CONNECTICUT DMHAS · INTEGRATED CARE SERIES

CLINICAL REVIEW FOR PRESCRIBING CLINICIANS

Aging, SUD & Medications

Age-related changes in pharmacology, the rising prevalence of substance use disorders in older adults, and implications for prescribing in primary care, psychiatry, and addiction medicine.

PRESENTED BY

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DISCLOSURES

No relevant financial relationships to disclose.

Dr. Fahed has no relevant financial relationships with ineligible companies to disclose. This activity was independently planned and reviewed to be balanced, evidence-based, and free of commercial bias. Some agents discussed are used off-label in older adults; such use is identified and reflects published evidence rather than product labeling.

CLINICAL CONTEXT

Standard adult dosing frequently inappropriate for the older patient.

Substance use disorders among adults aged 65 and older have risen markedly over the past two decades. Concurrently, age-related changes in pharmacokinetics, pharmacodynamics, and polypharmacy patterns place this population at elevated risk for iatrogenic harm from standard psychotropic and medication-assisted treatment regimens.

3.9M
ADULTS ≥65 WITH SUD (2022)

2×
SUD PREVALENCE ≥50, 2009→2020

190%
↑ TX ADMISSIONS ≥55 ('08–'18)

SAMHSA 2022 · HAN 2009 · WEBER 2022

OBJECTIVES

At the end of this session, learners will be able to…

01

Describe epidemiologic trends

Prevalence and admissions data in adults aged 55 and older.

02

Apply age-related PK principles

Absorption, distribution, metabolism, and elimination.

03

Recognize PD vulnerabilities

GABA, opioid, anticholinergic, and blood–brain barrier.

04

Identify substance–drug interactions

Alcohol, opioid, cannabis, and stimulant effects on psychotropics.

05

Select medications for addiction

Buprenorphine, naltrexone, methadone, and acamprosate in older adults.

06

Mitigate drug–drug interactions

QTc, serotonin, anticholinergic burden, falls, hepatic, and renal.

07

Integrate into daily practice

Screening, monitoring, and deprescribing strategies.

08

Reference authoritative guidelines

Beers 2023, SAMHSA TIP 26, ASAM, STOPP/START.

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01 / 08

SECTION 1

Epidemiology of substance use in older adults.

Rising prevalence across nearly every category, driven by a baby-boomer cohort with greater lifetime exposure to illicit substances than any prior generation.

EPIDEMIOLOGICAL TRENDS · 2002 → 2023

SUBSTANCE USE IN OLDER ADULTS

A rising, and routinely missed, clinical problem

+1233%
past year cannabis use, adults 65+, 2002 to 2022

3x
rise in opioid use disorder among Medicare enrollees, 2013 to 2018

31%
of older benzodiazepine users take them long term

Why it is missed, and how to catch it

1. DSM-5 criteria lean on work and family roles. In retired, isolated older adults those markers disappear, so problematic use can be hidden a little easier.

2. Build screening into routine primary care and the emergency department, using tools such as the NIDA screener and NIAAA Rethinking Drinking.

3. Check the prescription drug monitoring program, and probe the stressors that drive use: grief, retirement, chronic pain, money.

APA Resource Document on SUD in Older Adults 2023; Lehmann & Fingerhood, NEJM 2018; Han, JAMA Intern Med 2020; NSDUH 2002–2022.

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SECTION 2

Age-related pharmacokinetic changes.

At every ADME stage (absorption, distribution, metabolism, elimination): greater exposure, prolonged half-lives, and amplified toxicity risk with age.

MANGONI & JACKSON 2004 · MCLEAN & LE COUTEUR 2004

II.01 · ADME · AGE-RELATED CHANGES

All four stages of Pharmacokinetics are impacted at different percetanges

A **ABSORPTION**

Modest, **except** first-pass.

First-pass metabolism declines ~ **1% per year after age 40** , increasing bioavailability of propranolol, verapamil, and some opioids.

Cusack 2004

D **DISTRIBUTION**

Body composition is **altered**.

Body fat **~doubles (men), ↑36% (women)** ; total body water falls 10–15%. Diazepam V_d rises 0.8 → **1.4 L/kg** ; t½ extends up to **96 hours**.

Mangoni 2004 · Gronich 2024 · Klotz 2009

M **METABOLISM**

Phase I is **impaired**.

Hepatic blood flow ↓**40%** , liver mass ↓ **30%** . CYP450 oxidation is impaired; Phase II conjugation is relatively preserved.

McLean & Le Couteur 2004 · Schmucker 2001

E **ELIMINATION**

GFR **silently declines**!

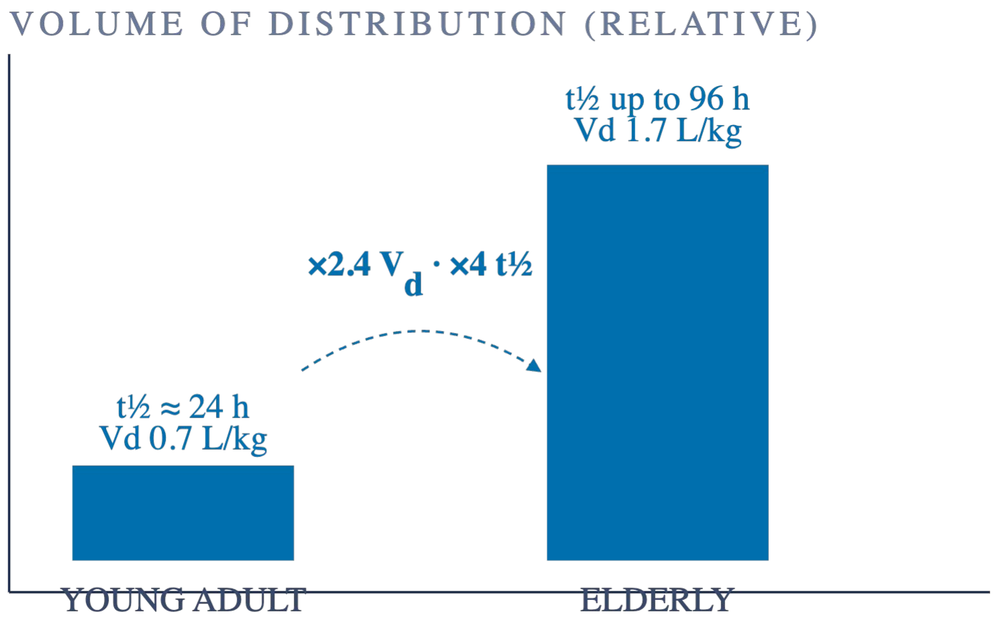
GFR falls **~0.75–1.0 mL/min/year** after age 30–40. Serum creatinine is **misleading**; use CKD-EPI.

BLSA Lindeman 1985 · Levey 2009

MANGONI & JACKSON BJCP 2004 · MCLEAN & LE COUTEUR PHARMACOL REV 2004

II.02 · DISTRIBUTION · LIPOPHILIC AGENTS

Diazepam's half-life:



> For lipophilic drugs, expanded fat mass becomes a reservoir. The same milligram dose lingers **longer** and accumulates over repeated dosing.

Decreased serum albumin simultaneously raises the **free fraction** of highly protein-bound drugs (**warfarin, phenytoin, valproate, diazepam**), amplifying clinical effect at the same measured total concentration.

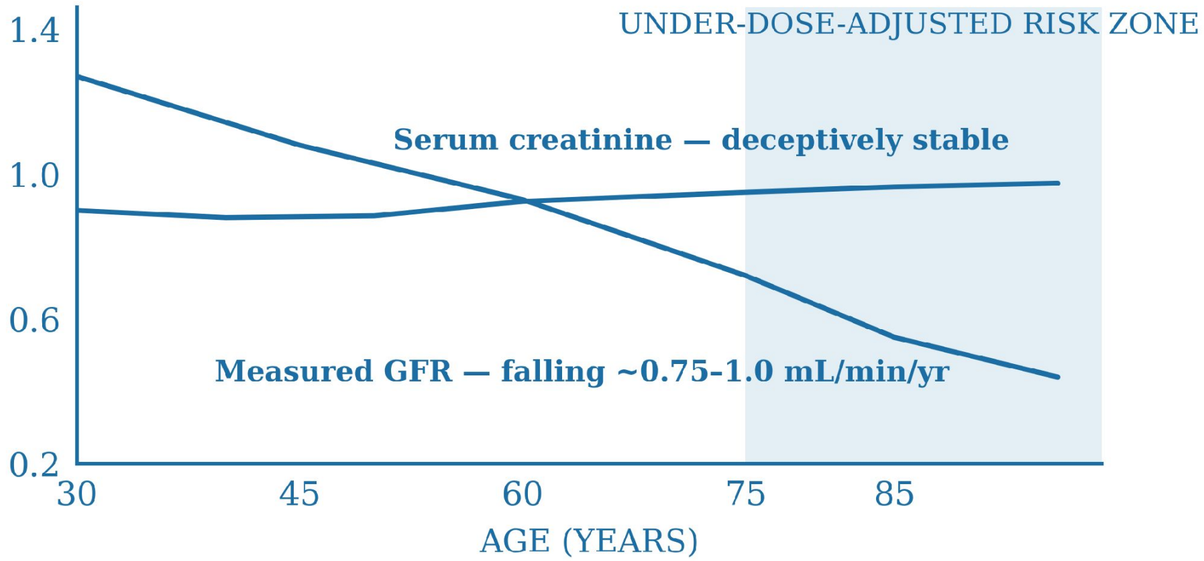
HYDROPHILIC AGENTS

Lithium, digoxin, ethanol: lower V_d yields **higher peak plasma** at any given dose. Start lower.

GRONICH DRUGS & AGING 2024 · KLOTZ DMR 2009 · MANGONI & JACKSON 2004

II.03 · ELIMINATION · SERUM CREATININE LIMITATION

Stable serum creatinine despite declining renal function.



Serum creatinine is held constant by **declining muscle mass** , masking real renal impairment. Estimate with **CKD-EPI**, not serum creatinine alone.

RENALLY-CLEARED DRUGS OF CONCERN

- Lithium
- Gabapentin
- Pregabalin
- Acamprosate
- Digoxin
- Varenicline

KDIGO recommends CKD-EPI (Levey *Ann Intern Med* 2009).

Dose-adjust; for lithium, shift trough target to **0.4–0.8 mEq/L** .

LINDEMAN BLSA 1985 · LEVEY 2009 · AYMANNS 2010 · SPROULE 2000

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SECTION 3

Pharmacodynamic vulnerability of the aging brain.

Pharmacodynamic shifts (receptor sensitivity, blood-brain-barrier permeability, impaired homeostasis), independent of drug concentration.

GABA-A · M-OPIOID · D2 · ANTICHOLINERGIC · BBB

PHARMACODYNAMICS

The aging brain responds more strongly at the same drug level

Even after adjusting for concentration, receptor biology and a more permeable blood brain barrier amplify CNS effects. These shifts are independent of plasma level.

2.8x

Opioid respiratory depression

Older adults often need 25 to 50% of younger adult morphine equivalents.

+24%

Benzodiazepine sensitivity

Greater impairment at equivalent plasma levels, and it lasts longer.

-6 to 7%

D2 density, per decade

Compounds with low cholinergic reserve; raises EPS and antipsychotic risk.

OR 3.27

Anticholinergic burden

ACB of 3 or more for 90 days or more is tied to mild cognitive impairment.

Freye & Levy 2004; Nikaido 1990; Montagne, Neuron 2015; Taylor-Rowan 2021.

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SECTION 4

Interactions between substances of use and psychotropic medications.

Alcohol, opioids, cannabis, stimulants, and increasingly misused gabapentinoids, each interacting with commonly prescribed medications.

COMPOUNDED RISK IN THE POLYPHARMACY CONTEXT

IV.01 · ALCOHOL · PREVALENT & UNDER-SCREENED

Alcohol interacts with virtually every psychotropic class.

WITH	MECHANISM	CLINICAL IMPACT	MAGNITUDE
Benzodiazepines	Dual GABA-A modulation; ↑ peak diazepam plasma	**Synergistic** CNS depression, not just additive	HIGH
SSRIs / SNRIs	Additive CNS depression; platelet & mucosal effects	Upper-GI bleed OR **1.55** (SSRI alone)	ELEVATED
Antipsychotics	Enhanced sedation; α-blockade	Orthostasis & **falls** , especially in elderly	ELEVATED
Mood stabilizers (Li)	Dehydration; CYP2E1/3A4 induction w/ chronic use	Unpredictable levels; lithium **toxicity risk**	HIGH
Anticonvulsants	Shared hepatic load; altered protein binding	Reduced seizure threshold post-binge	ELEVATED

AGABIO 2022 · JIANG 2015 · HOLTON 2017 · COUSINS 2019 · CHAN & ANDERSON 2014

IV.02 · THREE INTERACTION PATTERNS

Three principal interaction risks.

01

Serotonin syndrome.

Highest with **tramadol, fentanyl, meperidine** + SSRIs/SNRIs/MAOIs. **Morphine, oxycodone, hydromorphone** carry lower serotonergic load.

FDA 2016 DSC · Baldo & Rose 2020

02

Opioid + BZD depression.

FDA **Boxed Warning** (Aug 2016) covers ~400 products. In 2021, **>13%** of opioid-overdose deaths also involved benzodiazepines.

FDA DSC Aug 2016 · CDC WONDER 2021

03

QTc prolongation stacking.

Methadone blocks hERG → QTc **+12–42 ms** . Citalopram capped at **20 mg/day** in patients >60 years. Additive with QTc-prolonging antipsychotics.

Krantz 2009 · Beach 2014 · FDA 2012

BALDO & ROSE BJA 2020 · KRANTZ ANN INTERN MED 2009 · BEACH J CLIN PSYCHIATRY 2014

IV.03 · NALOXONE

Naloxone underused in older adults.

01

Higher overdose lethality.

Older adults clear opioids slowly and often stack them with benzodiazepines, alcohol, or sleep aids. **Overdose is more often fatal** here, with less respiratory reserve and **delayed presentation**. The antidote is naloxone.

CDC WONDER · SAMHSA 2023

02

Short half-life, re-dose.

Give **intranasal 4 mg or IM 0.4 mg**, repeating every 2 to 3 minutes if no response. The effect fades in **30 to 90 minutes**, shorter than methadone or ER opioids, so renarcotization can follow. Observe and re-dose.

Naloxone labeling · SAMHSA toolkit

03

Co-prescription for all at-risk patients.

The **2022 CDC opioid guideline** advises co-prescribing naloxone for patients on opioids who also use benzodiazepines, have OUD, or have lung disease. **Titrate to restore breathing**, not full alertness, and counsel a caregiver.

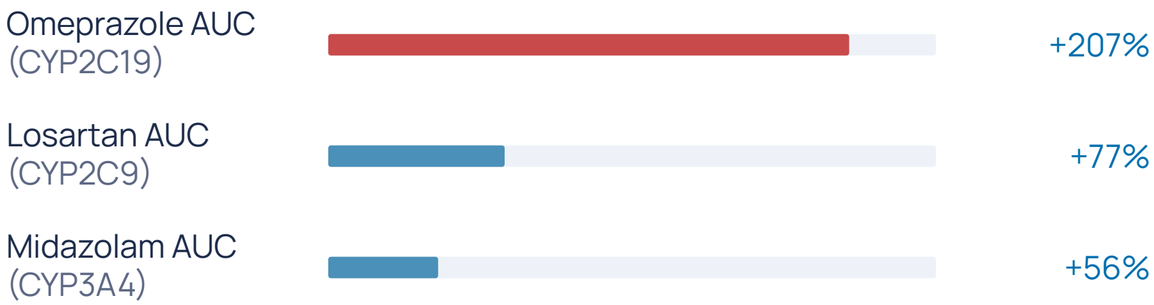
CDC 2022 · SAMHSA

CDC OPIOID GUIDELINE 2022 · SAMHSA TOOLKIT · NALOXONE LABEL

IV.04 · CANNABIS

CBD a potent CYP inhibitor, it is NOT a benign supplement.

CBD × CYP · SUBSTRATE AUC INCREASE (BANSAL 2023)



Healthy-volunteer probe-substrate study; bars proportional to % AUC increase.

CLINICALLY RELEVANT IMPACTS

CBD + valproate : increased hepatotoxicity; check LFTs at initiation and 1 month.

Antipsychotic non-adherence in cannabis users, OR **2.46** (Foglia 2017).

Psychosis risk, meta-analytic, OR **3.90** (Marconi 2016). Highest with high-THC, daily use.

THC in older adults, dose-dependent dizziness and lightheadedness **(IRR 2.04 at 10 mg/d)**, orthostatic hypotension, and falls (Velayudhan 2021).

BANSAL CLIN PHARMACOL THER 2023 · MARCONI SCHIZOPHR BULL 2016 · FOGLIA PSYCHOL MED 2017 · VELAYUDHAN JAMA NETW OPEN 2021

IV.05 · STIMULANTS

Cocaine: QTc prolongation; fatal MDMA + MAOI.

COCAINE

Cocaine independently prolongs **QTc** via cardiac sodium and hERG-channel effects, and stacks with QTc-prolonging antipsychotics (haloperidol, ziprasidone, IV droperidol).

Layered onto methadone or citalopram > 20 mg in patients > 60, risk of **torsades** is much higher..

> Baseline ECG before any QTc-prolonging psychotropic in a patient with stimulant exposure.

MDMA / METHAMPHETAMINE

MDMA or methamphetamine combined with an **MAOI** can produce fatal **serotonin syndrome** ; with SSRIs/SNRIs, risk is additive but lower.

Both raise sympathetic tone, additive cardiovascular load with stimulants prescribed for ADHD or weight, and with SNRIs.

≥3

BEERS 2023 · STRONG RECOMMENDATION

Avoid concurrent use of ≥3 CNS-active drugs. Stacking two or more raises recurrent falls, IDR **1.97** (95% CI 1.28–3.05; Thapa 1995).

BAUMAN AM J CARDIOL 2006 · MALCOLM & THOMAS PSYCHOPHARMACOLOGY 2022 · BEERS AGS 2023 · THAPA AM J EPIDEMIOL 1995

IV.06 · GABAPENTINOIDS

Gabapentinoids, also not benign (sorry).

01

Rising misuse.

Gabapentin and pregabalin are prescribed widely for pain and anxiety, but misuse is climbing, **especially alongside opioids**. Misuse runs near **15 to 22% among people with OUD**, far above the roughly 1% seen in the general population.

Evoy Drugs 2017 · FDA 2019

02

Respiratory depression.

FDA **December 2019 warning**: serious and fatal respiratory depression when combined with **opioids or CNS depressants**, especially with COPD or age ≥65.

FDA DSC Dec 2019

03

Dosing by renal function.

Both are **renally cleared**. Reduce dose as GFR falls; accumulation drives sedation, ataxia, and falls. **Re-check the CrCl** before escalating, especially with opioids on board.

Beers 2023 · CKD-EPI

FDA DRUG SAFETY COMMUNICATION 2019 · EVOY DRUGS 2017 · BEERS 2023

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SECTION 5

Medications for addiction in older adults.

Greater importance of agent selection in older adults, under-appreciated in guidelines recommending universal MAT.

BUPRENORPHINE · NALTREXONE · METHADONE · ACAMPROSATE · DISULFIRAM · VARENICLINE

THE OLDER ADULT MAT FORMULARY

Agent choice, reasoned for the aging patient

AGENT	CLASS AND USE	RECOMMENDATION	NOTES
Buprenorphine	Partial mu agonist, OUD	PREFERRED	Ceiling on respiratory depression, no QT effect, no serotonin transporter activity. XR injectable simplifies regimens.
Naltrexone	Mu antagonist, AUD and select OUD	PREFERRED	Only MAT with an older adult RCT; well tolerated. Blocks analgesia, contraindicated with opioids and in liver disease.
Acamprosate	NMDA modulator, AUD	PREFERRED	No hepatic metabolism, no CYP interactions. Dose by renal function; avoid at CrCl below 30.
Methadone	Full mu agonist, OUD	CAUTION	Effective but QT prolongation and a long variable half life. Serial ECGs; reassess above 100 mg/day.
Disulfiram	ALDH inhibitor, AUD	AVOID	Rare fatal hepatotoxicity. Contraindicated in any liver disease and severe cardiac disease.

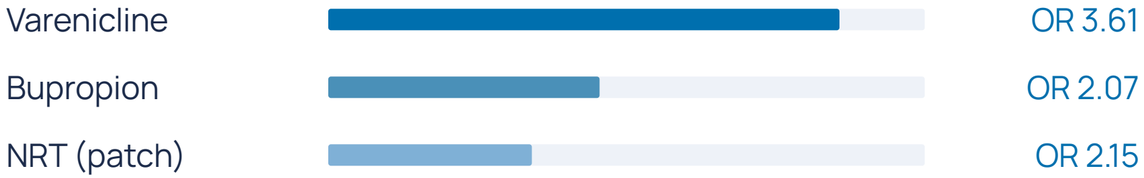
Oslin 1997; Krantz, Ann Intern Med 2009; Rieb, Can Geriatr J 2020; Lancet Healthy Longev 2023; Jophlin, Am J Gastroenterol 2024.

V.02 · VARENICLINE SAFETY

Varenicline boxed warning has been removed

The **EAGLES trial** (N = 8,144, incl. 4,116 with psychiatric disorders) found varenicline **did not significantly** increase neuropsychiatric adverse events vs placebo, and FDA subsequently removed the Boxed Warning.

CESSATION OR VS PLACEBO



IN ELDERLY MEDICARE BENEFICIARIES

No significant increase in AMI, stroke, or mortality with varenicline vs bupropion (Graham 2014).

DOSE

Renal dose adjust at **CrCl < 30 mL/min**.

CLINICAL BOTTOM LINE

In older adults with psychiatric comorbidity, **varenicline is both effective and well tolerated.**

ANTHENELLI LANCET 2016 · GRAHAM 2014 · FDA 2016 LABEL UPDATE

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SECTION 6

Key drug–drug interactions to monitor.

QTC · SEROTONIN · ACB · FALLS · HEPATIC · RENAL

VI.01 · THE PRESCRIBER'S SHORT LIST

Six commonly encountered patterns:

01 QTc stacking

HIGHEST

Methadone + antipsychotic + SSRI.

Additive ms push QTc past **500 ms** . Citalopram +8.5–18.5 ms; ziprasidone ~+15.9 ms.

Harrigan 2004 · Beach 2014

02 Serotonin syndrome

HIGH

MAOI + SSRI; tramadol, methadone + SSRI.

Hunter criteria **84%/97%** . Clonus distinguishes from delirium.

Dunkley QJM 2003

03 Anticholinergic burden

ACB ≥ 3 for ≥ 90 days.

Dementia OR: 1 → 2.18 · 2 → 2.71 · **3 → 3.27**.

Common hidden culprits: OTC diphenhydramine and doxylamine, oxybutynin, paroxetine, TCAs.

Boustani 2008 · Taylor-Rowan 2021 · Beers 2023

04 CNS-depressant falls

HIGH

Stacking doubles fall risk.

BZD OR 1.57 · AD 1.68 · AP 1.59. **≥2 CNS-actives: IDR 1.97.**

Woolcott 2009 · Thapa 1995

05 Hepatic impairment

Acamprosate is preferred; avoid **disulfiram** in any liver disease.

ACG Jophlin 2024

06 Renal impairment

Re-target lithium; dose-by-GFR.

Li trough **0.4–0.8 mEq/L** . Gabapentin · pregabalin · acamprosate · varenicline.

CKD-EPI · Beers 2023

WOOLCOTT 2009 · BOUSTANI 2008 · DUNKLEY 2003 · KRANTZ 2009 · JOPHLIN 2024

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SECTION 7

Practical considerations at the point of care.

Screening, monitoring,and tapering

SMAST-G · AUDIT · CKD-EPI · ACB · BEERS · STOPP/START

VII.01 · DOSING PRINCIPLE

Start LOW, go SLOW, but go all the way.

Initiate psychotropics at **25–50%** of the usual adult starting dose and titrate gradually, while still reaching therapeutic exposure. Steady state takes longer; plan for it.

SCREENING TOOLS

SMAST-G for alcohol (≥2 yes → problem). **AUDIT** : lower cutoffs in elderly: **≥5 men, ≥4 women**. **DAST-10**, **TAPS** for combined substances.

APPROPRIATENESS TOOLS

2023 AGS Beers Criteria, 2025 AGS alternatives · **STOPP/START v3** (190 criteria) · **Medication Appropriateness Index** · **AntiCholinergic Burden Scale**.

BLOW 1992 · VAN GILS 2021 · O'MAHONY 2023 · BOUSTANI 2008 · HANLON 1996

VII.02 · MONITORING & DEPRESCRIBING

Documentation and monitoring plan.

ROUTINE MONITORING

SYSTEM	TARGET / CADENCE
ECG / QTc	Baseline before any QTc-prolonging agent; flag threshold **500 ms**.
Hepatic (LFT)	Baseline & periodic for valproate, naltrexone. Disulfiram: **q10–14 days × 2 months**.
Renal (GFR)	CKD-EPI; dose-adjust lithium, gabapentin, acamprosate, varenicline.
Drug levels	Lithium trough **0.4–0.8** in elderly · free valproate given altered binding.

DEPRESCRIBING BENZODIAZEPINES

> Bruyère recommends deprescribing BZRAs in **all adults ≥65** , regardless of duration.

Suggested protocol: **25% dose reduction every 2 weeks** over **6–8 months** . Never abrupt in physically-dependent patients.

Bridge through Phase II agents. For patients on long-acting BZDs (clonazepam, diazepam), switch to **lorazepam, oxazepam, or temazepam** (glucuronidation, no active metabolites) to avoid accumulation during taper.

NON-PHARMACOLOGICAL ANCHOR

CBT-I is recommended by Beers and by deprescribing guidelines as first-line insomnia treatment in older adults.

POTTIE BRUYÈRE CAN FAM PHYSICIAN 2018 · CHEN ASAM JGIM 2025 · XIONG 2020

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SECTION 8

Guidelines and authoritative references.

BEERS · SAMHSA TIP 26 · ASAM 2020 · CANADIAN OUD · STOPP/START V3

Worthwhile desk references

2023 — **AGS Beers Criteria**
The reference standard for potentially inappropriate medications in adults 65 and older.

2023 — **APA Resource Document**
Substance use disorders in older adults: recognition, screening, and treatment.

2024 — **AFP, substance misuse**
A practical primary care approach to substance misuse in adults (Kowalchuk).

2023 — **STOPP/START v3**
190 criteria, a European complement emphasizing prescribing omissions.

2025 — **AGS Alternatives (Steinman)**
Companion to Beers; first line alternatives across 20 plus conditions. JAGS 2025.

2020 — **ASAM National Practice Guideline**
Opioid use disorder; all FDA approved medications should be available.

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