

# Late-onset schizophrenia Make the right diagnosis when psychosis emerges after age 60



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New evidence shows psychosis presents in later life more often than was once believed. Very late-onset schizophrenia remains underdiagnosed but responds well to treatment.

**M**r. B, age 73, repeatedly complained to his landlord that people were trying to poison him by pumping noxious gas into his apartment. He barricaded himself inside, taped up all air vents and windows, and left only when absolutely necessary. At night, he could hear people working the “apparatus” that pumped the gas, and could “smell” the vapors.

On examination, he was physically well but suffered from mild neural deafness and myopia. He was suspicious and guarded but oriented and not cognitively impaired. He expressed paranoid beliefs and experienced auditory and olfactory hallucinations. There was no evidence of affective disturbance.

At first he refused psychiatric care but eventually agreed to take risperidone, 0.5 mg at night. He tolerated the agent well, and his psychotic symptoms slowly resolved.

As Mr. B’s case illustrates, schizophrenia—once thought to be strictly an early-onset disorder—commonly manifests late in life (Box). Too often, however, very late-onset schizophrenia goes undiagnosed because older patients with the disorder tend to be socially isolated. Their symptoms of paranoia and reluctance by family members to intervene also can prevent them



Box

### PREVALENCE OF VERY LATE-ONSET SCHIZOPHRENIA

Most clinical samples of patients with schizophrenia cite few cases of onset after age 60, reflecting the confused and changing nosology of very late-onset schizophrenia.

DSM-III (1980) stated that the schizophrenia label could apply only if onset occurred before age 45. This stipulation was dropped in DSM-III-R (1987), but it undoubtedly led psychiatrists to believe that schizophrenia simply did not begin in late life. The International Late-Onset Schizophrenia Group<sup>1</sup> today recognizes the disorder's late-onset version as "very-late-onset schizophrenia-like psychosis."

General population studies report rates of "late paraphrenia" of around 1%, but these studies probably underestimate the true prevalence. One presumes that persons with paranoia are less likely than those without to participate in such a study.

The Camberwell Register First Episode Study,<sup>2</sup> performed in London, is one of the few to determine rates of nonaffective psychosis across all ages of onset. In this study, 12% of the 513 patients studied across 20 years had illness onset after age 60. Researchers suspect a similar incidence in the U.S. population.

from receiving treatment that could control psychotic symptoms and improve their quality of life.

Psychosis presenting at any age, but especially in later life, requires careful evaluation to exclude organic pathology. Very late-onset schizophrenia differs substantially from psychosis associated with dementia, as in Alzheimer's disease, both in terms of neuropsychological and brain imaging findings.

Although limited, data on late-life psychosis offer clues to its diagnosis and treatment. This article will address:

- risk factors and clinical presentations associated with late-onset schizophrenia
- pharmacologic and psychosocial treatment options based on available evidence.

#### Clinical presentation

Clinical presentation of schizophrenia with onset after age 60 differs from that of early-onset schizophrenia (*Table 1*). To those familiar with early-onset cases, the most obvious differences in late-onset patients are negligible rates of primary negative symptoms and formal thought disorder.

Persecutory delusions are common in both types and often are elaborate. The so-called "partition" delusion, which leads the patient to believe that people or objects can transgress impermeable barriers and access his or her home with malign intent, is more common in late-onset than in early-onset schizophrenia.<sup>3</sup>

Hallucinations in very late-onset schizophrenia are often prominent and can occur in multiple modalities, including auditory, visual, and olfactory. Sometimes the hallucination and delusion are clearly linked; for example, a patient claims to smell the noxious gas he believes is being pumped into his home.

Does the difference in presentation between early- and very late-onset schizophrenia reflect distinct disease processes or the disorder's impact at different stages of brain maturation and degeneration? To answer that question, researchers have compared late-onset patients with young early-onset patients and with older patients who developed schizophrenia in their youth. Similar phenomena have been found in both early-onset groups,<sup>4</sup> suggesting that age of onset causes the differences in clinical presentation.

#### Risk factors

As with early-onset schizophrenia, family history is the most common cause of very late-onset schizophrenia. Despite their limitations, family history studies almost all show a familial risk of very late-onset schizophrenia lower than that of early-onset patients but greater than that of the general population.<sup>5</sup> Published studies do not tell us whether age of onset is genetically determined, in part because not all patients at risk for very late-onset schizophrenia live long enough to manifest its symptoms.

Family history has been associated with affective disorder in some patients with very late-onset schizophrenia. One case-controlled series of family interviews<sup>6</sup> found an approximate 1.3% rate of schizophrenia in relatives—about the same rate as that of the control group. The rate of depression among relatives of patients with very late-onset schizophrenia was 16.3%, compared with only 4.4% for controls ( $p = 0.003$ ). Thus, late-onset psychosis and affective disorders may have etiologic links.<sup>7</sup>

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Other possible risk factors for very late-onset schizophrenia include sensory deficits, premorbid personality disorder, social isolation, neuropsychological abnormalities, and female gender.

**Sensory deficits.** Several studies have reported that hearing and vision loss is more prevalent in older patients with very late-onset schizophrenia than in similarly aged controls. Most of these studies have associated either auditory or sensory impairment with very late-onset schizophrenia,<sup>8</sup> but most did not include appropriate controls.

One case-control study (of younger patients)<sup>8</sup> found that only uncorrected sensory deficits were over-represented in late-onset cases. This finding implies that one should find out if the patient is willing or able to get medical help for the sensory deficit, as well as whether that treatment has been adequate, before calling the sensory deficit a sequela of late-onset schizophrenia.

**Premorbid personality disorder.** Patients with very late-onset schizophrenia are widely reported to have gone through life reclusive and paranoid.<sup>5</sup> Of interest is that unlike many of their early-onset counterparts, late-onset patients tend to have achieved fairly well in the workplace. Whether this success reflects a later onset of illness cannot be determined.

**Social isolation** is common among older persons and even more so among those with very late-onset schizophrenia.<sup>9</sup> Whether this finding reflects patients' premorbid personalities, the illness itself, or a risk factor for the disorder is open to conjecture.

**Neuropsychological abnormalities.** Assessments of patients with very late-onset schizophrenia reveal cognitive impairment patterns similar to those reported in patients with an earlier onset<sup>10</sup> but distinct from those reported in patients with psychosis associated with dementia. CT and MRI studies reveal focal (reduced left temporal lobe volume) and nonspecific (increased ventricular-to-brain ratios) structural abnormalities similar to those in younger patients.<sup>11</sup>

Table 1

### CLINICAL FEATURES OF SCHIZOPHRENIA: EARLY- VS. VERY LATE-ONSET TYPES

Clinical feature	Early onset	Very late onset
<b>Persecutory delusions</b>	Common (often elaborate)	Common (often elaborate)
<b>Partition delusions</b>	Rare	Common
<b>Negative symptoms</b>	Common	Rare
<b>Formal thought disorder</b>	Common	Rare
<b>Hallucinations</b>	Common, especially auditory	Often prominent (can manifest in multiple modalities)
<b>Gender differences</b>	Equally common in men, women	More common in women
<b>Family history of schizophrenia</b>	Common	Less common
<b>Uncorrected auditory, visual impairments</b>	No consistent relationship	Common; excessive in some patients
<b>Premorbid personality</b>	Maybe schizoid/schizotypal	Reclusive, suspicious
<b>Social abilities</b>	Social isolation	Social isolation
<b>Marital status</b>	Usually unmarried	Usually unmarried
<b>Cognitive deficits, structural brain abnormalities</b>	Similar for both groups	Similar for both groups

Researchers previously reported excessive white-matter abnormalities in late-onset patients compared with healthy controls—a consistent finding in patients with late-life depression. More recent studies that carefully excluded organic cerebral disorders have not replicated this finding, however.<sup>11</sup>

**Female gender.** Very late-onset schizophrenia is more common in women than in men.<sup>12</sup> Female-to-male ratios ranging from 2.2:1 to 22.5:1 have been calculated. Although women



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generally live longer than men, this predominance is still greater than one would expect. It might also hide important clues regarding schizophrenia and related disorders across the life span, including the fact that the brains of men and women show sex-specific patterns of aging.<sup>12</sup>

### Managing very late-onset schizophrenia

**Initial assessment.** Patients who present with a new-onset psychotic disorder at any age require careful evaluation to exclude an underlying organic cause. The following are strongly suggested in older patients with new-onset psychoses:

- comprehensive history (including medications)
- physical (including neurologic) examination
- laboratory investigations
- CT neuroimaging
- and cognitive screening, such as the Mini Mental State Examination.

**Drug treatment.** Despite the wealth of published data on the psychopharmacologic management of schizophrenia, few randomized, con-

Cognitive-behavioral therapy can help modify delusional beliefs and gain control over hallucinations



trolled trials have examined the use of drugs to treat the disorder's very late-onset form. Case reports or small open studies comprise the available literature. Significant flaws in treatment studies have included diagnostic heterogeneity, mixing of early- and late-onset patients, inadequate outcome criteria, and lack of control groups.<sup>13</sup>

As with early-onset schizophrenia, however, antipsychotics appear to improve the acute symptoms of very late-onset schizophrenia and reduce the risk of relapse.<sup>14</sup> Pearlson et al<sup>4</sup> reported at least partial remission in 76% of patients with late-onset schizophrenia after neuroleptic regimens (complete remission occurred in 48%). The presence of thought disorder or a premorbid schizoid personality predicted poor response to treatment, whereas gender, family history, and first-rank symptoms (auditory hallucinations, delusions, social withdrawal) did not significantly affect outcome.

Very late-onset patients respond to about one-half the antipsychotic dosage required for younger patients.<sup>13</sup>

Sweet and Pollock<sup>15</sup> found an average dosage of chlorpromazine equivalents, 148 mg/d, to be effective in older patients, compared with >300 mg/d in younger cohorts.

**Neuroleptic side effects.** Older patients are more susceptible than their younger counterparts to side effects and adverse reactions from typical neuroleptics, even at low dosages. Age-related differences in pharmacokinetics and pharmacodynamics, combined with the increased incidence of comorbid physical disease and polypharmacy among older patients, often complicate pharmacotherapy for late-onset schizophrenia.

Older patients taking antipsychotics face an increased risk of extrapyramidal symptoms (EPS), especially parkinsonism and akathisia.<sup>16</sup> Anticholinergics are poorly tolerated and may cause urinary retention, constipation, blurred vision, exacerbation of glaucoma, and delirium. Cardiovascular side effects, especially orthostatic hypotension, may lead to falls and significant injury and may exacerbate coexisting cardiovascular disease.

Neuroleptic-induced tardive dyskinesia (TD) is another potential complication. Jeste et al found the cumulative annual incidence of drug-induced TD to be five times greater

among older psychotic patients than among younger ones (26% vs. 5% after 1 year).<sup>17</sup> Duration of exposure and total cumulative amount of prescribed neuroleptics remain significant risk factors for TD in older patients.

**Atypical antipsychotics,** with their less-adverse side-effect profiles and lower risk of EPS (and probably TD as well) are the preferred first-line drugs for late-onset schizophrenia. These agents also have been associated with improved cognition in younger patients with schizophrenia, a potentially significant benefit in the older patient.

Table 2

### ANTIPSYCHOTIC DOSAGES RECOMMENDED FOR VERY LATE-ONSET SCHIZOPHRENIA

Drugs	Initial dosages	Maintenance dosages
Olanzapine	1 to 5 mg/d	2.5 to 15 mg/d
Risperidone	0.25 to 0.5 mg/d	0.5 to 3 mg/d
Quetiapine	12.5 to 25 mg/d	75 to 150 mg/d

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No well-controlled trials of clozapine in very late-onset schizophrenia have been performed. According to one literature review,<sup>18</sup> most older psychotic patients showed moderate to marked improvement at relatively low dosages (mean dosage 134 mg/d). The reviewers concluded that clozapine was safe and well tolerated but suggested that agranulocytosis may occur at higher rates in this group than in younger patients. Clozapine's potent anticholinergic action and its marked sedative effects limit its use in very late-onset schizophrenia to treatment-resistant patients or those with severe TD.

Data on the use of other atypical agents in very late-onset schizophrenia are limited. Risperidone has been associated with significant improvements in older patients with schizophrenia.<sup>16</sup> Risperidone, olanzapine, and quetiapine have all been found to be safe, well-tolerated, and effective in managing late-life psychotic disorders.<sup>16,19,20</sup> As with neuroleptics, recommended starting and maintenance dosages of the atypicals are lower than those used in younger patients (*Table 2*).<sup>13</sup>

A “start low, go slow” approach is warranted, and dosages should be adjusted according to clinical response. Communicate with the patient's primary care physician to learn of any potential drug-drug interactions with medications being given for comorbid illnesses.

Electroconvulsive therapy has been reported to be useful in several studies, but data on its use in very late-onset schizophrenia are limited.<sup>21</sup>

**Psychosocial interventions.** One review of the role of non-biological treatment in very late-onset schizophrenia<sup>22</sup> stressed the need to develop trust between patient and psychiatrist, so that the patient clearly views the treatment team as allies (*Table 3*).

Table 3

### DOs AND DON'Ts OF MANAGING AN OLDER PATIENT WITH SCHIZOPHRENIA

#### Do

- **Offer practical solutions** to perceived difficulties (e.g., help resolve familial conflicts or housing/financial difficulties rather than get involved with delusional interpretation of events)
- **Assess degree of loneliness** by exploring the patient's wishes/fears of social contact
- **Assess the patient's social needs** by talking with the patient, family physician, and (if applicable) nurse
- **Contact family members** early and involve them in planning
- **Correct visual and hearing impairments** as much as possible

#### Don't

- **Make initial demands on the patient.** Often the patient is hostile at first; this can undermine treatment
- **Confront delusional system directly.** Acknowledge concerns but don't directly challenge beliefs; otherwise the patient will become unresponsive
- **'Take sides'** in paranoid disputes the patient may be having with neighbors or others
- **Apply diagnostic labels early.** Build patient rapport before rendering a diagnosis
- **Act alone.** Involve primary care physician and family as appropriate

To treat late-onset schizophrenia, start low and go slow when prescribing antipsychotics

To that end, look for thoughts, feelings, or situations that may have precipitated the onset of psychosis, and explore their subjective meaning with the patient.

Address any clear losses that are identified, such as the recent death of a spouse or other family member.

Find out if the patient is isolated and to what degree he or she feels lonely. Encourage the patient to engage in activities that he or she once enjoyed, and subtly introduce the patient to an appropriate community support group.

Suggesting participation in group leisure activities may also help. Ascertain the patient's living arrangements and basic needs. You may need to refer the patient to a social agency for assistance with housing, finances, nutrition/diet, and transportation.

**Reminiscence therapy**, through which patients are encouraged to reflect on their lives, can be useful for patients with very



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late-onset schizophrenia. Through reflection, patients can review past successes and painful experiences and move toward ultimate resolution of conflict and current difficulties.<sup>22</sup>

As in younger patients with schizophrenia, cognitive-behavioral therapy can help to modify delusional beliefs, gain control over hallucinations, and identify high-risk situations and appropriate coping strategies.<sup>23</sup>

Include family members in the treatment plan, and offer them support, education, and practical assistance (e.g., strategies for dealing with delusions). Informed families can help patients comply with prescriptions and appointments and can also detect relapse in its early stages.

In some cases, the patient's longstanding paranoia and paranoid personality can lead to resentment and conflict within the family. Before treatment can begin, you may also need to address this conflict by educating family members on how a loved one's schizophrenia affects them. Counseling the family as a group may be appropriate in some cases.

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Very late-onset schizophrenia is underdiagnosed and has not been extensively studied. Premorbid personality, sensory deficits, family history, and social isolation are among the possible risk factors for new-onset schizophrenia in patients 60 and older. Atypical antipsychotics and psychosocial interventions can be effective treatments.

# BottomLine

### Related resources

- ▶ Howard R, Rabins PV, Castle DJ, eds. *Late onset schizophrenia*. Petersfield, UK: Wrightson Biomedical; 1999.
- ▶ Howard R, Rabins PV, Seeman MV, et al. Late-onset schizophrenia and very-late-onset schizophrenia-like psychosis: an international consensus. *Am J Psychiatry* 2000; 157:172-8.

### DRUG BRAND NAMES

Clozapine • Clozaril	Quetiapine • Seroquel
Olanzapine • Zyprexa	Risperidone • Risperdal

### DISCLOSURE

The authors report no affiliation or financial arrangement with any of the companies whose products are mentioned in this article, or with manufacturers of competing products.

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