Consensus Statement on Depression in the Elderly

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A consensus meeting of experts in the treatment of depression was held with the aim of providing primary care clinicians with a better understanding of depression in the elderly and to guide clinical practice with recommendations on management issues. The consensus statement is based on consideration of the review articles published in this supplement and the scientific literature relevant to these articles. The consensus statement identifies diagnostic indicators for depression in the elderly and an appropriate management strategy. Selective serotonin reuptake inhibitors are recommended as the antidepressants of first choice in the elderly, including those with severe depression, the very old, and hospitalized patients. Psychosocial support and psychotherapy, where available, are other components of a comprehensive strategy. Early intervention is important in late-life depression, and the more pervasive, persistent, or severe the depression, the greater is the need to start drug therapy without delay.
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Late-life depression is chronic and disabling and is an important risk factor for elderly suicide. Yet, older people and many physicians share the misconception that depression is a normal feature of aging. This means that older adults with depressive symptoms are even less likely to seek medical help than are younger depressed adults, and, when they do consult a physician, they are less likely to receive appropriate treatment because their depression is seen as explicable. With the increase in the proportion of the elderly in the population, late-life depression will continue to increase in importance as a public health problem.

A consensus development meeting brought together a panel of experts on the treatment of depression and the management of depression in the elderly. Our objective was to consider evidence on issues concerning late-life depression to provide clinicians with a better understanding of depression in the elderly and guide clinical practice with recommendations on management issues. The review articles in this supplement were produced for discussion by the consensus group. Key issues were identified for further debate and discussion to arrive at a consensus view. A consensus statement was produced by the group and reviewed by the external panel, and this article presents the final statement approved by the contributors.

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DEFINING THE ELDERLY POPULATION

Late-life depression can refer to a population ranging in age from 60 to 85 or more years. What is an appropriate definition of *elderly*? As a group, we were unable to endorse a single age, whether 60, 65, or 70 years, to define when an adult can be considered elderly. Apart from physiologic issues, there are many confounding factors, such as physical illness and medication. One approach, accepted in the United States, is to define the elderly by age of retirement, an approach that is endorsed by the World Health Organization. Although it may be considered arbitrary, this definition has utility because the period between 60 and 65 years marks a social transition for most people. Similarly, we can delineate a biological transition, which is most likely to occur between 75 and 80 years. During this period, meaningful changes start to occur in neurotransmitters in the central nervous system and in drug metabolism due to delayed and inefficient hepatic and renal clearance. Adults over the age of 80 years are definitely old in terms of physiologic changes. The "young-old" versus the "old-old" provides a useful conceptual dichotomy.

PREVALENCE OF DEPRESSION IN THE ELDERLY

The prevalence of depression in the elderly has attracted extensive research effort and yielded a wide range of estimates, depending on the diagnostic criteria, the method of detecting depression, the experience and expertise of the interviewers, and, most importantly, the characteristics of the population sample. Some epidemiologic

studies had a full sample of the elderly, others stopped at the age of 80 years, but few included the very old (aged over 85 years).[1,2]

Major depression appears to be less common in the elderly than in younger adults. DSM diagnostic criteria require either depressed mood or loss of interest, but undue emphasis tends to be placed on depressed mood, which is less prominent in the elderly than are other symptoms of major depression. It is possible that societal and ethnic constraints make it as hard to endorse depressed mood in the elderly as it is in children and in younger adults in some ethnic groups. Reliance on depressed mood as the diagnostic criterion has contributed to the underrecognition of late-life depression by physicians and an underestimation of the size of the problem posed by depression in the elderly.

The prevalence of major depression in adults aged over 65 years is around 2%,[3] but the prevalence of subsyndromal depression, depressive symptoms that do not meet full diagnostic criteria, ranges from 15% to 30%.[4,5] Depression is increasingly recognized as a spectrum disorder in the elderly.[6] In the elderly, depressive symptoms appear to increase with increasing age over 65 years. The positive association with age appears to be related to motivation symptoms (loss of interest, poor concentration, and lack of enjoyment), which increase with declining cognitive function.[7]

DISTINGUISHING LATE-LIFE DEPRESSION FROM DEPRESSION IN YOUNGER ADULTS

The dichotomy between early- and late-onset depression is less helpful to clinicians than whether, for example, there is a vascular component to depression in the older patient. Some types of depression are more prevalent among the elderly, for example, vascular depression and depression associated with Parkinson's disease or after a stroke. Late-life depression is essentially heterogeneous. When depression is associated with vascular disorders, it tends to be chronic and recurring and carry a poor prognosis.[8–10] Other forms of depression in the elderly are more similar to depression earlier in life. These types of depression, when recognized, are responsive to treatment.

The underlying pattern of risk factors for different forms of depression varies with increasing age in the elderly; for example, the risk of physical illness and bereavement increases with age over 60 years. The change in the pattern of risk factors may affect prognosis and treatment outcome, but this hypothesis requires further research.

From a public health perspective, chronic medical illness and functional impairment in later life overwhelm the effect of other risk factors for depression, a finding that is consistent across countries and cultures. Comorbidity with physical illness such as cardiovascular disease or other psychiatric symptoms such as anxiety are defining characteristics of late-life depression,[11] and the presence of one or more medical illnesses is a negative prognostic factor in treatment studies.[12,13]

Subsyndromal Depression

Subsyndromal depression occurs frequently in the elderly,[4,5] and it is a clinical problem particularly pertinent to this population. Convincing evidence suggests that the elderly experience a fluctuating course of depression. Elderly depressed adults spend most of their time in periods of subsyndromal depression, whether minor depression, dysthymia, demoralization, or simply what has been termed a "persistent miserable syndrome."[14] Whatever the classification, however, the prognosis for subsyndromal depression is poor in some 50% of cases.[15–17] Periods of major depression are less frequent, but the rate is likely to have been underestimated owing to an insufficiently sensitive measure of dysfunction in the elderly.

We must not underestimate the suffering associated with subsyndromal depression in the elderly. It causes psychosocial distress and affects functional ability and quality of life to no less an extent than syndromal depression.[18,19] Not only is the general health of the elderly impaired by subsyndromal depression, but it may also predict worsening depression.[20] One recent report from the Longitudinal Aging Study Amsterdam provides good evidence of the impact on increasing mortality.[21]

Similarly, we must not underestimate the burden imposed by depressive symptoms that do not meet full diagnostic criteria.[4,6] Given the prevalence of these symptoms in the elderly, the morbidity associated with them outstrips the morbidity associated with major depression. Subsyndromal depression identifies a substantial at-risk population in late-life depression that imposes a substantial health care burden.

RECOGNIZING AND DIAGNOSING DEPRESSION IN THE ELDERLY

Diagnostic criteria for depression are more difficult to apply in the elderly than in younger adults, particularly in the very old (aged over 85 years) or those with concomitant physical illness.[22] DSM diagnostic criteria require the subject to show clinically significant impairment in social, occupational, or some other form of functional ability and to endorse depressed mood.[23] Establishing a diagnosis of depression in the elderly using DSM-IV diagnostic criteria is compromised by the problem of measuring functional impairment in subjects already impaired by concomitant medical illness and the difficulty in eliciting a report of depressed mood. Strict diagnostic criteria may be unhelpful in identifying clinically meaningful depression in older people, but, although we may need to modify items of existing diagnostic criteria to apply to the elderly, no justification exists for creating a specific diagnostic

system for depression in the elderly. Late-life depression is not a specific disorder.

In our view, the clinical diagnosis of depression in the elderly should not depend primarily on the spontaneous expression or endorsement of depressed mood. Depressed mood can be elicited by a sensitive interviewer. It demands taking the time to talk to older people about what they are feeling and taking the care to frame questions in a language and manner that are appropriate. There are alternative ways in which the experience of depression is expressed in the elderly, and these may be more common than the spontaneous expression or endorsement of depressed mood. They are the presence of anxiety, irritability, and a change in functional ability, either a loss of capacity to enjoy life or a loss of interest in usual activities. In the elderly, these are the more appropriate diagnostic indicators of depression.

The "atypical" clinical presentation of depression in the elderly as anxiety or somatic symptoms[24,25] can be misleading for the clinician and mask an underlying mood disorder. Careful psychopathologic examination is needed to determine whether depressive symptoms are recognizable beyond the anxiety or somatic symptoms. As an incentive to the recognition and diagnosis of depression in the elderly, the primary care physician must appreciate that late-life depression is an eminently treatable disorder. As the starting point for identifying depression in the elderly, we recommend that the physician ask general questions, such as "Are you getting out as much as you used to?" or "Are you enjoying life as much as you used to?" The physician will need the appropriate skills to ask elderly people how they are feeling, in a clinically relevant way, and also the time to ask more than a single question. We recognize, however, that the time available for primary care physicians to spend with their patients is decreasing. The average consultation time is currently 9 minutes in the United Kingdom and no more than 6 to 7 minutes in the United States.[26]

Brief screening questionnaires have been developed to help detect depression in the elderly and the 15-item version of the Geriatric Depression Scale is recommended by the Royal College of General Practitioners for use in the over-75 health check in the United Kingdom.[27] Trained practice nurses can carry out this health check. In nursing homes, depression in the elderly is often more likely to be detected by the experienced geriatric nurses who are 24-hour caregivers and, therefore, most sensitive to the changes in functional ability of the elderly residents.[14] It is likely that screening will help improve recognition rates.

Pseudodementia

Apparently reversible cognitive impairment is sometimes seen in late-life depression. This "pseudodementia" is clinically important since it may result in failure to recognize and treat either depression or the underlying dementia. The cognitive impairment, however, is a marker of high risk of subsequent dementia, and many of these patients will experience more clear-cut irreversible dementia over the next 2 to 5 years.[28] The use of the diagnostic category of pseudodementia rather than recognizing the coexistence of dementia and depression is increasingly criticized.

We support the view that pseudodementia is an inappropriate term and recommend that it should not be used. When depression and dementia occur together, both diagnoses should be made.

Neuroimaging techniques (such as nuclear magnetic resonance or computed tomography) should be implemented at a diagnostic level, if possible, to differentiate clinical or subsyndromal depressive states from primary or secondary dementing processes. More pronounced abnormalities at frontal and/or other brain regions would suggest the need for subsequent reevaluation of the diagnosis with closer clinical follow-up.

Bereavement Depression

Life events such as divorce, loss of employment, or the development of a physical handicap are accepted by DSM diagnostic criteria as stressors precipitating a major depressive disorder,[23] whereas bereavement disbars a diagnosis of major depression.

One of the most common underlying conditions for major depression in later life is the loss of a loved one. When depression is associated with bereavement, it is disabling, chronic, and/or recurring,[29,30] and we feel strongly that it should be recognized as a major depressive episode and treated appropriately. Combined treatment with antidepressant medication and psychotherapy is reported in one study[31] to produce the best outcome. The existence of an explanation for the depression—bereavement—is not a reason to deny diagnosis or treatment.

MANAGEMENT GUIDELINES FOR LATE-LIFE DEPRESSION

The social context in which depressive symptoms arise in the elderly is important, since it can influence treatment outcome. Whether the patient has depressive symptoms that meet diagnostic criteria for major depression or is suffering from a subsyndromal condition, depression causes serious dysfunction. The physician should discuss the social context and individual stressors that give rise to depression and institute a management program that takes account of the context of late-life depression.

Any comprehensive management program should include social and psychological approaches in addition to appropriate drug therapy. Physicians must maintain a psychotherapeutic relationship with their patients and understand the importance of their role in supporting patients and their families throughout the continuum of depression and treatment into the longer term. We believe there are

certain minimum requirements for good clinical practice. The physician should provide their elderly patients with psychological support, which extends from exploring background problems to educating patients and their families about depressive disorders and the different treatment options. During the acute phase of treatment, the physician can encourage patients to continue and complete an adequate course of pharmacotherapy by maintaining an appropriate level of contact with them, aiming for 5 follow-up visits rather than 3 over the first 10 weeks. Again, it is important for the physician to gain the support of patients' families in encouraging compliance.

Psychotherapy in Late-Life Depression

There is clinical evidence that cognitive-behavioral therapy (CBT) and interpersonal therapy (IPT) are effective forms of psychotherapy in elderly adults with major depression.[32–34] Although further data on nonpharmacologic treatments are needed, recent placebo-controlled evidence suggests that a combination of IPT and medication is superior to medication alone in preventing the recurrence of depression in the elderly and that IPT may help patient compliance with antidepressant drug therapy.[34]

Independent of the evidence for the effectiveness of psychotherapy in the elderly, there is the issue of the accessibility of treatment. Both CBT and IPT are sophisticated techniques, and primary care physicians and their support staff generally lack the training to apply them. Specialist services within health care systems vary in their capacity to provide personnel trained in these psychological techniques, and currently these services are not readily or widely available to the primary care physician. This lack of provision could be addressed with training programs for therapists to work in groups.

When we consider subsyndromal depression, we note that there have been some studies of nonpharmacologic treatment of minor depression in the elderly in nursing home and assisted care settings. However, there is a lack of controlled studies of different forms of psychotherapy, particularly in elderly adults living independently in the community.

Drug Therapy in Late-Life Depression

Antidepressants are as effective in older patients with depression as they are in younger depressed adults. Double-blind, placebo-controlled data from clinical trials in major depression, including subjects aged more than 85 years, support the efficacy of selective serotonin reuptake inhibitors (SSRIs) in late-life depression.[35] Older double-blind data, largely derived from clinical trials of nortriptyline, also imply efficacy for tricyclic antidepressants (TCAs) in older subjects, although studies of long-term treatment with nortriptyline showed a lack of efficacy compared with placebo.[36] More recent data support the efficacy of nortriptyline in long-term treatment.[36,37] Some clinical experience supports the efficacy of newer antidepressants in late-life depression (Table 1), but we recognize that elderly adults are largely an understudied population and that more data are needed to define the potential role of these newer agents in general practice. Over the last decade or so, it has been normal practice to establish the safety of newer antidepressants in the elderly prior to licensing. The elderly are prone to receive polypharmacy, and, therefore, careful scrutiny is needed of the concomitant medication for potential effects on physical and psychiatric state. For any newly prescribed medications, it is important to make a physical and laboratory assessment (such as thyroid and anemia measurements), as well as considering potential depressogenic effects.

Tolerability is an important determinant of choice of antidepressant therapy in late-life depression because the elderly have higher sensitivity to the side effects of treatment than younger adults. Physicians need to be aware of secondary effects, most notably with TCAs, to improve adherence with treatment in the medium and long term.[38] We recognize that the side effects of TCAs, in particular anticholinergic effects, often make it difficult to achieve a therapeutic dose of antidepressant therapy in the elderly. Also, clinicians have justifiable concerns about using and increasing the dose of TCAs because of potential cardiac toxicity.[39] SSRIs have a far more favorable side effect profile than TCAs, as meta-analyses of comparator data have shown.[40–43] All these meta-analyses show the same general effect, some statistically significant, and others not. There may be differential effects in older patients, such as hyponatremia or extrapyramidal symptoms, but these occur infrequently.[44]

Treatment that is well tolerated encourages patient compliance, an important consideration when treatment is prolonged to prevent relapse and recurrence of depressive episodes. Compliance may be compromised when the patient has to take multiple drugs for coexisting medical conditions. The physician must ask about concomitant drug therapy and document what the patient is taking. The aim is to simplify treatment by prescribing antidepressant therapy with a simple once-daily regimen and, when anxiety is a component of the clinical picture, selecting therapy that is effective against symptoms of both depression and anxiety.

We propose well-tolerated effective treatments such as SSRIs as the antidepressant therapy of first choice in late-life depression. There is no qualification to our recommendation: it applies equally to the elderly patient with severe depression and the elderly depressed patient in hospital. It is essential for the physician to remember that *elderly* denotes a heterogeneous population and that treatment should be individualized. Although they share a common mode of action, SSRIs are a structurally diverse class with different pharmacokinetic profiles that underline differences in their clinical profiles (see Table 1).[45,46] Elderly depressed

Table 1. Comparison of Antidepressant Profiles in the Elderly Population[a]

	TCAs		SSRIs					Others	
Variable	Desipramine	Nortriptyline	Citalopram	Fluoxetine	Fluvoxamine	Paroxetine	Sertraline	Mirtazapine	Venlafaxine
Clinical efficacy in elderly	◗	◗	●[b]	●	●	●	●[+]	●[c]	◗[+]
Efficacy in late-life depression comorbid with									
Cardiovascular disease				□		◗			◗[+]
Dementia/Alzheimer's			●[b]	◗		●	◗		
Indicated for anxiety disorders									
Panic disorder			◆			◆			
OCD				◆	◆	◆			
Social anxiety disorder						◆			
Once-daily dosing			■	■		■	■		
Good tolerability				■		■	■		
Pharmacokinetics									
Lack of active metabolites					■	■			
Optimal half-life @ 1 day						■	■		

[a]Abbreviations: OCD = obsessive-compulsive disorder, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant.
Symbols: ◗ = small comparative studies < 100 patients, ● = large comparative studies ≥ 100 patients, [+] = single comparative, □ = open-label study, ◆ = U.K. Monthly Index of Medical Specialities classification (April 1999), ■ = the drug meets the criteria.
[b]Same study population.
[c]Includes a study of patients aged ≥ 55 years.

patients will commonly have a comorbid condition, and in selecting treatment, the physician will have to take account of the cardiovascular effects or anxiolytic profile of the SSRI selected.

We do not agree with earlier recommendations that treatment of any concomitant medical illness take priority over the treatment of depression.[13] Early intervention is important, and the more persistent, pervasive, and severe the depression, the greater is the need to start drug therapy without delay. The more physically ill the patient, the more detrimental is concomitant depression, as illustrated by the predictive value of major depression for mortality after myocardial infarction.[9] The clinician may have a legitimate concern about the possibility of drug interactions in the older adult who is taking many other medications and will need to take into account the cytochrome P450 isoenzymes involved in the metabolism of SSRIs and other drugs. However, the risks of not treating depression appropriately are prolonged morbidity and potentially increased mortality, and these are risks that would be unacceptable for any other medical illness.

As in younger adults, depression in the older patient should be treated aggressively. The clinician should start treatment with a low dose, particularly with TCAs, and increase the initial dose of therapy slowly, with appropriate attention to possible adverse effects or drug interactions, given the sensitivity of the population and the likelihood of concomitant medication. The tradition of starting low and going slow was necessary for the poorly tolerated antidepressants, but is unnecessary with the SSRIs. It is the opinion of some investigators that the time to response to antidepressant therapy is prolonged in the elderly[47] and that typically it may take 8 to 12 weeks for a therapeutic response rather than 6 to 8 weeks as in younger adults. This emphasizes the importance of continuing treatment to obtain an adequate trial of antidepressant therapy. The clinician must not give up too soon.

When the depression is severe and protracted and there is no response to an appropriate trial of the initial choice of antidepressant therapy, the clinician should try another antidepressant, either selecting a different SSRI or switching to an alternative therapy. There are, however, very few studies of resistant depression in the elderly to inform the choice. In this context, we feel the move toward restricting formularies to a single SSRI is detrimental to the patient. Again, we stress that this population is a heterogeneous one, and the clinician may have to try a number of treatment options. In our opinion, there is currently neither the clinical data nor the clinical experience on which to base an algorithm appropriate to late-life depression, given the heterogeneity of the population, and we remain skeptical about the value of any algorithm defined for the elderly at this time.

There is growing evidence for the efficacy of antidepressants and, to a lesser extent, psychotherapy in maintenance treatment of late-life depression.[48] In the elderly as in the younger adults, treatment should be continued at the antidepressant dose that produced a therapeutic response to prevent relapse of the depressive episode and further maintained to prevent the development of new episodes of depression. The recommendation of several consensus groups is that the first episode of depression should be treated for at least 6 months following response.[6,27,47] In those with recurrent depression in whom the risk of new episodes is high, maintenance therapy at the same dose should be indefinite. Late-life depression is chronic and often recurrent. Once an older patient is responsive to antidepressant therapy, we recommend maintaining that patient on the effective dose of therapy for as long as possible, assuming that no drug interaction or other adverse effect interferes with treatment.

Subsyndromal depression. Subsyndromal depression is part of the spectrum of depressive disorders and represents a significant proportion of late-life depression. Clinical experience suggests that many elderly depressed subjects move from periods of subsyndromal depression to major depression, which implies that there could be a role for intervention when the depressive disorder is still subsyndromal. While there is clinical evidence for the efficacy of antidepressant therapy in dysthymia, we feel that there are insufficient data overall to generalize our recommendations in major depression (see above) to the subsyndromal population. There is an important gap in our knowledge about this at-risk population, and further research is needed.

CLINICAL SUMMARY

The consensus development group agreed on the following key clinical points:

- Depression in the elderly is underrecognized and undertreated. Major depression may be less common in older than in younger adults, but subsyndromal depression is more prevalent. In the elderly, it may be more difficult for patients to endorse depressed mood, which is a core symptom of DSM-IV diagnostic criteria for major depression. Great care is needed by physicians to find the appropriate wording that will allow the elderly to acknowledge their depression. The phraseology used in the criterion of DSM-IV has the effect of lowering the number with major depression and increasing the proportion with subsyndromal depression. The diagnostic indicators of depression in the elderly are anxiety, irritability, and a withdrawal of interest in habitual activities. The DSM-IV criterion for major depression that the depression must cause clinically significant distress or impairment in social, occupational, or other areas of functioning is sometimes difficult to assess in the elderly who have limited social role, and this criterion may also need to be modified.
- Subsyndromal depression identifies a substantial at-risk population in late-life depression. Not only does subsyndromal depression cause psychological distress and functional disability, but it also affects the quality of life and general health of the elderly and may be predictive of worsening depression. Some clinical evidence shows efficacy of antidepressant therapy in subsyndromal depression, but further research is needed.
- Depression in the elderly is essentially heterogeneous. When depression is associated with vascular disorders, it tends to be chronic, recurring, and carry a poor prognosis. Other forms of depression in the elderly are more similar to depression earlier in life. They may be related to life events, and they are generally responsive to treatment. It is difficult to select an appropriate definition of *elderly* since age is a continuous variable and there is no single cut-off to denote the change from adult to elderly. The elderly population can be defined, for example, in the context of a social transition (60 to 65 years) or a biological transition (75 to 80 years). This provides a basis for the concepts of "young-old" and "old-old."
- Chronic medical illness and functional impairment in later life overwhelm the effect of other risk factors for depression. Depression in the elderly is frequently comorbid with physical illness such as cardiovascular disease and/or other psychiatric symptoms such as anxiety. The presence of one or more medical illnesses is a negative prognostic factor for response to antidepressant therapy.
- Antidepressants are as effective in the elderly as they are earlier in life. SSRIs are the antidepressants of first choice for depression in the elderly, including those with severe depression, the very old, and hospitalized patients. In selecting appropriate treatment, the physician must take account of concomitant illness and concurrent therapy and prescribe an agent with a simple once-daily regimen and one with anxiolytic activity and/or lacking cardiovascular effects, as appropriate.
- Depression in the elderly must be treated aggressively with an appropriate dose of antidepressant therapy for an appropriate duration. If a TCA is used, the physician should start treatment with a low dose and increase that dose slowly with an attention to possible drug interactions or adverse effects. Starting with a low dose is not necessary with SSRIs. Since there is some evidence that the time to respond to antidepressant therapy is prolonged in the elderly, the clinician must not give up too soon. Once a response is seen, the patient should be maintained on the effective dose of therapy to prevent relapse and recurrence of depression.
- Early intervention is important in late-life depression, and the more pervasive, persistent, or severe the depression, the greater is the need to start drug therapy without delay. This recommendation applies irrespective of the presence of concomitant medical illness. Primary treatment of depression, particularly if it has the characteristics of a major depressive disorder, should not be deferred in the elderly until somatic conditions have been treated.
- CBT and IPT appear to be effective forms of psychotherapy in elderly adults with major depression. With appropriate training, these techniques could be made more widely available to the primary care physician. Psychotherapy such as IPT can help elderly adults to comply with antidepressant drug therapy.
- Any comprehensive management program should include psychological support from the physician. This includes exploring stressors for depression and educating patients and their families about depressive illness and its treatment.

- Bereavement is a common life event in the elderly, some of whom will develop symptoms meeting diagnostic criteria for depression. When depression is associated with bereavement, it is chronic and disabling and should be recognized as a major depressive episode and treated appropriately.

Drug names: citalopram (Celexa), desipramine (Norpramin and others), fluoxetine (Prozac), fluvoxamine (Luvox), mirtazapine (Remeron), nortriptyline (Pamelor and others), paroxetine (Paxil), sertraline (Zoloft), venlafaxine (Effexor).

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