	Rationale	Recommendation	Quality of Evidence (Low/Moderate/High)	Strength of Recommendation (Strong/Weak)
Aspirin (Cardio-Protection)	 Risk of major bleeding increases markedly in older age. Several studies suggest lack of net benefit when used for PP in older adults with CV risk factors, but evidence is not conclusive. Generally indicated for secondary prevention in older adults with established CVD 	Use with caution in patients >/= 70yo	Moderate	Strong
Antipsychotics, carbamazepine, SNRIs, SSRIs, TCAs, diuretics, & tramadol	May exacerbate or cause SIADH or hyponatremia	 Use with caution Monitor sodium closely when starting or changing dosages in older adults 	Moderate	Strong



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Elderly PIMs Due to Drug-Drug Interactions Pain Management Related

Drug Class	Interacting Drug	Rationale	Recommendation	Quality of Evidence (Low/Moderate/High)	Strength of Recommendation (Strong/Weak)
Corticosteroids	NSAIDs	Increased risk of PUD or GI bleed	AvoidIf avoidance not possible, utilize PPI/miso	Moderate	Strong
Warfarin	NSAIDs	Increased risk of bleeding	 Avoid If avoidance not possible, monitor closely for bleeding 	High	Strong



Elderly PIMs Due to Drug-Drug Interactions Pain Management Related

Drug Class	Interacting Drug	Rationale	Recommendation	Quality of Evidence (Low/Moderate/High)	Strength of Recommendation (Strong/Weak)
Opioids	Benzos & Gabapentinoids	Increased risk of severe sedation, respiratory depression/death	 Avoid Rare exception when converting from opiate to gabapentin 	Moderate	Strong
Antidepressants, Antipsychotics, AEDs, Z-Hypnotics, Benzos, & Opioids	Any combination	Increased risk of falls and fractures	 Avoid total of 3 or more CNS active drugs Minimize CNS active drugs 	High	Strong



Pain Management Drug Interactions Opioids & Benzos (Black Box Warnings)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration 10903 New Hampshire Ave Building 51 Silver Spring, MD 20993

Leana Wen, M.D. M.Sc.
Commissioner of Health
Baltimore City Department of Health
1001 E. Fayette St.
Baltimore, MD 21202

AUG 3 1 2016

Nicole Alexander-Scott, M.D., M.P.H. Director Rhode Island Department of Health 3 Capitol Hill Providence, RI 02908

RE: Docket No. FDA-2016-P-0689



Pain Management Drug Interactions Opioids & Benzos (Black Box Warnings)

WARNING: RISKS FROM CONCOMITANT USE WITH OPIOIDS

Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death [see Warnings and Precautions (5.X), Drug Interactions (7.X)].

- Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.
- Limit dosages and duration to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.

WARNING: RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

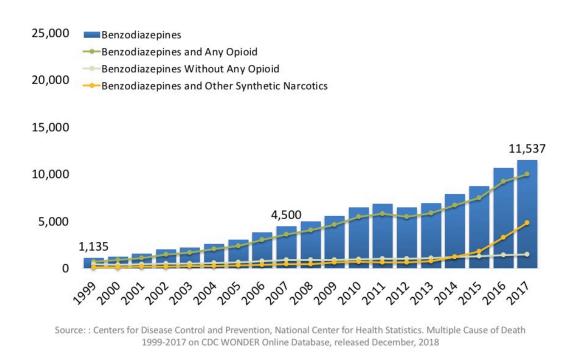
Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death [see Warnings and Precautions (5.X), Drug Interactions (7.X)].

- Reserve concomitant prescribing of TRADENAME and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.
- Limit dosages and duration to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.



Pain Management Drug Interactions Opioids & Benzos (CDC Warnings)

Figure 8. National Drug Overdose Deaths Involving Benzodiazepines, by Opioid Involvement,
Number Among All Ages, 1999-2017



CDC GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN

ASSESSING RISK AND ADDRESSING HARMS



AVOID CONCURRENT OPIOID AND BENZODIAZEPINE PRESCRIBING

Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.



Pain Management Drug Interactions

Hepatic & Serotonergic

CYP-450 Enzyme	Common Substrates	Common Inhibitors	Common Inducers
IA2	Tizanidine	Major: ciprofloxacin & fluvoxamine	Major: Smoking Minor: rifampin & barbiturates
2D6	codeine, hydrocodone, oxycodone, trazodone, & venlafaxine	cocaine, cimetidine, fluoxetine, paroxetine, & sertraline	Not Inducible
3 A 4	Fentanyl, oxycodone, etc.	grapefruit juice, azoles, clarithromycin, diltiazem, erythromycin, & verapamil	garlic & prednisone
Serotonergic Opioids		meperidine, methad	one, & tramadol



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Medications That Should Be Avoided/Adjusted with Reduced Kidney Function in Older Adults Pain Management Related

Drug	CrCl Requiring Action	Rationale	Recommendation	Quality of Evidence (Low/Moderate/High)	Strength of Recommendation (Strong/Weak)
Duloxetine	< 30 mL/Min	Increased GI ADEs (N/V & Diarrhea)	Avoid	Moderate	Weak
Gabapentin	< 60 mL/Min	CNS ADEs	Reduce Dose	Moderate	Strong
Levetiracetam	= 80 mL/Min</td <td>CNS ADEs</td> <td>Reduce Dose</td> <td>Moderate</td> <td>Strong</td>	CNS ADEs	Reduce Dose	Moderate	Strong
Pregabalin	< 60 mL/Min	CNS ADEs	Reduce Dose	Moderate	Strong
Tramadol	< 30 mL/Min	CNS ADEs	IR: Reduce Dose ER: Avoid	Low	Weak
Colchicine	< 30 mL/Min	GI, Neuromuscular, & Bone Marrow Toxicity	Reduce Dose Monitor ADEs	Moderate	Strong
Probenecid	< 30 mL/Min	Loss of effectiveness	Avoid	Moderate	Strong



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Drugs with Strong Anticholinergic Properties Pain Management Related

- 1. TCA
 Antidepressants
- 2. 1st Generation Antihistamines
 - -Brompheniramine
 - -Chlorpheniramine
 - –Diphenhydramine
 - -Doxylamine
 - -Hydroxyzine
 - -Meclizine

- 3. Antipsychotics
 - Chlorpromazine
 - Clozapine
 - Olanzapine, etc.
- 4. "Muscle Relaxants"
 - Cyclobenzaprine
 - Orphenadrine

Anticholinergic Medication Scales		
ADS	Anticholinergic Drug Scale	
ACB	Anticholinergic Cognitive Burden Scale	
ARS	Anticholinergic Risk Scale	



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Medications/Criteria Removed Since 2015 AGS Beers List Pain Management Related

- Pentazocine (Oral product no longer on US Market)
- Avoidance for patients with chronic seizures (Not unique to older adults)
 - -Bupropion, Chlorpromazine, Clozapine, Olanzapine, Thioridazine, and Tramadol
- Avoidance for patients with Dementia
 - –H2 Antagonists (Weak Evidence)
- Stimulants (Not unique to older adults)
 - -Phenylephrine & Pseudoephedrine
 - -Amphetamine, Armodafinil, Caffeine, Methylphenidate, Modafinil, Phenylephrine, Pseudoephedrine, & Theophylline



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Medications/Criteria <u>Added</u> Since 2015 AGS Beers List Pain Management Related

SNRI

-Associated with an increased risk of falls/fractures in older adults

Tramadol

-Use with Caution, Risk of SIADH/Hyponatremia

Opioids & Benzos

–Increased risk of overdose

Opioids & Gabapentinoids

–Increased risk of overdose



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Medications/Criteria Modified Since 2015 AGS Beers List Pain Management Related

- Meperidine
 - Removed caveat from recommendation
- NSAIDs in Patients with Heart Failure
 - Distinguished COX-1 & COX-2 Inhibitors
 - Changed recommendations
- Opioids in Patients with a Fall/Fracture History
 - Increased strength of recommendation to Strong
- ASA Cardio Primary Prevention
 - Modified age, etc.
- Combination of 3 CNS Medications
 - Replaced individual/specific criteria with one universal criteria





Table	Descriptions
I	 Designations Of Quality Of Evidence And Strength Of Recommendations Quality: Low, Moderate, Or High Strength: Weak Or Strong
2 (5 Pages)	Potentially Inappropriate Medication Use In Older Adults (PIMs)
3 (3 Pages)	 Potentially Inappropriate Medication Use In Older Adults (PIMs) Due To Drug-disease Or Drug-syndrome Interactions That May Exacerbate The Disease/Syndrome
4	Potentially Inappropriate Medication: Drugs To Be Used With Caution In Older Adults
5	Potentially Inappropriate Drug-Drug Interactions That Should Be Avoided In Older Adults
6	Medications That Should Be Avoided or Have Dosage Reduced With Varying Levels of Kidney Function in Older Adults
7	Drugs With Strong Anticholinergic Properties
8	Medications/Criteria Removed Since 2015 AGS Beers List
9	Medications/Criteria Added Since 2015 AGS Beers List
10	Medications/Criteria Modified Since 2015 AGS Beers List



If not anything, then something?

Patient by patient scenarios

- -Clinical judgment
- -Monitoring
- –Documentation

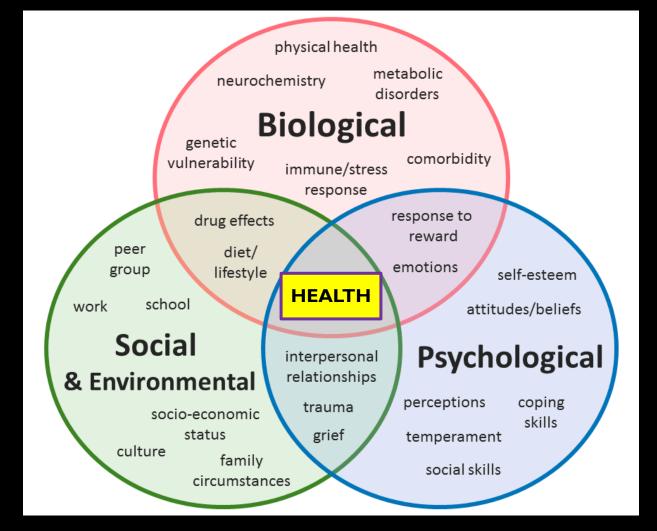






Painweek.

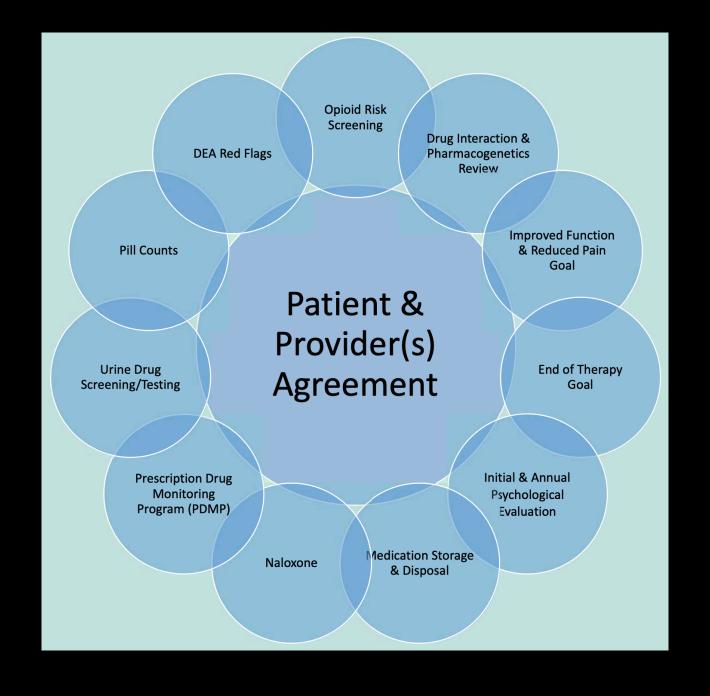
BioPsychoSocial Model of Pain





Risk Reduction Strategy

www.sempguidelines.org









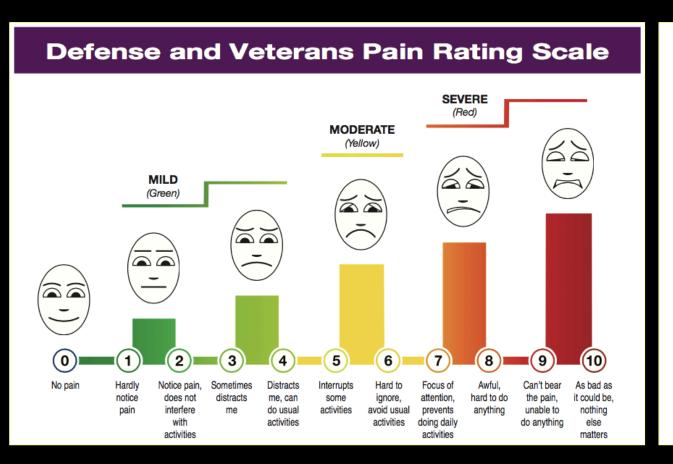




Pain Scales



DVPRS



DoD/VA Pain Supplemental Questions

For clinicians to evaluate the biopsychosocial impact of pain

1. Circle the one number that describes how, during the past 24 hours, pain has interfered with your usual ACTIVITY:

0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10

Does not interfere

Completely interferes

2. Circle the one number that describes how, during the past 24 hours, pain has interfered with your SLEEP:

0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10

Does not interfere

Completely interferes

3. Circle the one number that describes how, during the past 24 hours, pain has affected your MOOD:

0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10

Does not affect

Completely affects

4. Circle the one number that describes how, during the past 24 hours, pain has contributed to your STRESS:

0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10

Does not contribute

Contributes a great deal

*Reference for pain interference: Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. Ann Acad Med Singapore 23(2): 129-138, 1994.

v 2.0



Pain Management Treatment Tool Box Non-Pharmacological Options

Active

Cardio/Resistance Exercise

Aquatic Exercise

Walking Aids

Yoga

Tai Chi

Qigong

Meditation

Hypnosis

Relaxation

Cognitive Behavioral Therapy

Acceptance & Commitment Therapy

Biofeedback

Graded Motor Imagery

Occupational/Physical Therapy

Passive

Nutrition

Heat or Cold

TENS/EMS Devices

Hyperbaric Oxygen

Spinal Manipulation (Chiropractor)

Massage

Ultrasound

Paraffin Wax

Infrared Light

Spinal Traction

Acupuncture





Painful Paperwork

Living Wills

Advanced Directives for healthcare, life sustainment, treatment, etc.

Power of Attorney

Invalid if patient becomes incompetent

Durable Power of Attorney

Valid if patient becomes incompetent

Durable Power of Attorney for Healthcare Decisions

Valid if patient becomes incapacitated

DNR Orders

- Do No Resuscitate Orders, made by patient while competent
- Made by Family/Practitioner if not competent



Geriatric Care Resources

- Geriatric Medication App
 - IGeriatrics
- Geriatric Books & Textbooks
 - http://www.ccgp.org/content/geriatric-books-and-textbooks
- Geriatric Journals
 - http://www.ccgp.org/content/geriatric-journals
- American Geriatric Society
 - http://www.americangeriatrics.org
- Silver Book
 - http://www.silverbook.org



Which of the following tricyclic antidepressant adjuvant pain medications is the most appropriate chronic pain management medication for a 75yo male patient with syncope concerns?

- a) Amitriptyline
- b) Doxepin
- c) Imipramine
- d) Nortriptyline



Which of the following tricyclic antidepressant adjuvant pain medications is the most appropriate chronic pain management medication for a 75yo male patient with syncope concerns?

- a) Amitriptyline
- b) Doxepin
- c) Imipramine
- d) NORTRIPTYLINE [CORRECT ANSWER]



Which of the following NSAIDs is the most appropriate chronic pain management medication for a 75yo male patient?

- a) celecoxib
- b) ibuprofen
- c) meloxicam
- d) naproxen



Which of the following NSAIDs is the most appropriate chronic pain management medication for a 75yo male patient?

- a) CELECOXIB [CORRECT ANSWER]
- b) ibuprofen
- c) meloxicam
- d) naproxen

celecoxib is the most "COX-2 Selective" NSAID listed, thus relatively safest on GI system



Discussion

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