




GERIATRIC POLYPHARMACY

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No Disclosures

A photograph of an elderly woman, Betty Davis, with short, curly white hair, wearing a white t-shirt and blue jeans. She is wearing large, bright red boxing gloves and is captured in a dynamic, forward-leaning pose, as if she is boxing or running. Her expression is one of intense focus and determination, with her mouth slightly open. The background is a solid, deep blue. The image is framed by a thick black border.

Old age is no place for Sissies ~~ Betty Davis

There is no instruction manual for growing old.....



Objectives:

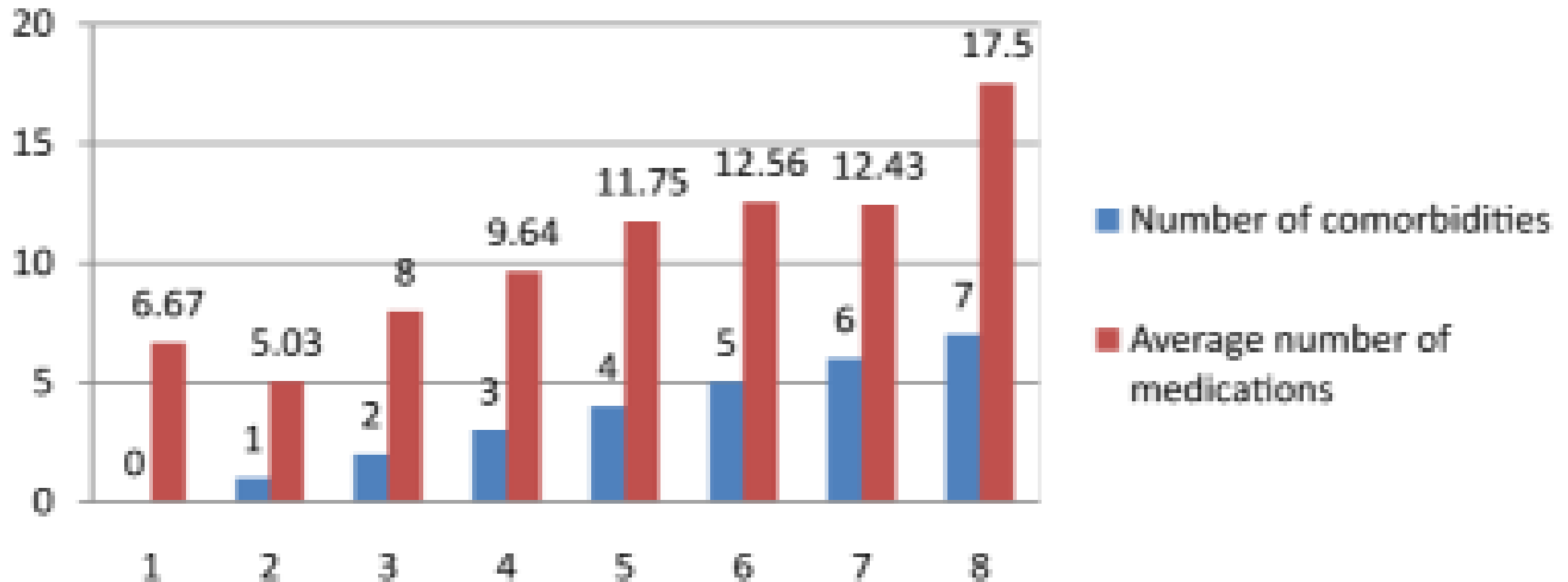
- Explore geriatric polypharmacy prevalence and its dangers
- Examine some of the more problematic medications given to the aging population
- Develop a systematic approach to evaluating the risks and benefits of problematic common medications that are frequently prescribed
- Introduce helpful tools to assist in reducing problematic medications with support and safety.

Note: Any changes in medications must be clinically appropriate relative to the individual patient and be approved by patient's provider.

Polypharmacy is associated with.....

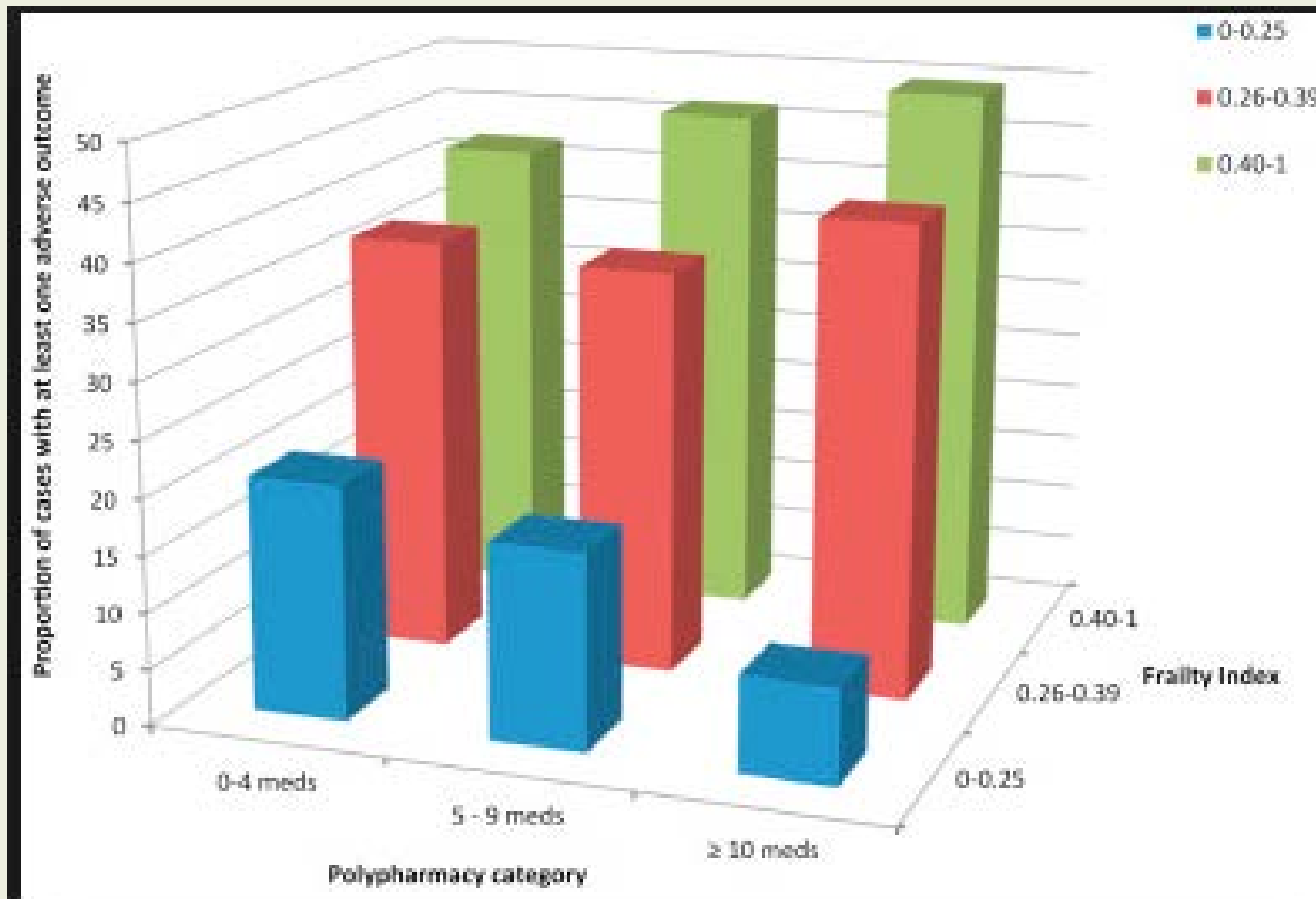
- increased risk of using potentially inappropriate medications (PIMs)
- negative effects on long-term physical and cognitive functioning
- Polypharmacy also results in medication nonadherence
- increased risk of drug duplication, drug–drug interactions and adverse drug reactions (ADRs)
- higher health care costs

Polypharmacy and Comorbidities

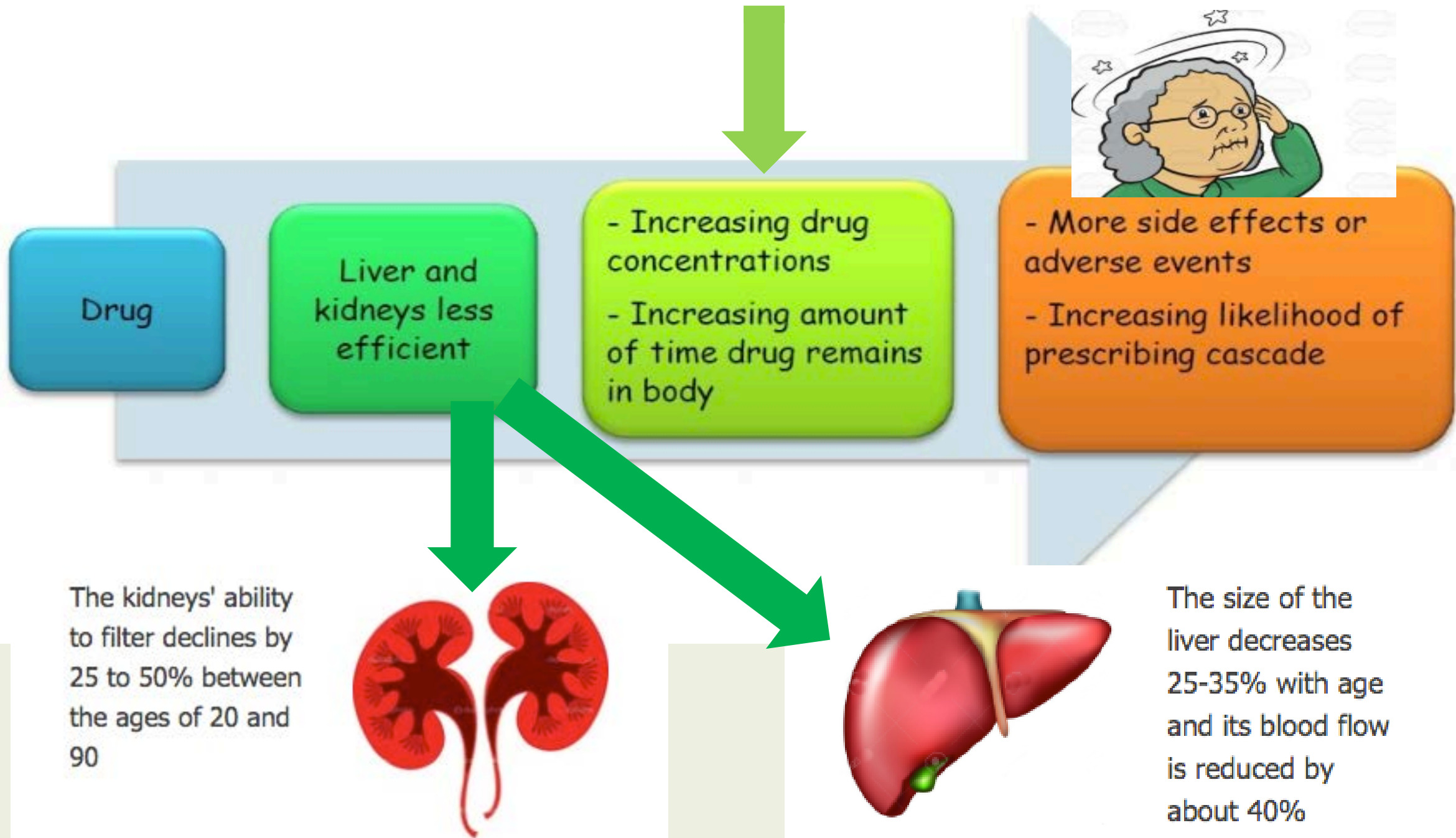


Journal of Pharmacy and Pharmaceutical Sciences 2014

Al Ameri MN, Makramalla E, Albur U, Kumar A, Rao P (2014) Prevalence of Poly-pharmacy in the Elderly: Implications of Age, Gender, Co-morbidities and Drug Interactions. SOJ Pharm Pharm Sci, 1(3), 1-7. DOI: <http://dx.doi.org/10.15226/2374-6866/1/3/00115>



Adverse Outcomes in Relation to Polypharmacy in Robust and Frail Older Hospital Patients
Author links open overlay panel Arjun Poudel PhD, Nancye Peel PhD, Lisa Nissen PhD, Charles Mitchell, Leonard Gray Ph D, Ruth Hubbard MD.
Journal of American Medical Directors Association 1 August 2016, Pages 767.e9-767.e13



Problematic Medications for the Aging Population



1. Opioids
2. Benzodiazepines
3. Anticholinergics
4. Antipsychotics for
Insomnia or Dementia

Opiates and the aging

- From 1996 through 2010, the number of opioid prescriptions provided to older patients increased 9-fold.
- More alarming, 35% of patients aged older than 50 years with chronic pain reported misuse of their opioid prescriptions in the past 30 days.
- According to the American Geriatric Society, nearly 80% of elderly patients in long-term care settings have substantial pain, yet 25% do not receive any treatment.

Opiates

and the aging

- Nausea
- Constipation
- Urinary retention
- Pruritus
- **Central nervous system adverse effects**

Sedation and mild cognitive impairment are the other common side effects of opioids in elderly

Combinations of opioids and other central nervous system (CNS) depressant drugs such as barbiturates, benzodiazepines, antidepressants, and antipsychotics often have additive effects on sedation.

Opiates

and the aging

- **Respiratory depression – COPD/asthma - greater danger hypoxia**

- **Opioid-induced hyperalgesia**

Patients who are receiving increasing doses of opioids may have opioid-induced hyperalgesia. This is the phenomenon of increasing sensitivity to both pain (hyperalgesia) and non-painful stimuli (allodynia).

The mechanism of action is due to toxic metabolites of opioid (morphine-3-glucuronide (M3G) or hydromorphone-3-glucuronide (H3G), activation of N-methyl-D-aspartate (NMDA) receptors in the CNS. Since it is due to the effect of toxic metabolites, the other opioid hyper excitability effects such as myoclonus,

Opiates

and the aging

- **Cardiovascular system** - Less well known adverse effects include cardiovascular instability- Opioid therapy increases catecholamine secretion via the hypothalamus and brain stem
- **Skeletomuscular system** - headache and muscle spasm of both smooth and striated muscle, leading to urine retention, slowing of gut motility and myoclonic jerks. Furlan AD, Sandoval JA, Mailis-Gagnon A, et al. Opioids for chronic non-cancer pain: a meta-analysis of effectiveness and side effects. Can Med Assoc J 2006; 174: 1589–1594.
- **Endocrine**- opioids exert this effect via the hypothalamic-pituitary-gonadal axis. Additional effects on adrenal hormones, weight and blood pressure.
- **Diminished bone density**

Opiates

and the aging

- Non-opioid pharmacotherapy and non-pharmacological therapy are the preferred modalities of treatment for chronic pain. However, in the proper contexts, opioids can be a useful treatment option. They are most beneficial in the short term for acute injuries, including the management of pain postoperatively.
- Use should be time-limited, except in managing certain cancer-related pain syndromes and as a part of end-of-life care
































































Opiates

and the aging

- Titrate down in small amounts - Cutting 10-20% weekly, more if tolerated.
- Follow-up with patient every 2 weeks -If only cutting the dose by a small fraction – That is still success.
- Add on other medications to assist with pain relative to injury or dysfunction such as Tylenol “Arthritis,” Lidocaine patches, lidocaine gel, capsaicin cream, Aspercreme, Diclofenac Cream, CBD oil/cream
- Non-oral med Modalities: Physical therapy, chiropractor, stretching/exercise therapy, Geriatric centric yoga, tai chi or qigong, epidural steroid injections, platelet rich plasma injections

TAPERING-OFF PROGRAM

We recommend that you follow this schedule under the supervision of your doctor or your pharmacist.

WEEKS	TAPERING SCHEDULE							✓
	MO	TU	WE	TH	FR	SA	SU	
1 and 2								
3 and 4								
5 and 6								
7 and 8								
9 and 10								
11 and 12								
13 and 14								
15 and 16								
17 and 18								

EXPLANATIONS

 Full dose  Half dose  Quarter of a dose  No dose

Deprescribing.org

Benzodiazepines/ Hypnotics





You May Be at Risk

You are taking one of the following
sedative-hypnotic medications:

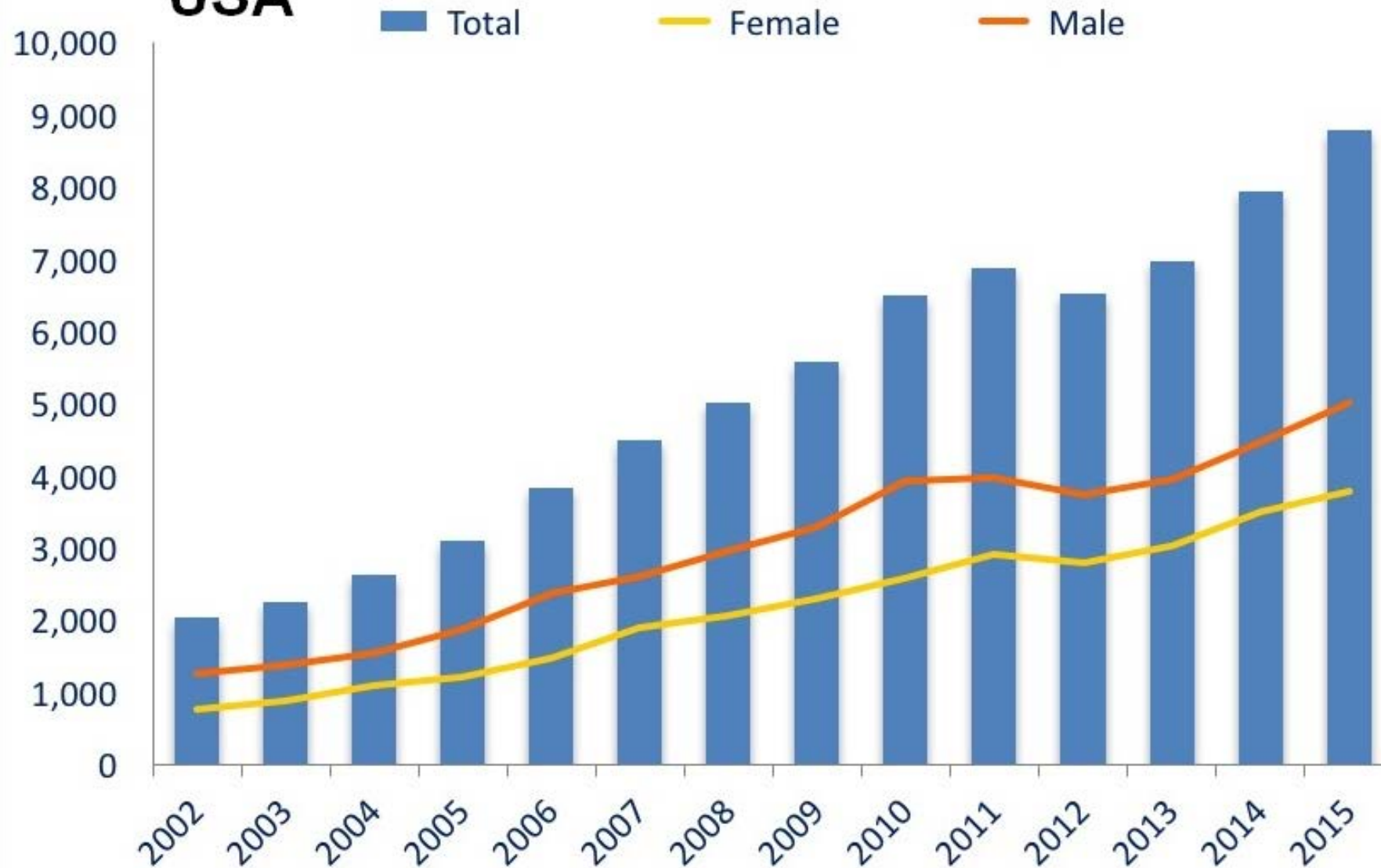
- | | | |
|--|---|---|
| <input type="radio"/> Alprazolam (Xanax®) | <input type="radio"/> Diazepam (Valium®) | <input type="radio"/> Temazepam (Restoril®) |
| <input type="radio"/> Bromazepam (Lectopam®) | <input type="radio"/> Estazolam | <input type="radio"/> Triazolam (Halcion®) |
| <input type="radio"/> Chlorazepate | <input type="radio"/> Flurazepam | <input type="radio"/> Eszopiclone (Lunesta®) |
| <input type="radio"/> Chlordiazepoxide-
amitriptyline | <input type="radio"/> Loprazolam | <input type="radio"/> Zaleplon (Sonata®) |
| <input type="radio"/> Clidinium-chlordiazepoxide | <input type="radio"/> Lorazepam (Ativan®) | <input type="radio"/> Zolpidem (Ambien®,
Intermezzo®, Edluar®,
Sublinox®, Zolpimist®) |
| <input type="radio"/> Clobazam | <input type="radio"/> Lormetazepam | <input type="radio"/> Zopiclone (Imovane®,
Rhovane®) |
| <input type="radio"/> Clonazepam (Rivotril®,
Klonopin®) | <input type="radio"/> Nitrazepam | |
| | <input type="radio"/> Oxazepam (Serax®) | |
| | <input type="radio"/> Quazepam | |

Benzodiazepines /Hypnotics

[Deprescribing.org](https://deprescribing.org)

Number of Deaths from Benzodiazepines

USA



Source: National Center for Health Statistics, CDC Wonder

Benzodiazepines

Anxiety often a nonspecific symptom – adaptive

No evidence base for use in behavioral disturbances in dementia.

- 1989 study indicates can worsen attention in Dementia
- Highly correlated with delirium and somnolence
- Can increase confusion
- Definitely increases risk of falls
- Can disinhibit patient

Table. Mortality Risk Depending on Use of Benzodiazepine.

Table. Mortality Risk Depending on Use of Benzodiazepine

Benzodiazepine Use	Mortality, RR (95% CI)*	
	All-Cause	Fracture-Related
Any benzodiazepine	0.77 (0.51-1.17)	2.71 (0.37-19.76)
Diazepam equivalents, >5 mg/d†	0.98 (0.64-1.51)	3.82 (0.52-27.80)
More than 1 benzodiazepine	1.21 (0.49-2.97)	7.75 (0.75-79.86)
Benzodiazepine with long half-life‡	1.38 (0.73-2.63)	NA

Abbreviations: CI, confidence interval; NA, not available because no deaths were observed; RR, relative risk.

*From Cox proportional hazards model using the annually observed use of benzodiazepine as the time-dependent covariate, adjusted for sex.

†Equivalents calculated per Salzman.⁹

‡Diazepam, chlordiazepoxide, flunitrazepam, flurazepam, and nitrazepam.

Vinkers, D. J. et al. JAMA 2003;290:2942-2943

JAMA

**Why is patient taking a BZRA?**

If unsure, find out if history of anxiety, past psychiatrist consult, whether may have been started in hospital for sleep, or for grief reaction.

- Insomnia on its own OR insomnia where underlying comorbidities managed
- For those ≥ 65 years of age:** taking BZRA regardless of duration (avoid as first line therapy in older people)
- For those 18-64 years of age:** taking BZRA > 4 weeks

- Other sleeping disorders (e.g. restless legs)
- Unmanaged anxiety, depression, physical or mental condition that may be causing or aggravating insomnia
- Benzodiazepine effective specifically for anxiety
- Alcohol withdrawal

Engage patients (discuss potential risks, benefits, withdrawal plan, symptoms and duration)

Recommend Deprescribing**Continue BZRA**

- Minimize use of drugs that worsen insomnia (e.g. caffeine, alcohol etc.)
- Treat underlying condition
- Consider consulting psychologist or psychiatrist or sleep specialist

Taper and then stop BZRA

(taper slowly in collaboration with patient, for example $\sim 25\%$ every two weeks, and if possible, 12.5% reductions near end and/or planned drug-free days)

- **For those ≥ 65 years of age** (strong recommendation from systematic review and GRADE approach)
- **For those 18-64 years of age** (weak recommendation from systematic review and GRADE approach)
- Offer behavioural sleeping advice; consider CBT if available (see reverse)

Monitor every 1-2 weeks for duration of tapering**Expected benefits:**

- May improve alertness, cognition, daytime sedation and reduce falls

Withdrawal symptoms:

- Insomnia, anxiety, irritability, sweating, gastrointestinal symptoms (all usually mild and last for days to a few weeks)

Use non-drug approaches to manage insomnia

Use behavioral approaches and/or CBT (see reverse)

If symptoms relapse:**Consider**

- Maintaining current BZRA dose for 1-2 weeks, then continue to taper at slow rate

Alternate drugs

- Other medications have been used to manage insomnia. Assessment of their safety and effectiveness is beyond the scope of this algorithm. See BZRA deprescribing guideline for details.

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Pottle K, Thompson W, Davies S, Grenier J, Sadowski C, Welch V, Holbrook A, Boyd C, Swenson JR, Ma A, Farrell B (2016). Evidence-based clinical practice guideline for deprescribing benzodiazepine receptor agonists. Unpublished manuscript.





BZRA Availability

BZRA	Strength
Alprazolam (Xanax®) ^T	0.25 mg, 0.5 mg, 1 mg, 2 mg
Bromazepam (Lectopam®) ^T	1.5 mg, 3 mg, 6 mg
Chlordiazepoxide (Librax®) ^C	5 mg, 10 mg, 25 mg
Clonazepam (Rivotril®) ^T	0.25 mg, 0.5 mg, 1 mg, 2 mg
Clorazepate (Tranxene®) ^C	3.75 mg, 7.5 mg, 15 mg
Diazepam (Valium®) ^T	2 mg, 5 mg, 10 mg
Flurazepam (Dalmane®) ^C	15 mg, 30 mg
Lorazepam (Ativan®) ^{T, S}	0.5 mg, 1 mg, 2 mg
Nitrazepam (Mogadon®) ^T	5 mg, 10 mg
Oxazepam (Serax®) ^T	10 mg, 15 mg, 30 mg
Temazepam (Restoril®) ^C	15 mg, 30 mg
Triazolam (Halcion®) ^T	0.125 mg, 0.25 mg
Zopiclone (Imovane®, Rhovane®) ^T	5mg, 7.5mg
Zolpidem (Sublinx®) ^S	5mg, 10mg

T = tablet, C = capsule, S = sublingual tablet

BZRA Side Effects

- BZRAs have been associated with:
 - physical dependence, falls, memory disorder, dementia, functional impairment, daytime sedation and motor vehicle accidents
- Risks increase in older persons

Engaging patients and caregivers

Patients should understand:

- The rationale for deprescribing (associated risks of continued BZRA use, reduced long-term efficacy)
- Withdrawal symptoms (insomnia, anxiety) may occur but are usually mild, transient and short-term (days to a few weeks)
- They are part of the tapering plan, and can control tapering rate and duration

Tapering doses

- No published evidence exists to suggest switching to long-acting BZRAs reduces incidence of withdrawal symptoms or is more effective than tapering shorter-acting BZRAs
- If dosage forms do not allow 25% reduction, consider 50% reduction initially using drug-free days during latter part of tapering, or switch to lorazepam or oxazepam for final taper steps

Behavioural management

Primary care:

- Go to bed only when sleepy
- Do not use bed or bedroom for anything but sleep (or intimacy)
- If not asleep within about 20-30min at the beginning of the night or after an awakening, exit the bedroom
- If not asleep within 20-30 min on returning to bed, repeat #3
- Use alarm to awaken at the same time every morning
- Do not nap
- Avoid caffeine after noon
- Avoid exercise, nicotine, alcohol, and big meals within 2 hrs of bedtime

Institutional care:

- Pull up curtains during the day to obtain bright light exposure
- Keep alarm noises to a minimum
- Increase daytime activity & discourage daytime sleeping
- Reduce number of naps (no more than 30mins and no naps after 2pm)
- Offer warm decaf drink, warm milk at night
- Restrict food, caffeine, smoking before bedtime
- Have the resident toilet before going to bed
- Encourage regular bedtime and rising times
- Avoid waking at night to provide direct care
- Offer backrub, gentle massage

Using CBT

What is cognitive behavioural therapy (CBT)?

- CBT includes 5-6 educational sessions about sleep/insomnia, stimulus control, sleep restriction, sleep hygiene, relaxation training and support

Does it work?

- CBT has been shown in trials to improve sleep outcomes with sustained long-term benefits

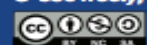
Who can provide it?

- Clinical psychologists usually deliver CBT, however, others can be trained or can provide aspects of CBT education; self-help programs are available

How can providers and patients find out about it?

- Some resources can be found here: <http://sleepwellns.ca/>

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Pottie K, Thompson W, Davies S, Grenier J, Sadowski C, Welch V, Holbrook A, Boyd C, Swenson JR, Ma A, Farrell B (2016). Evidence-based clinical practice guideline for deprescribing benzodiazepine receptor agonists. Unpublished manuscript.



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How to get a good night's sleep without medication





Anticholinergic Medications

Anticholinergic drugs competitively inhibit binding of the neurotransmitter, acetylcholine. They target either muscarinic acetylcholine receptors or, less commonly, nicotinic acetylcholine receptors. Muscarinic receptors are found on nerve endings to smooth muscles cells, secretory glands and the eye.

ANTICHOLINERGIC SIDE EFFECTS



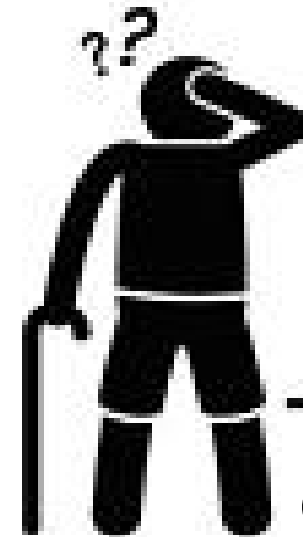
Hot as a hare



Dry as a bone



Dizziness



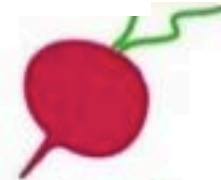
Cognition Changes



Can't urinate



Blind as a bat



Red as a beet



Constipation



Lose Appetite

Anticholinergic Risk Scale					
Score 1		Score 2		Score 3	
alprazolam	Xanax	amantadine	Symadine	amitriptyline	Elavil
atenolol	Tenormin	belladone alkaloids	All	amoxapine	Asendin
brompheniramine maleate	Veltane	carbamazepine	Carbatrol, Teril	benztropine	Cogentin
bupropion hydrochloride	Wellbutrin, Zyban	cyclobenzaprine	Amrix, Flexeril	carbinoxamine	Clistin
captopril	Capoten	cyproheptadine	Periactin	chlorpheniramine	antihistamine
chlorthalidone	Thalitone	loxapine	Loxitane	clemastine	Tavist
cimetidine hydrochloride	Tagamet	meperidine	Demerol	clomipramine	Anafranil
clorazepate	Tranxene	methotrimeprazine	Levoprome, Nozinan	clozapine	Clozaril
codeine		molindone	Moban	darifenacin	Enablex
colchicine	Colcrys	oxcarbazepine	Trileptal	desipramine	Norpramine, Pertofrane
diazepam	Valium	pimozide	Orap	dicyclomine	Bentyl
digoxin	Lanoxin			dimenhydrinate	
dipyridamole	Persantine			diphenhydramine	Benedryl
disopyramide phosphate	Norpace	Key		doxepin	Sinequan, Zonalon
fentanyl				flavoxate	Urispas
isosorbide	Ismotac	1 Point = low risk of anticholinergic side effects		hydroxyzine	Atarax, Vistaril
loperamide	Imodium			imipramine	Janimine, Tofranil
metoprolol	Lopressor, Toprol-X			meclizine	Antivert
morphine		2 Points = moderate risk of anticholinergic side effects		nortriptyline	Pamelor
nifedipine	Adalat, Procardia			olanzapine	Zyprexa
prednisone				orphenadrine	Disipal, Norflex
quinidine	Duraquin, Quinora	3 Points = high risk of anticholinergic side effects		oxybutynin	Ditropan
risperidone	Risperdal			paroxetine	Paxil
theophylline	many brands			perphenazine	Trilafon
trazodone	Desyrel, Trialodine			procyclidine	Kemadrin
triamterene	Dyrenium			promethazine	Phenergan, Zipan
References				quetiapine	Seroquel
1. Rudolph JL, Salow MJ, Angelini MC et al. The anticholinergic risk scale and anticholinergic adverse effects in older persons. <i>Arch Intern Med</i> . 2008;168(5):508-13.				Scopolamine	motion sickness
				thioridazine	Mellaril
2. Indianapolis Discovery Network for Dementia. Anticholinergic cognitive burden list. www.indydiscoverynetwork.org/anticholinergiccognitiveburdenscale.html (accessed 2013 Oct 3).				tolterodine	Detrol
				trifluoperazine	Stelazine
				trihexyphenidyl	Artane, Tremin
3. Kansas Foundation for Medical Care, Inc. Anticholinergic Risk Scale for Commonly Prescribed Medications. http://www.kfmc.org/qio/images/docs/Providers/ADE/Anticholinergic%20Risk%20Scale%20Table.pdf (accessed 2013 Oct 3).				Trimipramine	Surmontil

Anticholinergic Side Effects	Potential Complications
PERIPHERAL	
Decreased salivation	Dental caries, ulceration of gums and buccal mucosa
Decreased bronchial secretions	Mucous plugging of small airways in patients with asthma or bronchitis
Increased pupil size	Photophobia, precipitation of acute narrow angle glaucoma
Visual Changes	Blurred vision, especially when reading small print
Increased heart rate	Angina, myocardial infarction
Difficulty urinating	Bladder distention, urinary retention
Decreased GI motility	Constipation
COGNITIVE	
Cognitive Impairment	Impaired concentration, confusion, attention deficit, memory impairment

Betty 74 yr old female

Hypertension

- Metoprolol XL (Toprol) 100mg qd
- HCTZ/ ~~Triamterene 25mg/37.5mg qd~~

Anticholinergic Risk Scale

+1 point
+1 point

Depression with Anxiety

- Zoloft 50 mg qd
- Wellbutrin 150 mg qd

0 points
+2 points

High Risk
Total points:
9 points

Stress/ Urge Incontinence

- ~~Oxybutynin 5 mg bid~~

+3 points

Lower risk
Total
points:
3 points

Back Strain

- ~~Cyclobenzaprine 10 mg qhs prn~~

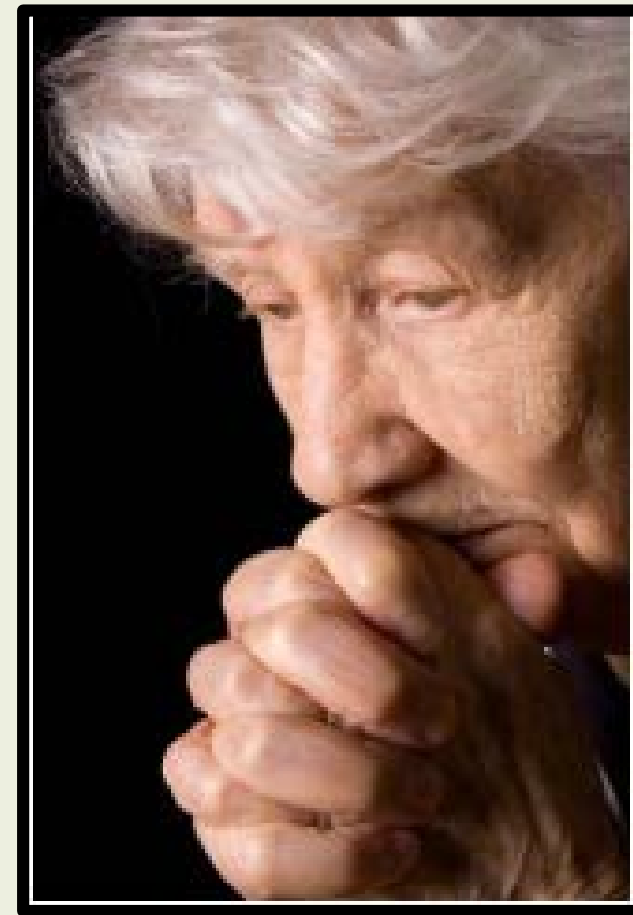
+2 points

Geriatric Polypharmacy

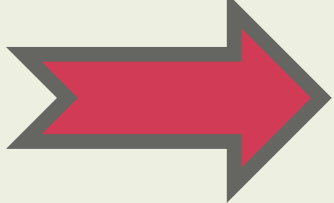
Disease State	Preferred Drug (drugs to avoid in parenthesis)
Allergies	loratadine, cetirizine (avoid diphenhydramine and 1st generation agents)
Depression	SSRIs including sertraline, escitalopram, or fluoxetine or an SNRI (avoid TCAs, paroxetine)
Insomnia	Trazodone (avoid antihistamines)
Movement disorder	Dopamine agonists, levodopa
Nausea	Ondansetron, metoclopramide (avoid meclizine, promethazine)
Pain	Tylenol, Gabapentin for neuropathic pain, short term oxycodone/acetaminophen, morphine (avoid meperidine)
Psychotic symptoms	Risperidone, paliperidone, Ziprasidone, Lurasidone (phenothiazines, clozapine and olanzapine have the highest burden)
Urinary Incontinence	Trospium (Sanctura) or solifenacin (Vesicare) are more selective for the bladder (avoid oxybutynin or tolterodine)
Reflux disorder	PPIs such as esomeprazole, omeprazole, lansoprazole (avoid H2 antagonists such as cimetidine, ranitidine)

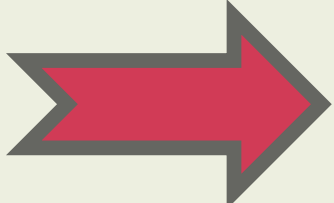
Note: Any changes in medications must be clinically appropriate relative to the individual patient and be approved by patient's provider.

Antipsychotics



Antipsychotics use with Dementia

Antipsychotic drugs  challenging behaviors
associated with dementia

FDA warns
antipsychotics  increased risk of death
severe muscle contractions
Increased incidence of falls

Non-drug treatments are often more effective and safer than antipsychotics

Antipsychotics and Aging

- The use of antipsychotics has **serious** concerns about safety in elderly patients affected with dementia for possible risks for stroke and sudden death.
- In the case of elderly patients affected with dementia, every antipsychotic treatment must be prescribed at the **lowest** effective dosage and for the **shortest** period possible. The severity and frequency of symptoms and the global functioning and quality of life, as reported by caregivers, must be always **monitored** during treatment

Shin JY, Choi NK, Jung SY, Lee J, Kwon JS, Park BJ. Risk of ischemic stroke with the use of risperidone, quetiapine and olanzapine in elderly patients: a population-based, case-crossover study. J Psychopharmacol. 2013;27(7):638–644.

7. Ray WA, Chung CP, Murray KT, Hall K, Stein CM. Atypical antipsychotic drugs and the risk of sudden cardiac death. N Engl J Med. 2009;360(3):225–235. Pub Med

Consider these practical strategies for improving sleep behaviour:

For a person who lives in the community:

- Go to bed only when sleepy
- Do not use bed or bedroom for anything but sleep (or intimacy)
- If not asleep within 20-30 min on going/returning to bed, exit the bedroom
- Use alarm to awaken at the same time every morning
- Do not nap
- Avoid caffeine after noon
- Avoid exercise nicotine, alcohol, and big meals 2 hours before bedtime

For a person who lives in long-term care or hospital:

- Pull up curtains during the day for light exposure
- Keep alarm noises to a minimum
- Increase daytime activity
- Reduce the number of naps (no more than 30 min and no naps after 2 pm)
- Use toilet before going to bed
- Have regular bedtime and rising times
- Avoid waking at night for direct care
- Try backrubs, or gentle massages

Personalized antipsychotic dose reduction strategy

www.deprescribing.org

Bjerre LM, Farrell B, Hogel M, Graham L, Lemay G, McCarthy L, et al. Deprescribing antipsychotics for behavioural and psychological symptoms of dementia and insomnia: Evidence-based clinical practice guideline. Can Fam Physician 2018;64:17-27 (Eng), e1-e12 (Fr).

Problematic Medications for the Aging Population



1. Opioids
2. Benzodiazepines
3. Anticholinergics
4. Antipsychotics for
Insomnia or Dementia

As You Age...

A Guide to
Aging, Medicines,
and Alcohol



SAMHSA

Substance Abuse and Mental Health
Services Administration

<https://store.samhsa.gov/product/As-You-Age-A-Guide-to-Aging-Medicines-and-Alcohol/SMA04-3940>

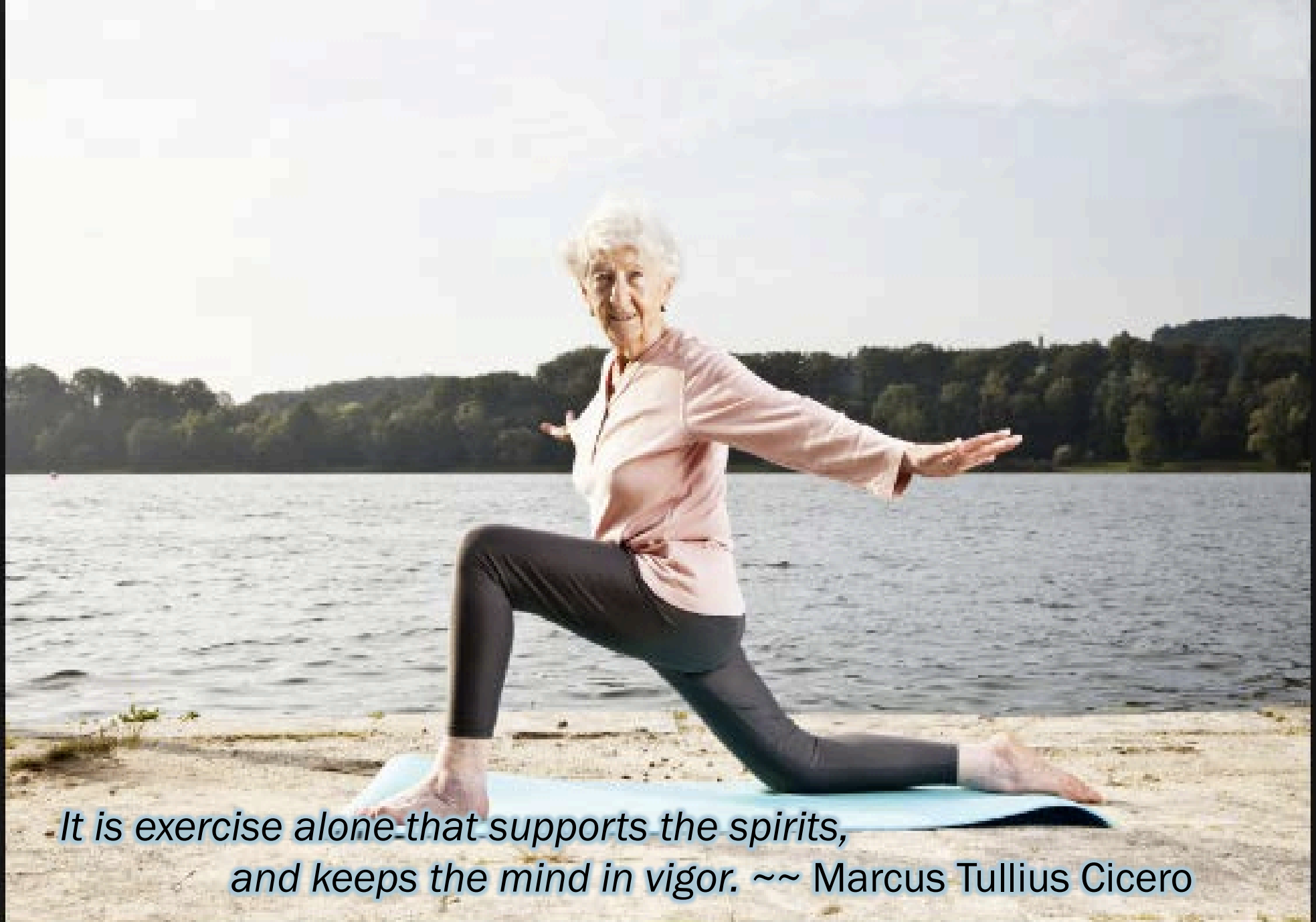
Informed Consent for all treatment including pharmacological

Discussion and documentation of discussion with patient, family or surrogate decision-maker of:

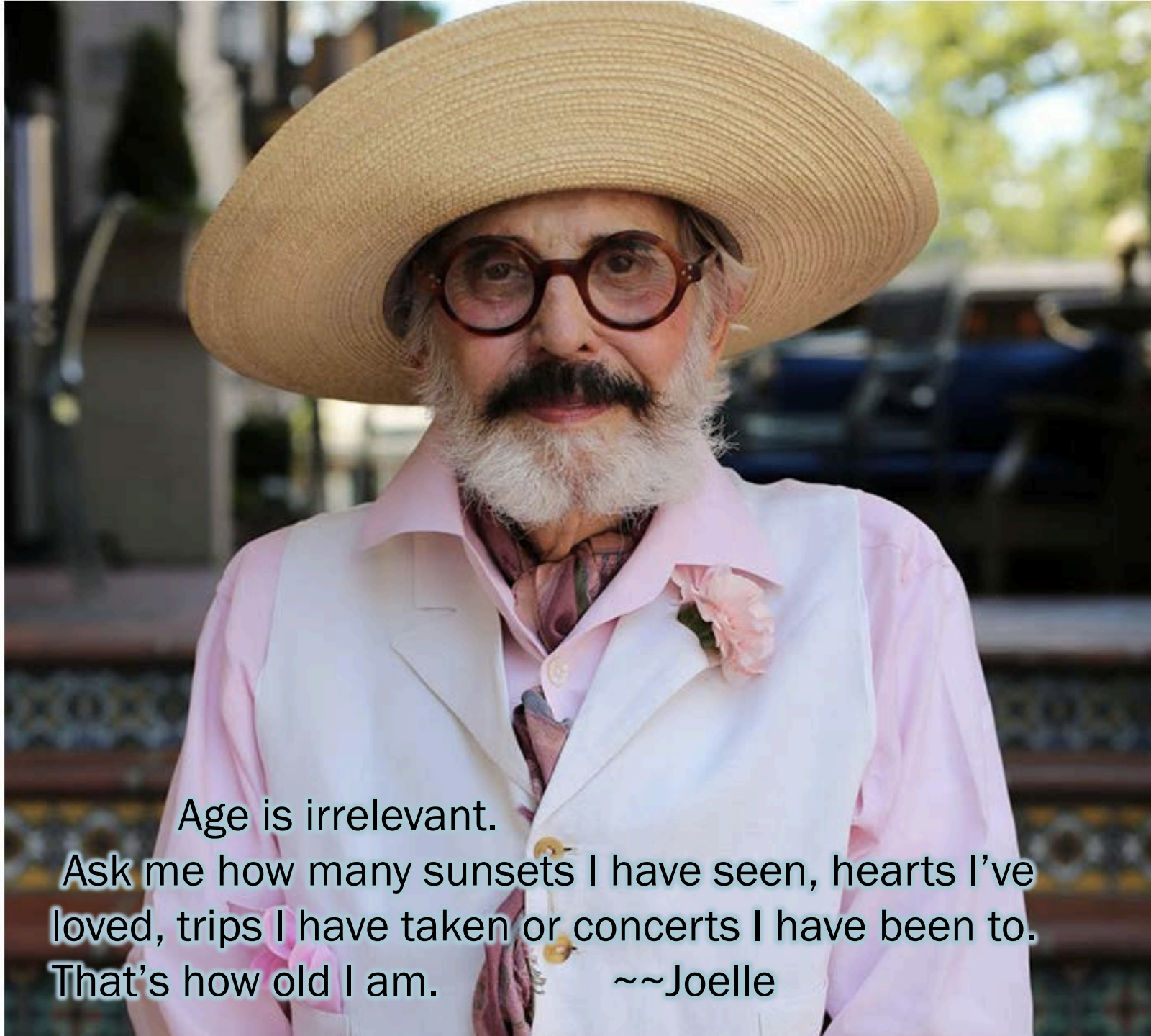
- Risks
- Benefits
- Alternatives (including the risks of no treatment)
- Most important to discuss and document – common risks and most dangerous risks

Appropriate prescribing

- Medications have clear, scientific-based indication (efficacy)
- Well tolerated (safety)
- Cost effective
- Respect patient's preferences, individualized
- Renal and liver function monitoring
- Recommend a medication card that is given for purse/wallet and educating patient to give to every provider at every visit.
- Recommend a medication reconciliation and drug interaction overview at every medication change and at every transition of care.



*It is exercise alone that supports the spirits,
and keeps the mind in vigor. ~~ Marcus Tullius Cicero*



Age is irrelevant.
Ask me how many sunsets I have seen, hearts I've
loved, trips I have taken or concerts I have been to.
That's how old I am. ~~Joelle



“Anyone who keeps the ability to see beauty
never grows old.” ~Franz Kafka

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