Fatigue is very common in patients with cancer. Current guidelines suggest that psychostimulants are “reasonable to consider for severe fatigue.” This randomized, double-blind placebo-controlled trial investigated the hypothesis that dexamphetamine in fatigued patients with advanced cancer would produce a clinically significant improvement with minimal side effects. Fifty patients with advanced cancer, who were receiving palliative care, were randomized to dexamphetamine 10 mg twice daily or placebo for eight days. Effectiveness was assessed using the Brief Fatigue Inventory (BFI) and the McGill Quality-of-Life Questionnaire (MQOL). The side effects were recorded. The results were analyzed on an intention-to-treat basis. The baseline demographics, fatigue levels, and quality-of-life scores were similar between the two arms. Patients were elderly, had impaired performance status (Eastern Cooperative Oncology Group score \( = 3 \)), and were taking a range of neurologically active medications. Thirty-nine patients completed the trial. There was a transient improvement in the fatigue levels on day 2, but no significant difference in fatigue (\( P = 0.267 \)) or quality of life (\( P = 0.579 \)) by the end of the study. Statistical modeling did not reveal any significant predictors of response to dexamphetamine. These results suggest that dexamphetamine 20 mg daily, although well tolerated, does not significantly improve fatigue or quality of life in patients with advanced cancer, as measured by the selected instruments.

Strengths
- Problem very prevalent in cancer patient
- Study well designed and analyzed
- Dexamphetamine as a good choice for the trial with usually tolerable side-effects (4/25 did not complete the study in D-arm vs 7/25 in placebo arm)
- Good evaluation with the BFI and the MQOL

Weaknesses
- Small sample size (21 and 18 in each arm)
- Age of the patients (elderly)
- No information on primary tumor site, Pain management and list of medication
- Dexamphetamine dosage could have been increased
- Significant difference in number of the days in hospital for D-arm not explained

Relevance to Palliative Care

This trial provides information to palliative care physicians who are dealing daily with fatigued cancer patients. The unsuccessful results obtained here with dexamphetamine prescribed to elderly patients confirm the complexity of the fatigue symptom and its multifactorial aspects. In view of some previous results obtained with younger HIV patients where dexamphetamine was improving their mood and energy, it suggests that fatigue in cancer patients may have a different pathophysiology than in HIV. Further studies will need to be done with younger cancer patients to confirm this hypothesis.