Terminally ill patients usually suffer from numerous underlying diseases and symptoms that decrease their quality of life. Literature suggests that among cancer patients, 25% experience severe depression and the incidence increases to 77% in those who are terminally ill.1 Anxiety is another common psychiatric issue which must be considered when treating patients nearing the end of their lives. There is a lack of literature that specifically addresses how to best improve quality of life in palliative care settings by controlling the "symptom cluster" of anxiety and dyspnea.2 At this time, morphine is considered the preferred pharmacologic treatment for refractory dyspnea, with adjunct anxiolytics provided as needed to control anxiety.3,4 A 2010 study by Navigante and colleagues suggests that midazolam by intramuscular injection may improve the quality of life in terminally ill patients who are enrolled in a hospice service. We hypothesize that treatment of hospice patients with benzodiazepines compared with opiates will result in an increased improvement in quality of life.

Study Design
This will be a prospective, randomized, double-blind, clinical trial conducted through an outpatient hospice service in Scranton, PA. The study protocol will be approved by the institutional review board, and all participants, or legal guardians acting on their behalf, will be required to provide written informed consent.

Study Population
Participants will include all patients 18 years of age or older who are terminally ill, enrolled in a hospice service, diagnosed with the symptom cluster of anxiety and dyspnea, and able to take oral medications. Patients with a life expectancy of 14 days or less, severe respiratory depression, uncontrolled asthma, upper airway obstruction, uncontrolled bleeding, GI obstruction, hyperventilation, heart failure due to chronic lung disease, cardiac arrhythmias, increased intracranial pressure, head injuries, brain tumors, seizure disorders, or narrow angle glaucoma will be excluded. Those receiving concomitant therapy with azelastine, paraldehyde, olanzapine, or sodium oxybate will also be excluded.

Randomization and Treatment
This trial will enroll patients. Subject randomization will be performed by a computerized random number generator. Study subjects, investigators, and all those involved in the care of the subject during their hospice stay will be blinded to treatment. Regimen treatments were adapted from the trial by Navigante and colleagues and are shown in figure 1, below.1,4,5

Materials & Methods (cont.)

**Introduction**

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**Symptom reduction** will be evaluated using the Edmonton Symptom Scale, a validated assessment tool for determining the effectiveness of patients' relief from physical and psychological distress.6

**Outcomes**
The primary outcome to be studied is the change in patients' perception of their quality of life. This will be assessed using the FACIT-Pal, a validated quality of life questionnaires specially designed for use in patients receiving palliative care.7 Patients will be assessed at baseline and after 7 and 14 days of treatment. Patients will receive treatment for 14 days, after which blinding will be removed and they will be allowed to either remain on the study medication or change to an alternate therapy, after thorough statistical analysis.

**Statistical Analysis**
Enrollment of 35 patients will be necessary to detect an increase of 3 points in quality of life score on the FACIT-Pal questionnaire with a two-sided alpha of 0.05 and 80% power following treatment. The sample size will be increased to 40 patients for analysis of the primary outcome. The sample size was calculated using the Open Epi software (www.OpenEpi.com) and was increased to ensure adequate power (80%) to detect an improvement of 3 points in quality of life score with a standard deviation of 8. In a 2010 paper, Navigante and colleagues suggested that midazolam might improve the quality of life in terminally ill patients who are enrolled in a hospice service. We hypothesize that treatment of hospice patients with benzodiazepines compared with opiates will result in an increased improvement in quality of life.

**Strengths & Limitations**
Quality of life is an understudied outcome in the hospice population and literature on this topic is lacking in this area. As Harding and colleagues note, “A primary reason for this dearth of evidence is the lack of appropriate and validated outcome tools, among other logistical and methodological challenges...in this population”.7,8 By using a validated tool, this study will decrease the literature deficit in this area.9,10

This study avoids common limitations encountered in research by ensuring adequate power, blinding practitioners and patients to treatment, and using a robust randomization protocol to increase the change in quality of life. Additionally, the results of this study will be able to compare the effects of lorazepam and morphine on the entire symptom cluster, rather than only dyspnea, as do prior publications.

Despite attempts to control confounding factors and outside influences, a potential limitation of this study is the geographic location from which the sample will be recruited. Most patients will likely be Caucasian which will limit the generalizability of the results to other ethnicities. Additionally, the findings of this study cannot be applied to patients in care settings other than hospice services or patients who have one or more of the exclusion factors.

**Disclosure Statement**
Authors of this presentation have the following to disclose concerning potential financial or personal relationships with the commercial entities that may have direct or indirect interest in the subject matter of this presentation: Eliza S. Daubert: Nothing to disclose; Scott Bolesta: Nothing to disclose.

**References**

**Effect of Lorazepam Versus Morphine on Quality of Life in Hospice Patients with Dyspnea and Anxiety**
Eliza S. Daubert, Pharm.D. Candidate, 2014[1], Scott Bolesta, Pharm.D., BCPS[1,2]


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