

2000

# Low Blood Pressure and Depression: Comorbidity and Competing Outcomes

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## Repository Citation

Robbins, M. A., Elias, P. K., & Elias, M. F. (2000). Low blood pressure and depression: Comorbidity and competing outcomes. *Journal of the American Geriatrics Society*, 48, 336-337.

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## Low Blood Pressure and Depression: Comorbidity and Competing Outcomes

The study by Stroup-Benham et al.<sup>1</sup> makes several important contributions to the literature on depressive symptom-reporting in relation to blood pressure (BP). Their findings support the existence of an association between low BP and higher levels of depressive symptomatology and a constellation of somatic and psychosocial variables. Their study design took into consideration important variables that must be controlled when examining these relationships. Analyses were conducted with statistical adjustment for the effects of possible confounders, including gender, age, marital status, obesity, self-reported diagnosis of hypertension, current use of antihypertensive medication, and current use of central nervous system active medication.

Stroup-Benham et al. measured depressive symptoms with the Center for Epidemiological Studies-Depression Scale (CES-D),<sup>2</sup> a well validated self-report measure. In contrast, several earlier studies examined only a few specific symptoms associated with depression. Results of the Stroup-Benham et al. study for an older Mexican-American sample are consistent with results obtained in samples with different age ranges and other ethnic groups. Because there is evidence that cultural belief systems are relevant to depression,<sup>3</sup> this additional evidence of generalizability across ethnic groups is important. Their findings are also consistent with the continental European medical view with respect to BP, that is, lower is not necessarily better.<sup>4</sup> However, it is important to note that hypotension was defined by Stroup-Benham et al. as systolic BP less than 120 mm Hg or diastolic BP less than 75 mm Hg.

Using this definition, both systolic hypotension and diastolic hypotension were associated with higher levels of self-reported depressive symptoms for their large sample of Mexican-American women and men aged 65 and older. Individuals whose systolic and diastolic BP values were both in the hypotensive range were particularly at risk for scores in the depressed range (CES-D score  $\geq 16$ ), for lower self-esteem, and for reporting problems with waking up feeling tired. The comparison group comprised normotensives (systolic BP of 120 to 139 mm Hg; diastolic of 75 to 84 mm Hg) for all analyses. The depression scores for individuals with elevated BP values were reported as intermediate between those for individuals described as hypotensive and those described as normotensive.

The similarity of this curvilinear association between BP and depression to reports of J- or U-shaped functions between BP and mortality<sup>5,6</sup> and cognitive functioning<sup>7</sup> is of interest and raises the following issues: (1) what is the optimal goal for blood pressure lowering with antihypertensive treatment when psychological as well as medical goals, e.g., reduction of stroke, are considered; (2) is age an important

consideration in relation to associations between BP and outcome measures such as depression, mortality, and cognitive functioning?

It is clear that the findings reported by Stroup-Benham et al. are not attributable to lowering of BP via current antihypertensive medication use. These investigators were careful to point out that their results should not be construed as indicating that treatment designed to increase BP values might be beneficial in reducing levels of depressive symptoms. However, they did suggest that their results indicate that there may be an optimal cut point for defining "well controlled" BP. A question may be raised as to whether this cut point is dictated by BP level or by the amount, or types, of medication required to reduce BP.

Indeed, there is a commonality between the possible side effects related to medication use and the symptoms associated with both hypotension and depression. Among the side effects most commonly associated with antihypertensive medications are drowsiness, weakness, fatigue, and impaired concentration and memory.<sup>8,9</sup> Thus, lowering BP to the point of hypotension might affect depression via the low BP levels, increased side-effects from higher dosages of medication, or both.

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### See also p 250

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However, the definition of hypotension used by Stroup-Benham et al. may not commonly be accepted as such by the healthcare community. The BP ranges defined as hypotensive by Stroup-Benham et al. correspond closely to the ranges classified as optimal (SBP values less than 120 mm Hg and DBP values less than 80 mm Hg) in the Sixth Report of the Joint National Committee (JNC) on Prevention, Detection, and Treatment of High Blood Pressure.<sup>10</sup> The JNC report does caution that unusually low BP values should be evaluated for clinical significance, but no criteria are given. The initial goal for treatment advocated in the JNC report is to lower BP into the normotensive range (SBP less than 140 mm Hg and DBP less than 90 mm Hg). Further lowering of BP, if tolerated by the patient, is recommended primarily "to prevent stroke, to preserve renal function, and to prevent or slow heart failure progression" (p. 20). Most would agree that these are high priority objectives. Clearly, the range of BP values optimal with respect to reducing risk for some possible outcomes (e. g., stroke) may not be optimal for other outcomes (e.g., depression). Therefore, one must consider the risk from the perspective of competing outcomes. For example, can we tolerate some depression to reduce the likelihood of stroke, an often catastrophic event? From this perspective, the age of the patient becomes a major consideration.

In the Stroup-Benham study, low BP level was associated with greater symptoms of depression for both age groups (65

to 74 years; 75 years or older), and the JNC report does not propose different target levels for BP depending on age. However, some studies do indicate that age is an important consideration with respect both to BP lowering<sup>11</sup> and to symptoms of depression and other psychological variables.<sup>12,13</sup> Orthostatic hypotension caused by antihypertensive medication use may be more common, and is also more serious, in older persons because of their increased risk of major injury (e.g., hip fracture) during syncope.<sup>11</sup> Some studies have shown that somatic symptoms (or correlates) of depression such as lowered energy levels and disturbances in sleep and appetite are more common in older people.<sup>14,15</sup>

Stroup-Benham et al. suggest that individuals with low BP may represent two populations. They speculate that their low BP sample might consist of individuals who represent a healthy population as well as chronically-ill individuals with higher levels of depressive symptoms and a higher risk of mortality. This is an important point because for some individuals, low BP may be the consequence of disease. Disease, in turn, impacts negatively on mortality, cognitive functioning, and psychological variables, including depression.<sup>16,17</sup>

As is true of high BP, low BP can be viewed as the common outcome of diverse processes. Increased risk for depression, cognitive impairment, and mortality might be specific to low BP that is concurrent with or secondary to other disease processes. If so, withholding treatment that would keep BP within optimal ranges (systolic BP less than 120 mm Hg and diastolic BP less than 80 mm Hg) may, for many patients, not pose a solution to depression, and it may increase the risk of other adverse outcomes such as stroke and coronary heart disease.<sup>18,19</sup> These adverse outcomes may then potentiate the problem with respect to depression. This point is arguable and, hopefully, a stimulus to further research. But it seems clear that treatment must take into account multiple outcomes, and outcomes must be assigned priorities based on the patient's age, unique risk profile, and medical history. Professor D. H. P. Streeten and colleagues argue this point with simplicity and elegance: "No population studies, of whatever size, will ever obviate the need for considering individual factors in making therapeutic decisions on patients with hypertension"<sup>11</sup> (p. 97).

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