

# Maintenance treatment with paroxetine, but not psychotherapy, prevented recurrent major depression in older persons

Reynolds CF 3rd, Dew MA, Pollock BG, et al. Maintenance treatment of major depression in old age. *N Engl J Med*. 2006;354:1130-8.

**Clinical impact ratings:** GIM/FP/GP ★★★★★☆☆☆ Geriatrics ★★★★★☆☆☆

## QUESTION

In older patients with major depression who respond to treatment, does maintenance therapy with paroxetine, psychotherapy, or a combination prevent recurrence of depression?

## METHODS

**Design:** Randomized, 2 × 2 factorial design, placebo-controlled trial.

**Allocation:** {Concealed}†.\*

**Blinding:** Blinded (clinicians, patients, and outcome assessors).\* Clinicians and patients were not blinded to the psychotherapy intervention.

**Follow-up period:** 2 years.

**Setting:** Specialized university-based clinic in Pittsburgh, Pennsylvania, USA.

**Patients:** 116 patients ≥ 70 years of age (mean age 77 y, 65% women) who had major depression according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV) criteria, score ≥ 15 on the Hamilton Rating Scale for Depression (range 0 to 52 [worst]), score ≥ 17 on the Folstein Mini-Mental State Examination (range 0 to 30 [best]), and a sustained clinical response after several months of treatment with paroxetine, 10 to 40 mg/d, and psychotherapy (weekly, then biweekly).

**Intervention:** Paroxetine plus psychotherapy ( $n = 28$ ), paroxetine plus clinical care ( $n = 35$ ), placebo plus psychotherapy ( $n = 35$ ), or placebo plus clinical care ( $n = 18$ ) for 2 years. Paroxetine was continued at the individually titrated dose. Psychotherapy or clinical care was provided monthly by the same clinician (nurse, social worker, or psychologist) who previously treated the patient.

**Outcomes:** Recurrence of major depression, according to DSM-IV criteria and a Hamilton score ≥ 15, confirmed by a geriatric psychiatrist.

**Patient follow-up:** 81% of patients completed the study (100% included in the intention-to-treat survival analysis).

## MAIN RESULTS

Major depression recurrence rates were lower in the 2 paroxetine groups than in the 2 placebo groups (relative risk 0.42, 95% CI 0.24 to 0.71; number needed to treat 4, CI 3

to 11) (Table). Psychotherapy did not reduce risk for recurrence (Table).

## CONCLUSIONS

In older patients with major depression who responded to treatment, long-term maintenance treatment with paroxetine prevented recurrence of depression. Monthly psychotherapy did not prevent recurrent depression or increase the efficacy of paroxetine treatment.

*Sources of funding:* National Institute of Mental Health and National Center for Minority Health and Health Disparities.

*For correspondence:* Dr. C.F. Reynolds, Western Psychiatric Institute and Clinic, Pittsburgh, PA, USA. E-mail reynoldscf@upmc.edu. ■

\*See Glossary.

†Information provided by author.

## Paroxetine or placebo plus psychotherapy or clinical care to prevent recurrence of major depression in older persons at 2 years

Outcome	Paroxetine + psychotherapy	Paroxetine + clinical care	Placebo + psychotherapy	Placebo + clinical care
Depression recurrence	35%‡	37%‡	68%	58%

‡ $P = 0.03$  vs placebo + psychotherapy; all other between-group comparisons were not significant.

## COMMENTARY

Although major depression is less common in older adults than in those who are middle-aged, relapse rates are higher in older adults, increasing the associated disability. A meta-analysis of 31 randomized discontinuation trials in mixed-aged populations showed that maintenance antidepressant medication decreases 12-month relapse rates from 41% to 18% (1). The risk for relapse is greatest in the first 12 months, but the benefit of continued treatment has been shown for up to 3 years. In older adults, antidepressant maintenance treatment had similar benefits in 3 of 4 trials. Reynolds and colleagues previously showed that combined antidepressant medication plus interpersonal psychotherapy (IPT) was more effective than IPT alone or placebo, but subgroup analysis showed higher risk for and more rapid relapse in patients ≥ 70 years of age (2).

The current study by Reynolds and colleagues tested relapse prevention treatments in this older subgroup and had several notable findings. First, with aggressive, acute-phase treatment, including paroxetine, IPT, and medication augmentation (35% of patients), almost 60% of patients achieved partial or complete remission. Second, in the maintenance phase, 58% of patients relapsed with placebo. Paroxetine was

highly effective, but IPT was not more effective than placebo. This outcome is surprising because of the efficacy of IPT for acute-phase treatment and the authors' previous finding of added benefit in somewhat younger, less medically ill patients. IPT therapists were highly skilled, so the lack of benefit is probably related to patient characteristics.

Clinical implications are that aggressive treatment of major depression is required to achieve remission in older adults; treatment should be continued for at least 1 year, as older adults are at high risk for relapse; and IPT is an efficacious choice for acute-phase treatment but not for maintenance treatment. Further studies of combined antidepressant medication and psychotherapy are needed to determine the role of psychotherapies in relapse prevention in older adults.

John W. Williams Jr., MD, MHS  
Duke University Medical Center  
Durham, North Carolina, USA

## References

- Geddes JR, Carney SM, Davies C, et al. *Lancet*. 2003;361:653-61.
- Reynolds CF 3rd, Frank E, Perel JM, et al. *JAMA*. 1999;281:39-45.