Mitigating Risks While Optimizing the Benefits of Pharmacologic Agents to Manage Pain in the Elderly

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Learning Objectives

1. Describe the pharmacokinetic and pharmacodynamic changes associated with aging, including absorption, distribution, metabolism and excretion.
2. Propose non-pharmacologic and pharmacologic avenues for optimizing pain management in older adults and patients near the end-of-life.

Are our elderly in pain?

- NIH study found 53% of people ≥ 65 years old reported having bothersome pain in the last month
  - Three-quarters of them reported having pain in more than one loation
  - Bothersome pain was associated with decreased physical capacity
- Complicating things – 75% of people ≥ 65 years have ≥ 2 chronic conditions
- We are undertreating pain in older adults, especially those with severe dementia

Diseases associated with chronic pain

Organ System	
Dermatology	
Gastrointestinal	
Cardiovascular	
Pulmonary	
Rheumatology	
Endocrine	
Nephrology	
Immune	
Neurology	
Oncology	
Miscellaneous	

Diseases associated with chronic pain

Organ System	Examples
Dermatology	Pressure or ischemic ulcers, burns, scleroderma
Gastrointestinal	Constipation, irritable bowel disease, diverticulitis, inflammatory bowel disease
Cardiovascular	Advanced heart disease, peripheral vascular disease
Pulmonary	Advanced chronic obstructive pulmonary disease, pleurisy
Rheumatology	Osteoarthritis, rheumatoid arthritis, gout, pseudogout, polymyalgia rheumatica, spinal stenosis/LBP, osteoporotic fracture
Endocrine	Diabetic neuropathy, Paget's disease
Nephrology	Chronic cystitis, end stage renal disease
Immune	Herpes zoster, post-herpetic neuralgia, HIV/AIDs neuropathy
Neurology	Headache, peripheral neuropathies, compressive neuropathies, radiculopathies, Parkinson's disease, post-stroke pain
Oncology	Cancer
Miscellaneous	Depression, tendonitis, bursitisz

Elements of a comprehensive geriatric pain assessment

- **Sensory**
  - Please tell me all of the places you experience pain or discomfort
  - What does it feel like?
  - What words come to mind?
  - Is your pain or discomfort with you all of the time or does it come and go?
  - How long has it been present?
  - What makes it better, what makes it worse?
- **Emotional Impact**
  - Has pain affected your mood, sense of well-being, energy level?
  - Are you worried about your pain or what may be causing it?

Elements of a comprehensive geriatric pain assessment

- **Functional Impact**
  - Has pain affected your ability to do every day activities? To do things you enjoy?
  - How about relating with others? If so, how?
- **Sleep**
  - Has pain affected your sleep?
  - Do you have trouble falling asleep or need to take drugs to help you sleep on account of your pain?
- **Coping Styles**
  - What things do you do to help you cope with your pain? This could be listening to your favorite music, praying, sitting still, or isolating yourself from others

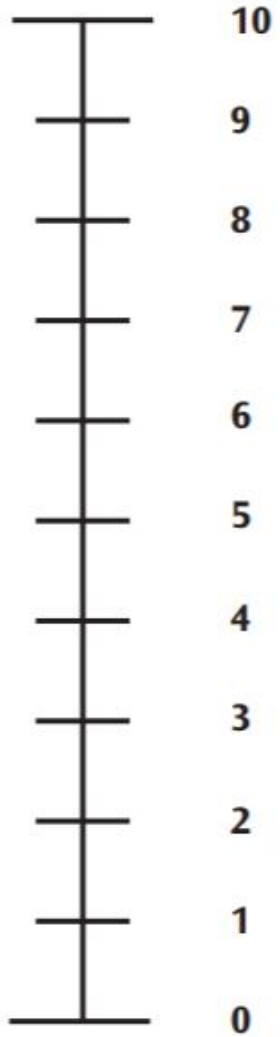
Elements of a comprehensive geriatric pain assessment

- **Attitudes and Beliefs**
  - Do you have any thoughts or opinions about experiencing pain at this point in your life that you believe would be important for me to know?
  - Do you have any thoughts or opinions about specific pain treatments that you believe would be important for me to know?
- **Treatment Expectations and Goals**
  - What do you think is likely to happen with the treatment I have recommended?
  - What are the most important things you hope will happen as a result of the treatment?
- **Resources**
  - Is there anyone at home or in the community that you can turn to for help and support when your pain is really bad?

Elements of a comprehensive geriatric pain assessment

- **Emotional Impact**
  - Has pain affected your mood, sense of well-being, energy level?
  - Are you worried about your pain or what may be causing it?
- **Functional Impact**
  - Has pain affected your ability to do every day activities? To do things you enjoy?
  - How about relating with others? If so, how?

The Numeric Graphic Rating Scale (NGRS)



Say to the patient:

- This is a scale to measure pain.
- 0 indicates 'no pain at all'.
- The numbers on the scale indicate increasing levels of pain,
- up to 10 which is the most severe pain imaginable.
- Which point on the scale shows how much pain you have today?

To the administrator:

In your opinion was the person able to understand this scale?

Yes ☐ No ☐

Comment:

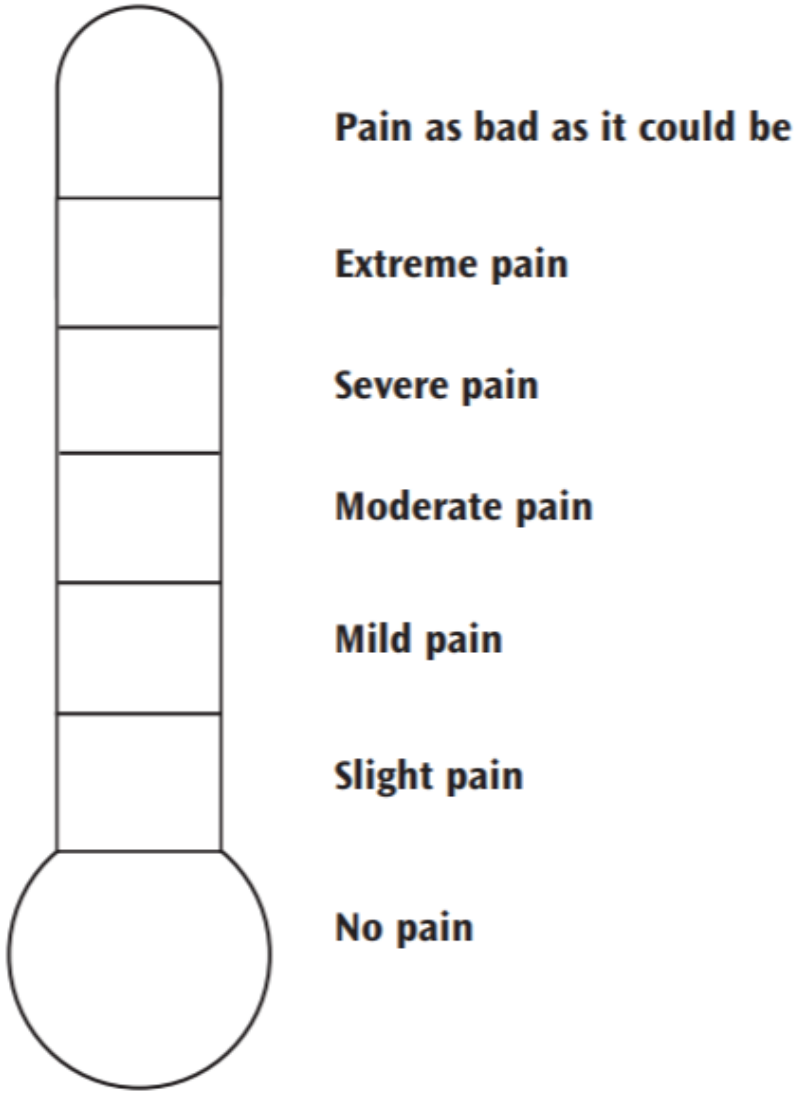
Verbal descriptor rating scale (5 points)

'How severe is your pain today?'

- ☐ None
- ☐ Mild
- ☐ Moderate
- ☐ Severe
- ☐ Very severe

Verbal numerical rating scale

'On a scale of 0 to 10, please tell me how severe your pain is today.'



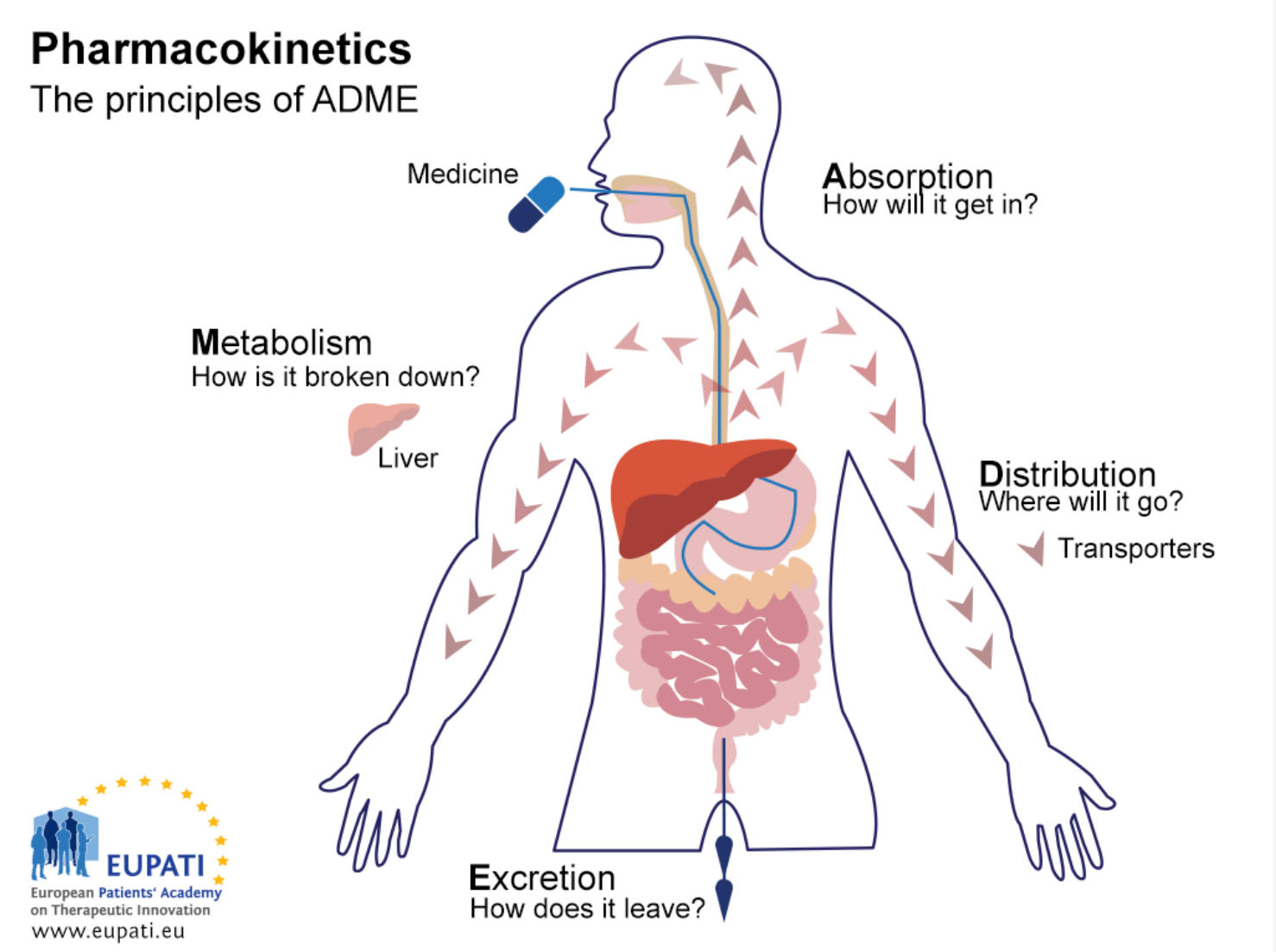
PAINAD score

Items*	0	1	2	Score
Breathing independent of vocalization	Normal	Occasional labored breathing. Short period of hyperventilation.	Noisy labored breathing. Long period of hyperventilation. Cheyne-Stokes respirations.	
Negative vocalization	None	Occasional moan or groan. Low-level speech with a negative or disapproving quality.	Repeated troubled calling out. Loud moaning or groaning. Crying.	
Facial expression	Smiling or inexpressive	Sad. Frightened. Frown.	Facial grimacing.	
Body language	Relaxed	Tense. Distressed pacing. Fidgeting.	Rigid. Fists clenched. Knees pulled up. Pulling or pushing away. Striking out.	
Consolability	No need to console	Distracted or reassured by voice or touch.	Unable to console, distract or reassure.	
			Total**	

Non-Drug Interventions

- Physical therapy
- Interventional approaches
- Exercise / Weight loss
- Psychological support
- Cognitive behavioral therapy
- Self-management programs

What about analgesics in older adults?



Pharmacokinetic Changes in the Elderly

- Absorption
  - Possibly reduced intestinal absorption of agents requiring active transport
  - Reduced first-pass metabolism
    - Increased absorption of some high-clearance drug
    - Decreased absorption of drugs from prodrugs

Clin Geriat Med 28 (2012) 273-286.

Pharmacokinetic Changes in the Elderly

- Distribution
  - Altered free fraction of some drugs
    - Increased free fraction of albumin-bound drugs
    - Decreased free fraction of alpha-1-glycoprotein bound drugs
  - Altered volume of distribution
    - Increased half-life for lipophilic drug
  - Increased permeability of blood-brain barrier

Clin Geriat Med 28 (2012) 273-286.

Pharmacokinetic Changes in the Elderly

- Metabolism
  - Delayed metabolism of high clearance drugs
- Excretion
  - Increased half-life for water-soluble drugs

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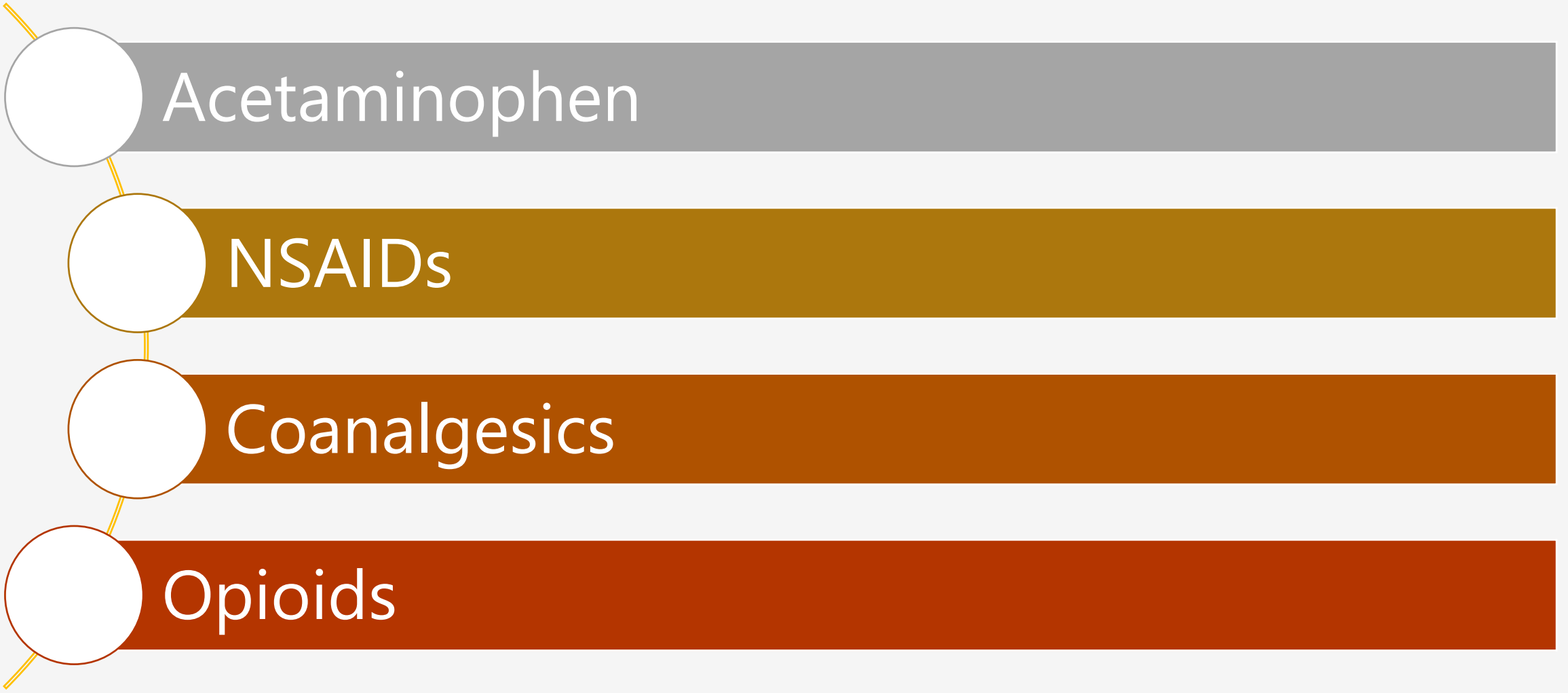
Safest? Most toxic?



Acetaminophen

- First line for older adults with mild to moderate pain
- Analgesic, antipyretic
- What's the maximum daily dose of acetaminophen?
- Caution with liver disease, alcoholism

NSAIDs

- Commonly used to treat musculoskeletal pain in older adults
- Heart disease, renal disease, GI issues
  - Only 40% of older adults on a NSAID have cytoprotective therapy prescribed
- Cardiovascular risk – COX-2 selective vs. nonselective NSAIDs?
- Drug-drug interactions
  - Aspirin, SSRIs, antihypertensives

Adjuvant Analgesics

- Antidepressants
  - SSRIs? TCA? SNRIs?
    - TCAs < 100 mg/day not shown to increase risk of cardiac death
    - > 100 mg was associated with greater number of cardiac deaths
- Gabapentinoids?
    - Dose-related adverse effects
    - Adjustment with renal impairment

Opioids

- Are opioids for chronic-non-cancer pain effective in older adults?
- Is precribing opioids safe in frail older adults?
- What are some guidelines for prescribing opioid for older adults?
- Are older adults are at risk for addiction to opioids?
- What is appropriate in renal disease (ESRD/dialysis)?

Step 2 - 3 Agents - Opioids

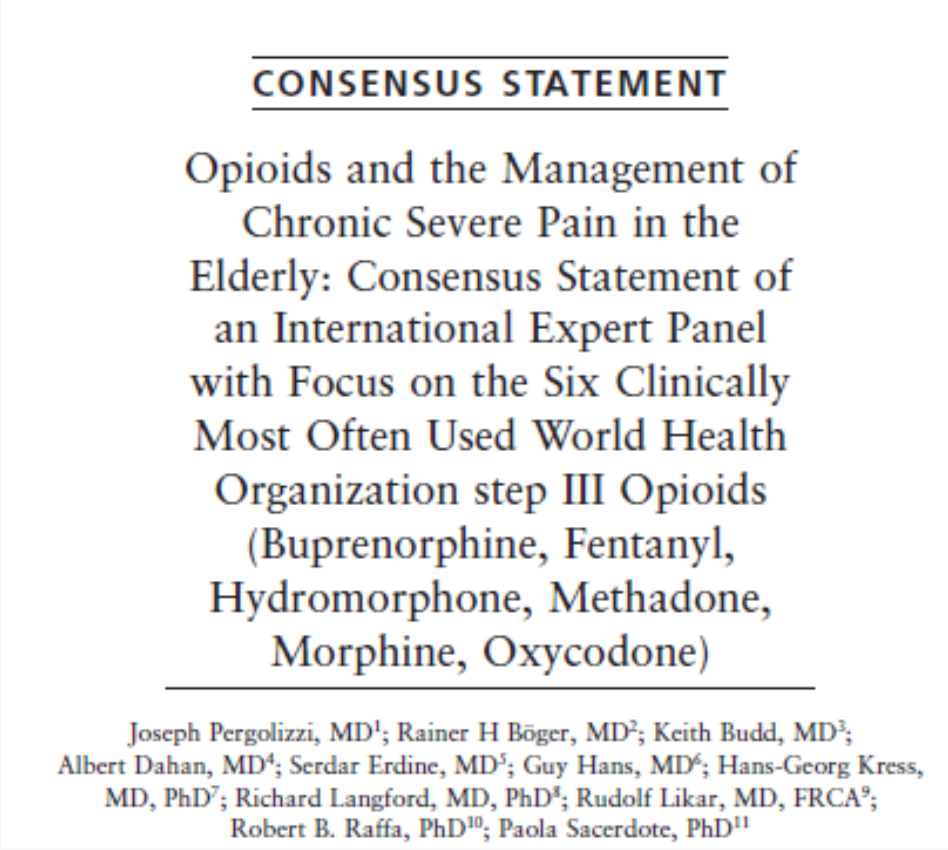
- Codeine
- Hydrocodone
- Oxymorphone
- Meperidine
- Morphine
- Hydromorphone
- Oxycodone
- Levorphanol
- Methadone
- Fentanyl
- Tramadol
- Tapentadol
- Agonist/Antagonist or partial agonists
  - Buprenorphine
  - Butorphanol

Variables Effecting Therapy

- Agent Variables
  - Mechanism of action and efficacy
  - Available dosage formulations
  - Pharmacokinetics (distribution, onset, peak and duration of action, t 1/2, method of elimination from body, presence of active metabolites)
  - Side effects and toxicities
  - Cost (Total cost impact)
- Patient Variables
  - Renal, hepatic function, body habitus
  - Pregnancy, breastfeeding

First Line Opioids

- Morphine
- Oxycodone
- Hydromorphone
- Methadone
- Buprenorphine
- Fentanyl



CONSENSUS STATEMENT

Opioids and the Management of Chronic Severe Pain in the Elderly: Consensus Statement of an International Expert Panel with Focus on the Six Clinically Most Often Used World Health Organization step III Opioids (Buprenorphine, Fentanyl, Hydromorphone, Methadone, Morphine, Oxycodone)

Joseph Pergolizzi, MD[1]; Rainer H Böger, MD[2]; Keith Budd, MD[3]; Albert Dahan, MD[4]; Serdar Erdine, MD[5]; Guy Hans, MD[6]; Hans-Georg Kress, MD, PhD[7]; Richard Langford, MD, PhD[8]; Rudolf Likar, MD, FRCA[9]; Robert B. Raffa, PhD[10]; Paola Sacerdote, PhD[11]

Pain Pract 2008;8:287-313

Morphine and Buprenorphine

- Majority glucuronidated
  - M3G (paradoxical neuroexcitatory effects)
  - M6G (analgesia)
- Buprenorphine
  - Up to 30% metabolized by 3A4
  - No clinically important drug interactios

Fentanyl and Methadone

- Fentanyl
  - Potent 3A4 inhibitors (ritonavir, ketoconazole, clarithromycin) increases fentanyl
  - Inactive metabolites
- Methadone
  - Metabolized by N-demethylation to inactive metabolite
  - 3A4 and 2D6 primary enzymes

Oxcodone and Hydromorphone

- Oxycodone
  - Extensively metabolized to noroxycodone, oxymorphone and glucuronide metabolites
  - Weakly analgesic
- Hydromorphone
  - Generally not involved in major drug interactions
  - HM3G can be a neuroexcitatory metabolite

Agent Related Variables

- Common Adverse Effects
  - Constipation
  - Nausea/vomiting
  - Sedation, confusion
- Uncommon Adverse Effects
  - Respiratory depression
  - Pruritus

Key Points

- Link potential treatment benefits with important patient goals (e.g., increased ability to perform activities of daily living)
- Use medication combinations (in which each analgesic works by a different mechanism) to enhance analgesic effectiveness
- Acetaminophen remains first-line pharmacologic treatment for older adults with mild-to-moderate pain
- Avoid long-term use of oral nonsteroidal anti-inflammatory drugs, given their significant cardiovascular, gastrointestinal, and renal risks
- Trial of opioid is appropriate for patients not responsive to first-line therapies and who continue to experience significant functional impairment due to pain

Key Points

- Consider serotonin-norepinephrine reuptake inhibitors or selective serotonin reuptake inhibitors in patients with comorbid depression and pain
- Implement surveillance plan (e.g., efficacy, tolerability, adherence) with each new treatment
- Physical activity (including PT, exercise, or other movement-based programs such as tai chi) constitutes a core component of managing persistent pain in older patients

Key Points

- Educate older patients about safety and efficacy of cognitive behavioral and movement-based therapies and identify local practitioners or agencies that provide them
- Determine whether treatment goals are being met; if goals are not met, medication should be tapered and discontinued, physical and occupational therapy prescription modified, or both.

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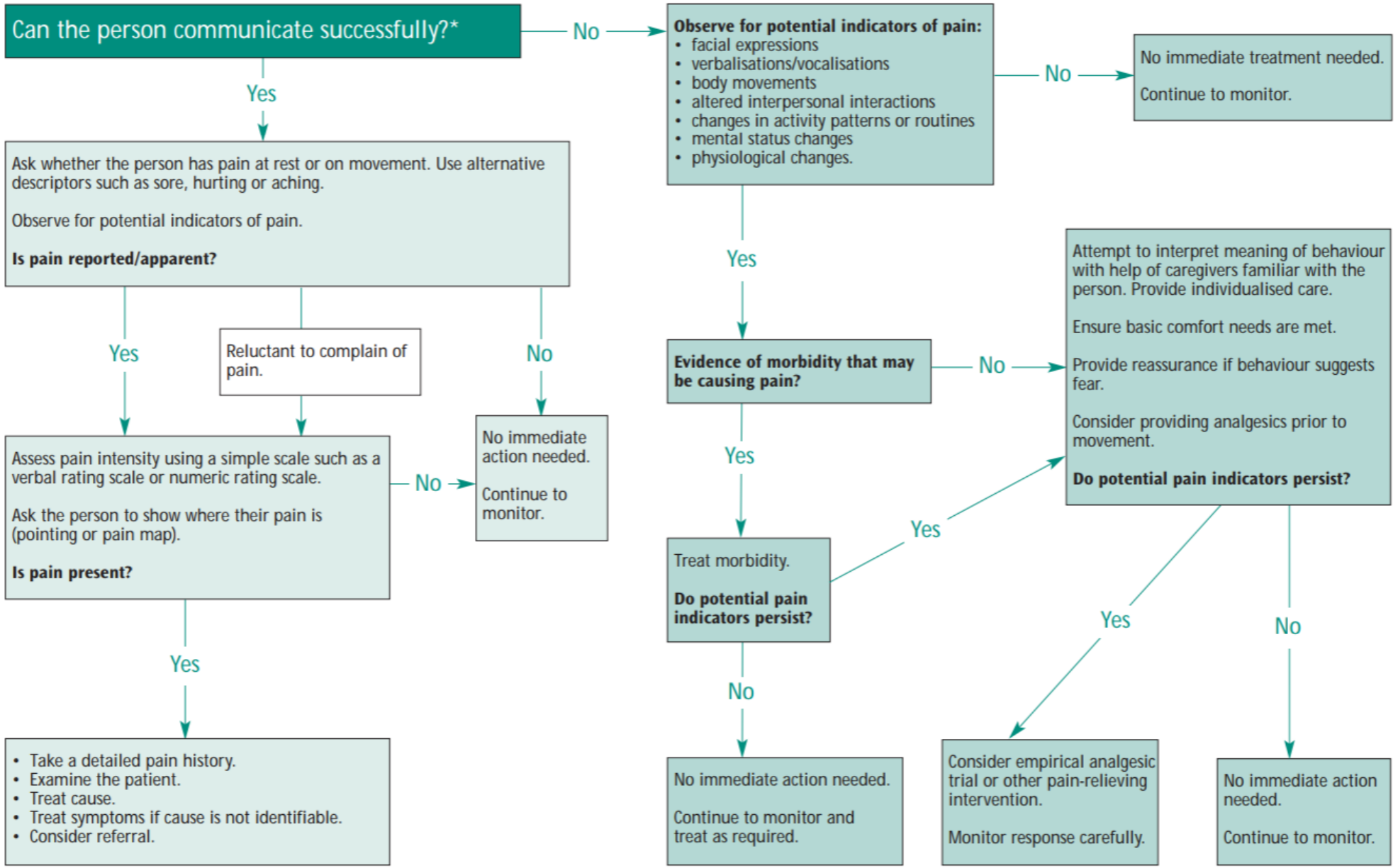
Appendix 2. Algorithm for the assessment of pain in older people



*If there is doubt about ability to communicate, assess and facilitate as indicated in Recommendations 4 and 5 of the Guidelines.