One Drug, Many Benefits: Reducing Polypharmacy Through Strategic Prescribing

Kentucky Medicaid Polypharmacy Initiative

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Depression is a significant and often underrecognized concern among older adults, with substantial implications for overall health, functional independence, and quality of life. Although depression is not an inevitable consequence of aging, its symptoms may be overlooked or attributed to normal aging, chronic medical conditions, grief, or cognitive decline. Untreated depression in older adults is associated with increased disability, impaired physical functioning, social isolation, reduced adherence to medical treatment, and greater healthcare utilization. It may also exacerbate existing chronic conditions and contribute to cognitive difficulties, further compromising an individual's ability to maintain independence and well-being.

Depression is common among older adults and often occurs alongside other conditions such as anxiety, sleep disturbance, appetite loss, and chronic pain. Choosing an antidepressant in this population often means finding one medication that can address several of these concerns at once. Selecting the right option can improve quality of life while reducing the need for multiple drugs. Careful attention is needed to balance benefits with potential risks such as sedation, falls, drug interactions, and age-related changes in drug response.

This newsletter highlights commonly recommended antidepressants for older adults—SSRIs, SNRIs, mirtazapine, and bupropion—and reviews their multipurpose uses, common side effects, and practical points to guide safe and effective care.

Pharmacokinetic Changes in Older Adults

Pharmacokinetics describes what the body does to a drug through absorption, distribution, metabolism and excretion. Aging can alter these processes with changes in body composition, organ function, presence of disease states, or other medications.

Figure 1: Summary of Drug Metabolism with Aging

Process	Change in Older Adults	Clinical Implications
Absorption	Decreased gastric acid production, slower gastric emptying, and reduced gastrointestinal motility	Usually minimal effects on the total amount of drug absorbed, but the onset of action may be delayed for some medications
Distribution	Decreased total body water and lean body mass; increased body fat; decreased serum albumin in some individuals	Water-soluble drugs may reach higher concentrations; fat-soluble drugs may have prolonged effects; highly protein-bound drugs may have increased free-drug concentrations when albumin is low
Metabolism	Reduced liver mass and hepatic blood flow in some older adults; decreased metabolism of certain medications	Reduced drug clearance and prolonged drug effects, particularly for some medications with extensive first-pass metabolism
Excretion	Decreased renal blood flow and glomerular filtration rate (GFR) in many older adult	Reduced drug elimination, increased risk of drug accumulation, and greater potential for toxicity

Pharmacodynamic Considerations & Side Effects

One of the most important factors to consider when choosing a new drug therapy for an elderly patient is the impact on anticholinergic effects[1]. These adverse effects include but are not limited to dry mouth, constipation, urinary retention, tachycardia, blurred vision, and confusion. Many of these adverse effects compound onto other conditions that are common in this specific patient population. One potentially severe concern is postural hypotension, or the sudden drop in blood pressure when transitioning from sitting to standing. In an already fall-susceptible patient population, this further increases the risk of falls and severe injury such as fracture. Tricyclic antidepressants (TCAs) were the first class of antidepressants, but the adverse effect profiles have pulled them out of favor.[11] Newer antidepressant drug classes like SSRIs (selective serotonin reuptake inhibitors) and SNRIs (serotonin norepinephrine reuptake inhibitors) have replaced TCAs as first-line options for depression. One exception that should be closely monitored is paroxetine. Although it is an SSRI and can be used to treat vasomotor symptoms (i.e. hot flashes), it should be avoided in older persons due to anticholinergic properties.

Clinical practice requires careful identification and management of high-risk adverse drug reactions (ADRs), guided by established geriatric criteria such as the AGS Beers Criteria[1] and STOPP/START[2]. Fall Risk Assessment Sedation and dizziness are the main contributors to falls and subsequent injury in older adults. Medications with strong H1 or alpha-1 blocking activity carry the highest risk and should only be used when sedation is clinically intended. Highly anticholinergic agents are discouraged due to their association with falls and confusion[1].

Figure 2: Comparative Fall and Sedation Risk Stratification

Risk Profile	Agent(s)	Primary Pharmacological Driver(s)
Lowest Risk	Bupropion (Wellbutrin)	Stimulating profile; no significant H1 or alpha-1 activity[3]
Low Risk	Escitalopram (Lexapro)	Minimal H1 antagonism; low anticholinergic burden[4]
Highest Risk	Mirtazapine (Remeron)	Potent central H1 antagonism causing pronounced sedation[5]

Specific Drug Interactions and Metabolic Concerns

Antidepressants must be reviewed for potential drug-drug interactions (DDI), especially via CYP enzyme inhibition. The STOPP/START criteria provide structured guidance for reviewing DDIs and general prescribing safety[2].

Figure 3: Key Metabolic and Interaction Risk Stratification

Safety Risk	Agent(s)	Clinical Action / Monitoring
Lowest Risk DDI	Escitalopram (Lexapro)	Preferred in patients on multiple medications[4]
Hyponatremia (SIADH)	Sertraline (Zoloft)	Monitor serum sodium at baseline and after dose changes[6]
Seizure Risk	Bupropion (Wellbutrin)	Contraindicated in patients with history of seizures or eating disorders[3]

Strategic Antidepressant Profiles

Selection should prioritize FDA-approved indications while leveraging secondary pharmacologic effects for comorbid conditions.

Figure 4: Summary of Primary Uses and Clinical Benefits

Agent/Drug Class	FDA Approved Indication	Key Clinical Benefit / Multipurpose Use
SSRIs	Escitalopram (Lexapro)	Preferred in patients on multiple medications[4]
SNRIs	Depression, Chronic Pain, Anxiety Disorders	Treats neuropathic or musculoskeletal pain[7],[8]
Mirtazapine (Remeron)	Bupropion (Wellbutrin)	Contraindicated in patients with history of seizures or eating disorders[3].
Bupropion (Wellbutrin)	Depression, Smoking Cessation, Seasonal Affective Disorder	Stimulating; avoids sedation, weight gain, sexual side effects[3]
Trazodone (Raldesy)	Depression	Off-label use for treating dementia with agitation/aggression or insomnia for sleep onset and maintenance

Agent-Specific Highlights

- SSRIs are generally first-line for depression and anxiety[4]. Escitalopram is preferred in patients with polypharmacy due to minimal DDI. Monitor for hyponatremia.
- SNRIs (e.g., duloxetine[7], venlafaxine XR[8]) treat depression concurrent with chronic pain. Monitor blood pressure due to norepinephrine effects
- Mirtazapine leverages H1 antagonism to improve sleep or appetite[5]. High fall risk; use when sedation or weight gain is therapeutic. It can also exacerbate hyponatremia/SIADH.
- Bupropion has instant-release, sustained-release, and extended-release formulations that are not therapeutically interchangeable. Monitor carefully for side effects when a patient has impaired liver or chronic kidney disease.
- Trazodone may require timing adjustments based on food. Patients should be monitored for drowsiness and hypotension. There is potential for CYP3A4 drug-drug interactions.

Conclusion

Effective treatment of depression is therefore an important component of comprehensive care for older people. Appropriate management can improve mood, daily functioning, quality of life, and engagement in social activities while potentially reducing the burden of coexisting medical conditions. However, pharmacologic treatment in older adults requires careful consideration due to age-related changes in drug metabolism and elimination, increased sensitivity to adverse effects, and the presence of multiple chronic conditions can increase the risk of medication-related harm. Collaboration with psychiatric specialists is essential for patients with complex conditions or medication regimens.

Polypharmacy further complicates treatment by increasing the potential for drug–drug interactions, adverse effects, and medication nonadherence. Consequently, treatment strategies that effectively address depression while minimizing medication burden are particularly valuable in this population. Optimizing antidepressant therapy, considering medications with established benefits for multiple coexisting indications when clinically appropriate, and regularly reviewing medication regimens may help balance therapeutic benefits with medication safety in older adults.

For suggested topics:

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