**BACKGROUND**: Angiotensin-converting enzyme (ACE) inhibitors are generally prescribed by physicians in doses lower than the large doses that have been shown to reduce morbidity and mortality in patients with heart failure. It is unclear, however, if low doses and high doses of ACE inhibitors have similar benefits.

**METHODS AND RESULTS**: We randomly assigned 3164 patients with New York Heart Association class II to IV heart failure and an ejection fraction $\leq 30\%$ to double-blind treatment with either low doses (2.5 to 5.0 mg daily, n=1596) or high doses (32.5 to 35 mg daily, n=1568) of the ACE inhibitor, lisinopril, for 39 to 58 months, while background therapy for heart failure was continued. When compared with the low-dose group, patients in the high-dose group had a nonsignificant 8% lower risk of death ($P=0.128$) but a significant 12% lower risk of death or hospitalization for any reason ($P=0.002$) and 24% fewer hospitalizations for heart failure ($P=0.002$). Dizziness and renal insufficiency was observed more frequently in the high-dose group, but the 2 groups were similar in the number of patients requiring discontinuation of the study medication. Conclusions-These findings indicate that patients with heart failure should not generally be maintained on very low doses of an ACE inhibitor (unless these are the only doses that can be tolerated) and suggest that the difference in efficacy between intermediate and high doses of an ACE inhibitor (if any) is likely to be very small.