

# 'Oldest Old' Have Less Serious Mental Illness

BY MIRIAM E. TUCKER

NATIONAL HARBOR, MD. — Long-term care residents aged 85 and older are less likely than younger residents to have a serious mental illness, more likely to have dementia, and equally likely to have depression or anxiety.

Up to 80% of long-term care (LTC) residents have diagnosable neuropsychiatric disorders, including dementia, according to an analysis of data from the 2004 National Nursing Home Survey. The new findings are among the first detailing the rates of these disorders among the "oldest old" population now making up the fastest-growing segment of the over-65 age group and disproportionately represented in nursing homes.

"As a rapidly growing subpopulation, the oldest old in LTC have what appears to be distinct characteristics relative to other age groups, and these no doubt affect their care," Catherine A. Yeager, Ph.D., and her associates said in a poster presented at the annual meeting of the Gerontological Society of America.

The 2004 National Nursing Home Survey, conducted between August and December 2004, is one in a series of nationally representative sample surveys of U.S. nursing homes conducted by the Centers for Disease Control and Prevention. A total of 1,174 nursing home facilities participated, producing data for 1,317,300 residents.

The population included 674,500 persons aged 85 and older. That group's average stay in those facilities was longer than that of their younger peers: 862 vs. 766 days. The survey data show "a few notable exceptions" to expected patterns of frailty and disability with age, said Dr. Yeager, of Robert Wood Johnson Medical School, Piscataway, N.J., and her associates.

The 85-plus group was made up of more women (82%) and more whites (90%), and was more likely to be widowed (72%) than were either the aged 75-84 or 65-74 groups. Of the 674,500 oldest old population, 17,300 had lived 100 years or more.

Only small proportions of all residents had neuropsychiatric diagnoses at the time they were admitted to LTC: 10% with dementia, 2% with schizophrenia spectrum, 0.3% with bipolar disorder, 0.2% with depressive disorder, and 0.2% with anxiety. However, neuropsychiatric diagnoses increased in all groups. At the time of the survey, depressive disorders were present in 35% of the oldest old, a percentage not significantly different from the 36% among the 75- to 84-year-old group and 32% of the 65- to 74-year-old individuals. Neither did rates of anxiety disorders differ by age, occurring in 12% of both the 85-plus and 75- to 84-year-old groups, and 11% of the 65- to 74-year-old group.

However, the oldest old were less likely than the two younger groups to have been diagnosed with a serious mental illness, including schizophrenia spectrum disorder (8.5% in 85-plus group, 13% in

75-84 group, and 17% in 65-74 group) and bipolar spectrum (1.2%, 2.3%, and 3.2%, respectively). Conversely, both the 85-plus and 75-84 groups were more likely than the 65- to 74-year-olds to have dementia (22% in the older groups vs. 13% in the youngest group).

In all three age groups—and especially among the oldest old—the survey found more clinical indicators of dementia and depression than formal di-

agnoses had indicated. The researchers reported moderate to severe impairment in decision making, an indicator of dementia, in 55% of the oldest old, 34% of the 75- to 84-year-olds, and 11% of the youngest group. Likewise, the proportions with "low mood not easily altered," a proxy for depressive disorder, were 49%, 37.5%, and 14%, respectively.

"Older residents are not admitted to LTC with neuropsychiatric diagnoses to

any degree," perhaps because of preadmission screening, reported the group led by Dr. Yeager, who works in the Essex County Hospital Medical Center, Cedar Grove, N.J. "Once in the LTC, all groups show an increased prevalence of formal neuropsychiatric conditions."

Residents with dementia diagnoses were more functionally impaired than their peers without dementia at all ages, the investigators reported. ■

## IMPORTANT CORRECTION OF DRUG INFORMATION ABOUT BYSTOLIC® (NEBIVOLOL) TABLETS

An advertisement in professional journal publications for Bystolic® (nebivolol) tablets for the treatment of hypertension was the subject of a Warning Letter issued by the U.S. Food and Drug Administration (FDA) in August 2008.

Forest would like to take this opportunity to clarify the content of this advertisement.

### Indications and Usage

Bystolic is indicated for the treatment of hypertension. Bystolic may be used alone or in combination with other antihypertensive agents.

### Unsubstantiated Superiority and Mechanism of Action Claims

The FDA objected to claims that Bystolic was a novel and next generation beta blocker with a unique mechanism of action including cardioselective beta blockade and vasodilation. The FDA stated that these claims were misleading because they suggested that Bystolic is different from and superior to other  $\beta$ -adrenergic receptor blocking agents in the treatment of hypertension, when these implications have not been demonstrated by substantial evidence or substantial clinical experience. In extensive metabolizers (most of the population) and at doses  $\leq 10$  mg, Bystolic is preferentially  $\beta_1$  selective. The FDA also stated that the presentation of the mechanism of action implied that it had been established, when the package insert states that the mechanism of action of the antihypertensive response of Bystolic has not been definitively established.

### Omission and Minimization of Risk Information

The FDA stated that the advertisement did not disclose the following important safety information, which is contained in Bystolic's full Prescribing Information:

**Warning:** In patients who have compensated congestive heart failure, Bystolic should be administered cautiously. If heart failure worsens, discontinuation of Bystolic should be considered.

**Precautions:** CYP2D6 Inhibitors: Use caution when Bystolic is co-administered with CYP2D6 inhibitors (quinidine, propafenone, fluoxetine, paroxetine, etc).

**Drug interactions:** Drugs that inhibit CYP2D6 can be expected to increase plasma levels of nebivolol. When Bystolic is co-administered with an inhibitor or an inducer of this enzyme, patients should be closely monitored and the nebivolol dose adjusted according to blood pressure response. Fluoxetine, a CYP2D6 inhibitor, administered at 20 mg per day for 21 days prior to a single 10 mg dose of nebivolol to 10 healthy adults, led to an 8-fold increase in the AUC and 3-fold increase in  $C_{max}$  for d-nebivolol.

The FDA objected to the claim, "Favorable tolerability profile with a low incidence of beta blocker-related side effects." The FDA determined that this claim implied that the tolerability profile of Bystolic is better than the tolerability profile of other  $\beta$ -adrenergic receptor blocking agents, when this has not been demonstrated by substantial evidence or substantial clinical experience. The FDA also objected to the claim, "Favorable tolerability profile," stating that it minimized the risks associated with Bystolic.

### Unsubstantiated Efficacy Claims

The FDA objected to the claim, "Efficacy demonstrated across a broad range of patients." The FDA stated that the cited claim implied that efficacy was demonstrated within each subgroup (obese, poor metabolizers, and diabetic) presented in conjunction with this claim, when this has not been supported by substantial evidence or substantial clinical experience. None of the efficacy trials for Bystolic were specifically designed to evaluate effectiveness in patients who were obese, poor metabolizers, or diabetic. The FDA is not aware of any studies with Bystolic demonstrating efficacy in the above referenced subgroups. Effectiveness was established in black hypertensive patients and was similar in subgroups analyzed by age and sex.

### Important Safety Information

Patients being treated with Bystolic should be advised against abrupt discontinuation of therapy. Severe exacerbation of angina and the occurrence of myocardial infarction and ventricular arrhythmias have been reported following the abrupt cessation of therapy with beta blockers. When discontinuation is planned, the dosage should be reduced gradually over a 1- to 2-week period and the patient carefully monitored.

Bystolic is contraindicated in severe bradycardia, heart block greater than first degree, cardiogenic shock, decompensated cardiac failure, sick sinus syndrome (unless a permanent pacemaker is in place), severe hepatic impairment (Child-Pugh  $>B$ ), and in patients who are hypersensitive to any component of this product.

Bystolic should be used with caution in patients with peripheral vascular disease, thyrotoxicosis, in patients treated concomitantly with beta blockers and calcium channel blockers of the verapamil and diltiazem type (ECG and blood pressure should be monitored), severe renal impairment, and any degree of hepatic impairment or in patients undergoing major surgery. In patients who have compensated congestive heart failure, Bystolic should be administered cautiously. If heart failure worsens, discontinuation of Bystolic should be considered. Caution should also be used in diabetic patients as beta blockers may mask some of the manifestations of hypoglycemia, particularly tachycardia.

When Bystolic is administered with CYP2D6 inhibitors such as fluoxetine, significant increases in d-nebivolol may be observed (ie, an 8-fold increase in AUC).

In general, patients with bronchospastic disease should not receive beta blockers.

Bystolic should not be combined with other beta blockers.

The most common adverse events with Bystolic versus placebo (approximately  $\geq 1\%$  and greater than placebo) were headache, fatigue, dizziness, diarrhea, nausea, insomnia, chest pain, bradycardia, dyspnea, rash, and peripheral edema.

**Please see the accompanying brief summary of Prescribing Information for full risk information.**



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