

# Recognizing and Treating Anxiety in the Elderly

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Anxiety in the elderly is often unrecognized and inadequately treated. Several factors complicate recognition and treatment, including concomitant medical illness, overlap with cognitive disorders, cohort effects, ageism, and comorbid depression. Although available data from controlled clinical trials are limited for anxiety patients in the geriatric age group, data from young adult studies and clinical experience indicate that pharmacologic treatments are safe and effective for anxious elderly patients. Age-related physiologic changes warrant modifications in dosing, including initial low doses increased in gradual increments. Education and psychotherapy are often recommended whether or not pharmacologic treatment is indicated.

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The thought of reaching old age probably elicits at least transient feelings of anxiety for most people. With age comes concerns about losses—loss of health, relationships, financial security, and mental faculties. Despite such worries and concerns, it is remarkable that relatively few elderly persons experience severe anxiety disorders. The impact of geriatric anxiety symptoms and disorders, however, is often unrecognized and inadequately treated.

As with depression of old age, geriatric anxiety is frequently disguised and presents with varied symptoms, particularly physical ones. A recent local effort to recruit community-dwelling elders for a study of “anxiety” was largely unsuccessful. Most potential volunteers did not perceive their difficulties as resulting from anxiety. Instead, they experienced palpitations or discouragement or worries about their physical conditions or safety. This anecdotal experience may well reflect the broader problem of recognition, both for patients themselves and their

health care providers. In this article, I describe factors complicating the recognition of geriatric anxiety and review some available therapies, both pharmacologic and nonpharmacologic.

## EPIDEMIOLOGY

Flint<sup>1</sup> reviewed data from random-sample community surveys in persons 60 years of age or older. Two age-group comparison studies<sup>2,3</sup> found overall prevalence of anxiety disorders to be lower in older compared with younger people living in the community. By contrast, the National Survey of Psychotherapeutic Drug Use<sup>4</sup> found total anxiety to be slightly higher in people age 65 years or older (10.2%) compared with all age groups combined (9.9%). However, the latter study included generalized anxiety disorder, which was frequent in the elderly sample and not measured in the other studies. Total anxiety rates vary considerably across studies and range from 0.7%<sup>5</sup> to 18.6%.<sup>6</sup> Several methodological issues contribute to such variability, including arbitrary case definition, hierarchical approach to diagnosis (i.e., patients with anxiety and another, higher level diagnosis are not counted), and varying survey methods (e.g., symptom elicitation, exclusion of institutionalized elderly).

Phobic disorder is the most common anxiety disorder for persons of all ages, including elderly persons, and the male-to-female ratio is 1:2. In fact, phobia is the second most common psychiatric disorder next to cognitive impairment in persons 65 years or older. The Guy's/Age Concern Survey<sup>7</sup> found a 10.0% prevalence of phobic disorder in elderly persons: agoraphobia was most common (7.8%), followed by simple phobia (2.1%) and social phobia (1.3%). Panic disorder and obsessive-compulsive disorder are less common in most surveys with less than a 1% prevalence for each.<sup>1</sup> By contrast, the prevalence of generalized

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anxiety disorder varies from 0.7% to 7.1%, and most cases begin before age 65 years.

### FACTORS COMPLICATING RECOGNITION OF GERIATRIC ANXIETY

#### Medical Illnesses

Most elderly people suffer from several chronic illnesses, especially arthritis, hypertension, and heart disease, and anxiety symptoms and disorders are frequent in the medically ill elderly. Although the prevalence of generalized anxiety disorder in medically ill elderly patients is lower than for young and middle-aged patients,<sup>8,9</sup> psychological reactions to the meaning and impact of the physical illness often cause worry and anxious symptoms. This phenomenon is further complicated by the fact that many anxiety symptoms are expressed as physical phenomena (Table 1), which may be mistakenly interpreted as resulting from an underlying organic illness.

Alternatively, physical illnesses may cause symptoms suggesting anxiety (e.g., dizziness, shortness of breath, palpitations; Table 2). For example, hypoglycemia, pheochromocytoma, and hyperthyroidism can cause trembling, tachycardia, or hyperexcitability. Silent myocardial infarction, pulmonary embolism, or stroke can lead to weakness, dizziness, respiratory distress, or diaphoresis. Another issue to consider is the overlap of physical symptoms with depression, which often occurs with anxiety in the elderly. Geriatric depression frequently has a "masked presentation," wherein the patient focuses on physical, rather than affective, complaints. Such patients also often display neutral moods but complain of constipation, back pain, or some other physical symptom.

#### Cognitive Disorders

In a study<sup>10</sup> of patients with mildly severe dementia and age-matched cognitively intact controls, significantly more anxiety was found among the patients: 16% had definite anxiety and 22% had possible anxiety. Alzheimer's disease, the most frequent cause of late-life dementia, afflicts at least 5% of people over age 65 years and accounts for the most striking rise in dementia incidence in the very old.<sup>11,12</sup> Anxiety and other psychological symptoms may occur in other forms of dementia, including vascular dementia.

Some degree of forgetfulness is considered a benign and normal aspect of aging. Pooled normative data from standard clinical memory tests indicate that the prevalence of age-associated memory impairment<sup>13</sup> is 41% for people aged 50 to 59 years, and 52% for those aged 60 to 69 years.<sup>14</sup> Many people experience worry and concern that these common age-related changes will progress to more severe forms of cognitive decline. Ironically, such worries may actually worsen objective memory test performance.<sup>15</sup> People with relatives who suffer from Alzhei-

**Table 1. Somatic Symptoms of Anxiety**

Tremor	Paresthesia
Body aches and pains	Nausea and vomiting
Fatigability	Frequent urination
Restlessness	Sweating
Palpitations	Facial flushing
Dizziness	Insomnia
Faintness	Dyspnea
Diaphoresis	

**Table 2. Some Medical Conditions Associated With Geriatric Anxiety**

Drug reactions
Stimulants
Antidepressants
Caffeine
Tobacco
Nonsteroidal antiinflammatory agents
Over-the-counter hypnotics
Withdrawal of central nervous system depressants
Alcohol
Barbiturates
Benzodiazepines
Physical illnesses
Endocrinologic disorders
Hyperthyroidism
Hyperparathyroidism
Hypoglycemia
Pheochromocytoma
Cerebral infarction
Neurologic conditions
Parkinson's disease
Epilepsy
Dementia
Infections
Influenza
Hepatitis
Encephalitis
Pneumonia
Cardiovascular disorders
Congestive heart failure
Myocardial infarction
Pulmonary embolism
Metabolic disturbances
Dehydration
Electrolyte imbalance
Other conditions
Constipation
Pain

mer's disease often express the greatest concerns, and, indeed, a family history of Alzheimer's disease may predict future cognitive decline.<sup>16</sup> Anxiety and memory complaints associated with aging may also be the first indication of a progressive cognitive decline. Early recognition will facilitate intervention and future planning.

#### Cohort Effects and Ageism

Today's cohort of elderly persons grew up in an era when mental health treatment was considered a stigma; they comprise a generation that tends to view psychiatrists and psychiatric treatments with suspicion. Many endorse the view that psychiatrists are reserved for "crazy people" only. Clinician biases may further complicate the problem.

Ageism or age-related prejudice is a reality of our society, and studies have shown that psychiatrists are not immune to such attitudes. The now classic Ford and Sbordone<sup>17</sup> study found that psychiatrists view elderly patients as less likely to respond to treatment than their younger counterparts. Negative attitudes may influence clinical judgment and decision making and lead to improper treatment. Ageism sometimes stems from the clinician's own fears of death and frustration or lack of knowledge about assessing and treating elderly patients.

### **Anxiety and Depression Comorbidity**

Anxiety often coexists with depression. Although the relationship is complex and controversial,<sup>18</sup> it is clear that depressive and anxious symptoms overlap in many older patients. In the Guy's/Age Concern Survey, up to 39% of phobic elderly patients experienced depression, compared with only 11% of nonphobic elderly.<sup>7</sup> In addition, there was a correlation between severity of generalized anxiety disorder and depression. Alexopoulos<sup>19</sup> found a 38% prevalence of anxiety disorders in elderly outpatients with major depression. Such prevalent comorbidity has implications regarding recognition and treatment. In particular, clinicians need to focus on treating anxiety symptoms in elderly patients with depression.

### **Age at Onset**

Most cases of agoraphobia in the elderly seem to begin late in life.<sup>7,20</sup> Because phobic disorders in the elderly are so strongly associated with depression, late-onset agoraphobia may arise, in many situations, secondary to a depression.<sup>1</sup> The clinician, however, should keep in mind that many of the fears of an elderly person are realistic. A frail elderly woman who is concerned about neighborhood crime may become housebound after learning that other local elders have become robbery victims.

Obsessive-compulsive disorder (OCD) usually begins early in life but does persist into old age.<sup>21</sup> It is of interest that the prevalence of OCD among institutionalized women is higher than among women in the community.<sup>3</sup> The high rate of dementia in nursing homes suggests that some of these patients may be experiencing obsessional symptoms secondary to a dementing illness. Clearly, new onset of panic disorder or OCD late in life should alert the clinician to the possibility of an underlying organic cause.

## **AGE-RELATED CHANGES AFFECTING DRUG DOSAGE**

### **Age-Related Changes Affecting Drug Actions**

Numerous physiologic and related changes will influence drug actions in old age.<sup>22</sup> Modest hypertrophy of the normal aging heart and diminished peripheral vascular resistance lead to reduced ventricular compliance and cardiac output, causing reduced blood flow to the brain, kid-

neys, liver, and muscles. Such changes contribute to pharmacokinetic alterations associated with aging. The heart's intrinsic rate slows, which may increase the risk for arrhythmias. Reduced  $\beta$ - and possibly  $\alpha_2$ -receptor sensitivity also occurs, which partly explains diminished baroreceptor reflex responses to acute arterial pressure changes. Thus, the heart has reduced cardioacceleration in response to hypotension and reduced deceleration in response to acute hypertension. Such changes contribute to sensitivity to drug-induced hypotension. Respiratory system changes include diminished cough, laryngeal reflexes, and central and peripheral responses to hypoxia and hypercapnia. Such changes result in sensitivity to suppressed respiratory drive from sedatives.

Xerostomia or dry mouth and sensitivity to anticholinergic effects are more likely with aging because of decreased oral mucosa and parotid gland secretion. This also increases the risk of dental caries and periodontal disease. Gastric acid secretion increases, perhaps increasing the risk of gastritis. Use of antacids is increased, which decreases absorption of some psychotropics. The alternative use of histamine Type 2 ( $H_2$ ) receptor antagonists (e.g., cimetidine) may reduce other drug metabolism. Complaints of constipation are common and may result from laxative misuse, inadequate fluid intake, or inadequate dietary fiber. Anticholinergic drug effects will worsen such symptoms. Relevant genitourinary changes include prostatic hypertrophy, which may lead to incontinence or retention, particularly with anticholinergic agents. Sedatives and adrenergic drugs can exacerbate incontinence.

Volume of drug distribution changes with age. Psychotropic drugs, except for lithium, are primarily lipid soluble and protein bound. Aging results in a relative decrease in total body water, reduction in lean body mass, and increase in body fat. With a larger volume of distribution, drugs take longer to reach steady-state levels, and plasma levels are lower at any given dose. If liver disease is present, protein synthesis may be impaired, causing decreased protein-binding in plasma. The resultant unbound active drug may have greater clinical effect at any given plasma level. Reduced hepatic blood flow and function diminishes the metabolism of benzodiazepines (e.g., chloridiazepoxide, diazepam) undergoing phase 1 biotransformation (i.e., hydroxylation). Phase 2 enzymes, which lead to conjugation of such drugs as oxazepam, lorazepam, or temazepam, are less influenced by age. Therefore, drugs metabolized through phase 2 enzymes are preferred for elderly patients.

Glomerular filtration rate declines with age so that elderly people may be more sensitive to effects from drugs requiring kidney clearance. Most psychotropic drugs do not require kidney clearance, but lithium, amantadine, atenolol, and to some extent, venlafaxine are cleared by the kidney. Digoxin may cause central nervous system toxicity and also undergoes renal clearance.

## Polypharmacy

The multiple physical illnesses that accompany aging often require medical treatments, and many older people receive several medications. The coadministration often results in drug interactions that worsen side effects. The various potential combinations of drugs and diseases are so numerous that systematic study is difficult; thus, conclusive data to guide clinicians in most circumstances are unavailable. Generally, clinical guidelines are used that generalize from data derived from patient populations that only partially resemble the clinical situation in question. Potential drug-drug interactions from medications commonly used in geriatric patients are numerous. For example, lithium in combination with a thiazide diuretic or nonsteroidal antiinflammatory drug will lead to increased plasma lithium levels and possible toxicity. Propranolol in combination with an antipsychotic drug could cause hypotension. Elderly patients are often confused about their many medications.<sup>23</sup> Educational programs that target health care providers appear to reduce polypharmacy.<sup>24</sup>

## PHARMACOLOGIC TREATMENTS

### Benzodiazepines

Benzodiazepines clearly have been the most frequently prescribed medicines for geriatric anxiety. In fact, epidemiologic data suggest overuse in the general elderly population.<sup>25</sup> Long-term benzodiazepine use has been particularly common in nursing homes, where surveys from the last decade indicate that nearly 80% of institutionalized sedative/hypnotic users received these drugs regularly.<sup>26</sup>

The elimination half-lives of benzodiazepines are indeed variable in elderly persons. The drugs can be classified according to half-life duration as long ( $\geq 20$  hours, e.g., clonazepam, diazepam, flurazepam, quazepam), intermediate (10–20 hours, e.g., alprazolam, lorazepam, temazepam), short (5–10 hours, e.g., oxazepam), and ultrashort ( $< 5$  hours, e.g., triazolam, midazolam). When agents with ultrashort, short and intermediate half-lives are used as sedatives, their effects do not carry over to the next day. Ultrashort benzodiazepines are generally used to treat insomnia rather than daytime anxiety and may cause rebound insomnia after abrupt discontinuation.<sup>27</sup> Adverse behavioral reactions from triazolam include confusion, agitation, and hallucinations, and safety concerns have led to its ban in several European countries including the United Kingdom.<sup>25</sup> Use of long-acting benzodiazepines confers a higher risk for hip fracture compared with use of short-acting benzodiazepines.<sup>28</sup>

Choosing a specific benzodiazepine depends on the patient's particular problems and the drug's particular side effects. Unfortunately, few clinical trials of benzodiazepines have included elderly anxious patients so that guidelines are based on clinical experience. In general, low-hepatic extraction compounds metabolized by conju-

gation (e.g., temazepam, oxazepam, lorazepam) tend not to contribute to pharmacokinetic drug interactions and are preferred for elderly patients. A potential disadvantage when treating insomnia is their slow oral absorption; however, the patient can be instructed to take the medicine an hour before bedtime. Some clinicians argue that the amnestic actions of lorazepam make it unsuitable for chronic use in older patients already concerned about memory impairment. Lorazepam has been used effectively in its intravenous form for patients requiring sedation during magnetic resonance imaging.

Alprazolam has been found to be more effective than placebo in the treatment of anxiety in depressed and anxious patients age 60 years and older, immediately after coronary bypass surgery.<sup>29</sup> Although one study found a relative absence of effects of alprazolam on cognitive and psychomotor functions in healthy elderly,<sup>30</sup> medically ill elderly patients may be more sensitive to such effects. Benzodiazepines (e.g., diazepam) that are metabolized in the hepatic microsomal enzyme system are best avoided in older patients. Such drugs and their active metabolites accumulate, have extremely long elimination half-lives, and cause a variety of untoward effects including ataxia, confusion, and worsening of depression. One study of nursing home residents found significant improvement in memory and cognitive functioning and no increase in anxiety, agitation, or sleeplessness when benzodiazepines were discontinued.<sup>31</sup>

### Other Anxiolytics and Sedative-Hypnotics

**Buspirone.** In a controlled, double-blind study of 40 anxious patients aged 65 years or older, buspirone was a significantly more effective anxiolytic than placebo.<sup>32</sup> The drug was also well tolerated by elderly patients receiving treatment for other chronic medical conditions. Buspirone has a relatively short half-life and thus requires multiple daily dosing (up to four times per day). In elderly patients, 20 to 40 mg/day is often an effective dose. Onset of action occurs in 1 to 3 weeks. Buspirone appears to have fewer side effects than other anxiolytics. There are no withdrawal symptoms, significant motor impairment, or cognitive effects.<sup>33</sup> Moreover, interaction with central nervous system depressants is negligible, and it has minimal abuse potential. Potential side effects reported in elderly patients include nausea, headache, dizziness, and fatigue. Case reports<sup>34,35</sup> and one open trial<sup>36</sup> have indicated its usefulness for agitated and possibly anxious demented patients. Buspirone is ineffective for panic attacks but useful for generalized anxiety disorder.

**$\beta$ -Adrenergic receptor antagonists.**  $\beta$ -Blockers do not diminish subjective, inner anxiety, but rather reduce autonomic concomitants of anxiety such as tachycardia and diaphoresis. Low doses of 5 to 10 mg of propranolol may be effective for elderly patients. These drugs should be avoided in elderly patients with cardiovascular disease

(e.g., heart failure, sinus bradycardia) or asthma. Potential side effects include falls and confusion.

**Chloral hydrate.** Chloral derivatives such as chloral hydrate have an onset of action of approximately 15 minutes and a half-life of about 8 hours, and they produce effective sedation in many situations. For elderly patients, a dose of only 250 mg is usually sufficient, but doses as high as 1.5 grams may be necessary. Disadvantages include gastric side effects such as nausea and flatulence and potential drug-drug interactions. Adequate studies comparing chloral hydrate with benzodiazepines have not been performed in elderly subjects.

**Alcohol.** Alcohol has been recommended for elderly persons as an aid for sleep or as an anxiolytic. However, elderly patients are at risk for abuse<sup>37</sup>; an estimated 15% experience alcohol problems. Its potential for drug interactions, diuretic effects, and other associated problems make it an anxiolytic with a relatively high risk-benefit ratio.

**Antihistamines.** Antihistamines are sometimes used to treat insomnia or anxiety in elderly patients. They are less effective than benzodiazepines, and their anticholinergic effects argue against their use for such symptoms, particularly for elderly patients who suffer from cognitive impairment or may be sensitive to anticholinergic effects.

**Barbiturates.** Barbiturates are inexpensive and effective sedatives but have numerous disadvantages when compared with other agents. Barbiturates have a high risk for physiologic dependence and serious withdrawal effects. They can cause cognitive impairment and ataxia, and overdose can be fatal. Despite such disadvantages, some clinicians still prescribe them for elderly persons.

### Antidepressant Drugs

Data from controlled trials of antidepressant medications for treating comorbid geriatric anxiety and depression are limited. Clinical experience and conclusions extrapolated from data of related populations, however, suggest that the initial choice of an antidepressant agent would be one that provides relative sedative and anxiolytic effects. Because of their tendency to stimulate patients, serotonin selective reuptake inhibitors (SSRIs) may not be the initial choice. Paroxetine may be more sedating than the other SSRIs. A recent analysis of baseline clinical predictors of antidepressant response in a large (671 patients) double-blind, placebo-controlled fluoxetine trial for geriatric major depression found that agitated depressed patients responded as well as those without agitation.<sup>38</sup> Studies of young adults also suggest that agitated depressed patients respond favorably to fluoxetine.<sup>39</sup>

Most of the older cyclic antidepressants that offer greater sedation also have greater anticholinergic and adrenergic properties that cause postural hypotension. Drugs such as amitriptyline or imipramine, therefore, are generally not recommended for elderly patients. Trazodone in low doses (25–50 mg/day) is sometimes used as a sedative

or anxiolytic for elderly patients, but the side effect of postural hypotension may limit its use. The newer phenylpiperazine compound and 5-HT<sub>2</sub> receptor antagonist, nefazodone, offers promise as a useful antidepressant for depressed elderly patients who have concomitant anxiety symptoms. It has acceptable levels of daytime sedation and minimal anticholinergic and other side effects. A recent study comparing nefazodone to imipramine in elderly persons found that imipramine but not nefazodone had a detrimental effect on driving and psychomotor performance.<sup>40</sup> Nefazodone does, however, inhibit P450 isoenzymes and has the potential to interact with terfenadine, astemizole, and antihypertensives. Coadministration of nefazodone and alprazolam will increase the plasma alprazolam level.

### NONPHARMACOLOGIC APPROACHES

Psychotherapeutic interventions for anxiety disorders are much better defined for younger populations than for older ones.<sup>41</sup> Investigation of cognitive-behavioral and psychodynamic group therapy for elderly depressed patients indicates that both forms of therapy achieve lower levels of anxiety and depression.<sup>42</sup> One meta-analysis identified 17 interventional studies for geriatric depression wherein the magnitude of effect for psychotherapy compared with no treatment was similar to that of studies comparing antidepressant medication with placebo.<sup>43</sup>

Because of their reluctance to acknowledge psychological problems, many elderly persons are more accepting of treatments presented as medical ones. To this end, education about the biological basis of anxiety may increase compliance. Anxiety about age-related memory loss also may improve with education. For example, a 50-year-old woman may worry that her forgetfulness will progress to the senility that her own mother developed at age 80 years. Knowledge that age at dementia onset within families is relatively consistent for familial Alzheimer's disease and that her mild memory complaints are not likely to progress may diminish her worries. Without such worries, her memory performance may even improve.

Elderly patients with concomitant physical illness are often sensitive to drug side effects and may not tolerate psychotropic medications. Moreover, many patients receiving psychotropic medications also have psychosocial issues requiring attention. Thus, many elderly anxious patients require some form of psychotherapy or education. No systematic data support the idea that elderly patients are too old for psychological change. Most experts agree that, provided cognitive function is intact, elderly patients respond well to psychotherapeutic interventions.

### INTERVENTION STRATEGIES

Despite the lack of adequate data on treatment of geriatric anxiety, clinicians can evaluate and treat these often

complicated patients with a conservative but rational approach. The following guidelines aim to provide a systematic approach that is based on the limited available controlled data and clinical experience.

- Careful psychiatric assessment is critical to identifying the presence or absence of standard diagnostic criteria for psychiatric disorders as well as physical symptoms of anxiety.
- A comprehensive history, physical examination, and appropriate laboratory tests will assist in identifying underlying physical illnesses that may be causing anxiety symptoms or may complicate their pharmacologic management.
- Collaborating with medical colleagues is particularly helpful when treating frail elderly patients with psychotropic medications.
- Minimizing polypharmacy may improve or even remove symptoms. Medication adjustments are most effective when simplified (i.e., one change at a time), which helps clarify whether a specific complaint results from a medication side effect or an underlying illness.
- Recognizing that anxiety often accompanies cognitive impairment will facilitate early recognition of complaints that may herald progressive cognitive decline. Many people who worry about age-related memory complaints improve with education and reassurance, provided that neuropsychological assessment proves normal.
- Choosing specific medications based on their side effect profile is a useful strategy. For example, an anxious depressed patient suffering from insomnia might respond well initially to a sedating antidepressant such as nefazodone. Sensitivity to anticholinergic effects can be minimized by using an SSRI rather than a tricyclic. Benzodiazepines metabolized by phase 2 enzymes (e.g., oxazepam, lorazepam, temazepam) are less influenced by age and therefore preferred to those undergoing phase 1 metabolism.
- Starting low and going slow is recommended to identify the optimal dosage for a particular patient without causing intolerable side effects. Age-related physiologic changes result in a wide range of dosages that will cause therapeutic or toxic effects in the elderly. Patients may respond to low or high daily dosages.
- Considering an alternate drug regimen may be necessary for patients who fail to respond to adequate doses of an initial medication. Because of the limited treatment data available on elderly anxious patients,

drug choices are often based on prior clinical experience rather than proven response predictors.

- Using nonpharmacologic approaches is essential in many situations. Because of sensitivity to side effects, physically ill geriatric patients often do not tolerate medications. In such situations, available nonpharmacologic approaches are preferred. Attention to psychological factors and family caregivers often facilitates positive effects of pharmacologic interventions.

*Drug names:* alprazolam (Xanax), amantadine (Symmetrel, Symadine), amitriptyline (Elavil and others), astemizole (Hismanal), atenolol (Tenormin), buspirone (BuSpar), chloral hydrate (Noctec), chlordiazepoxide (Librium and others), cimetidine (Tagamet), clonazepam (Klonopin), diazepam (Valium and others), digoxin (Lanoxin), fluoxetine (Prozac), flurazepam (Dalmane and others), imipramine (Tofranil and others), lorazepam (Ativan and others), midazolam (Versed), nefazodone (Serzone), oxazepam (Serax and others), paroxetine (Paxil), propranolol (Inderal and others), quazepam (Doral), temazepam (Restoril and others), terfenadine (Seldane), trazodone (Desyrel and others), triazolam (Halcion), venlafaxine (Effexor).

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