A Response to: "Prevalence, Severity and Correlates of Symptoms of Anxiety and Depression at the Very End of Life"

Dear Editor:

We read the recent paper titled "Prevalence, Severity and Correlates of Symptoms of Anxiety and Depression at the Very End of Life" by Kozlov et al.[1] with great interest. The authors concluded that psychological symptom management at the very end of life (EOL) is crucial to providing comprehensive hospice care.

Caregiver burden is defined by Zarit et al.[2] as "the extent to which caregivers perceived their emotional or physical health, social life and financial status as suffering as a result of caring for their relatives" and is associated with negative health outcomes in carers of people with common conditions. It is very interesting that Kozlov et al. reported that there is a relationship between caregiver burden and the intensity of patients' psychological symptoms at the very EOL that caregivers perceived. A previous study reported that the higher the caregiver burden of the caregivers, the higher the mental disorder risk.[3] Previous studies reported that the high risk group was defined as setting the cut-off point of caregiver burden.[4] Thus, we strongly agree with the author's opinion that providers caring for patients at the EOL need to pay attention to patient's psychological symptoms.

However, Kozlov et al. did not report the health status of caregivers. From the viewpoint of our clinical experiences, the caregiver's psychological symptoms of depression and anxiety are also important. In addition, recent research in the area of caregiving has emphasized not only the subjective burden, but also the importance of objective data such as physical burdens.[5] Therefore, we suggest that evaluating both mental and physical burdens of the caregivers will be able to reveal more beneficial results.

Furthermore, Kozlov et al. only reported the prevalence and intensity of psychological symptoms for patients at the very EOL. Caregiver burden consists of multidimensional aspects affected by emotional, social, and various other elements.[6] Therefore, we believe that it is crucial to evaluate the impact of various factors on caregiver burden. In future studies, we strongly recommend that collecting data from multidimensional aspects will be important to indicate ways to reduce caregiver burden.

Undoubtedly, it is important to focus on caregiver burden for caregivers working with patients at the very EOL. The study conducted by Kozlov et al. provided useful data in this regard. We believe that further evaluation of the caregiver burden will be beneficial for EOL caregivers in the future.

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Advance Care Planning Discussions in a Substance Use Disorder Recovery Program

To the Editor:

According to an article in the *British Journal of Medicine*, a randomized control trial of 309 patients

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showed that advanced care planning improved end-of-life care and reduced stress, anxiety, and depression in patients and their family members.[1] Unfortunately, there are still a surprisingly large number of individuals who do not engage in advance care planning. For instance, one study in *Health Affairs* found that only 36.7% of people in the U.S. had completed an advance directive.[2] Another study published in the *American Journal of Preventive Medicine* in 2014 found that of 7946 respondents, 73.7% did not have an advance directive because of lack of awareness.[3] Clearly, there is an awareness gap when it comes to advance care planning.

Organizations such as Respecting Choices in Wisconsin and Honoring Care Decisions[4] in New Hampshire have helped close this gap at the national and local level. With recent efforts to encourage locals to complete advanced directives, the rate of advanced directive completion in the Vermont and New Hampshire regions in January 2016 increased to 42%.[5] However, in discussions with Honoring Care Decisions, we determined that some local communities were still not receiving as much outreach as hoped primarily due to limited resources and access to care. We decided to reach out to individuals who were in a rehabilitation program receiving therapy for opioid use disorder. Our reasons for reaching out to this group were twofold. First, mortality rates are increased in individuals with opioid use disorder, so we thought that advance care planning discussions may be particularly beneficial to this group.[6] Second, we hypothesized that individuals in this group were likely to have below-average rates of advance directive completion. These recovery groups were reportedly not reached by the hospital advance care planning program, which primarily used health visits and local community events, such as religious gatherings, to engage in advance care planning. Thus, we suspected that our selected group members may have had fewer opportunities to engage in advance care planning.

Our goals were to provide information regarding advance care planning to this group and also to gather information about how this population perceives and completes advance care planning. We are unaware of literature that explores the perceptions and rates of advance care planning specifically in individuals who have substance use disorder.

Methods

Our initiative involved debunking myths around advance care planning and encouraging group members to fill out their own advance directive. We sought to empower the individuals to have these conversations with their loved ones and their primary care physician.

We led six 30-minute discussions about advance care planning at a Recover Together[7] branch in New Hampshire. Recover Together is a local treatment center that provides weekly group therapy sessions to people recovering from substance use. They exist in eight states across the country, and their purpose is to provide treatment for opiate use and weekly group therapy sessions to help maintain sobriety. There were approximately 10 to 15 attendees at each session. Each discussion began with a series of questions to promote conversation. These questions ranged from "what activities make you feel alive?" to "if you could control three things about your last day of life, what would they be?" Then, we provided details about advance care planning, such as choosing a health care agent, identifying one's values, beliefs, and preferences, and thinking about end-of-life scenarios. Next, we took turns going around the group discussing who they would identify as a potential health care agent and why. We then discussed the surrogacy law in New Hampshire and provided everyone with a New Hampshire or Vermont advance directive, depending on their state of residence. At the end of each session, we asked group participants to complete a paper-based survey, so that we could learn about their reactions to the session. The survey was designed by Honoring Care Decisions to ascertain baseline knowledge of advance care planning and to help determine the efficacy of the group session. 58 individuals completed the optional survey.

We obtained approval from the Committee for the Protection of Human Subjects. The study was designated as secondary research for which consent was not required.

Findings

For 86 percent of the participants, this was their first time ever attending a presentation about advance care planning (Table 1). Only 25 percent (14/55) of the participants had already completed an advance directive (Table 1). Only 10 individuals in total had given a copy of their advance directive to their health care provider (Table 1), and six of these individuals had discussed their preferences with their health care agent. Of the surveyed participants, 72 percent said they felt either very confident or somewhat confident that they were going to complete an advance directive in the next 30 days (Table 1). Over 98 percent of participants said that they found the session very useful or somewhat useful (Table 1). Nearly three-quarters (70.7%) of participants rated the importance of advanced care planning as either a 4 or 5 (with 5 being the most important), and 69 percent of participants said that they would recommend this presentation to others.

Table 1
Rates of Advance Care Planning Session Attendance and Advance Directive Completion and Effectiveness of Advance Care Planning Discussion

Prior Session Attendance and Advance Directive Completion		
	Yes	No
Have you attended a presentation or program to learn more advance care planning? ($n = 58$)	13.8%	86.2%
Do you already have an advance directive? ($n = 55$)	74.5%	25.5%
Does your health care provider have a copy of your advance directive? ($n = 11$)	90.9%	9.1%
Effectiveness of Advance Care Planning Discussion		
	Very confident/ useful	Somewhat confident/ useful
Attendee's confidence that he/she will update or complete an advance directive in the next 30 days ($n = 54$)	44.5%	16.7%
Usefulness of the information presented? ($n = 57$)	52.6%	45.6%

Comment

This project provides insights into the state of advance care planning in a population of individuals receiving therapy for opiate use disorder in New Hampshire. Moreover, it identifies an effective way to introduce the concept of advance care planning to them. We found the overall interest and appreciation for advance care planning to be very high and the rate of advance directive completion in this group to be quite low. These results suggest that individuals with substance use disorder should be provided with additional outreach and resources on this important issue. Additionally, even amongst those who had completed advance directives, few actually shared these with their physicians and even fewer discussed these with their listed health care agents. This further highlights the need for not only filling out an advance directive, but also the need for goals of care conversations and advance directive discussions with family members, health care agents, and physicians.

Qualitatively, these discussions were extremely well received by group participants. Group participants were very involved in the conversation, often providing personal and insightful perspectives into the discussion. Although we did not measure specific demographics, such as the ages of the group members, there was a large age range among group members. The discussions further fostered the bond between these group members, as individuals were able to learn personal and insightful details about their own values and beliefs. The depth of the discussions was often so great that it often came as a surprise even to the group counselor. For example, the group counselor occasionally would warn us that some of the groups were known to be on the quieter side. Surprisingly, many of these quieter groups turned out to produce lively and animated discussions.

Given that the Recover Together groups occur throughout the state of New Hampshire and also throughout the country, we think that this model could be scaled up so as to reach more participants. We propose that group counselors or volunteers be trained in advance care planning facilitation so that they can continue to lead these important discussions.

One limitation of our project is that we were unable to determine how many individuals actually completed their advance directive after the session. This challenge could be addressed by closely following up with participants or by having the participants report back to the group counselor after a certain period of time. Future projects should keep this limitation in mind and hope to maximize follow-up. We also did not obtain demographic data about the study group. Future projects should obtain such data, so that we can further ascertain how demographics, such as socioeconomic status and age, are associated with rates and perceptions of advance care planning in this population. Finally, our project only sampled 58 individuals. The generalizability of this project is therefore limited in part by the small sample size. Future studies should strive to obtain a larger number of participants from more than one location.

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Harms From Haloperidol for Symptom Management in Palliative Care—a Post Hoc *Pooled Analysis of Three Randomized Controlled Studies and Two Consecutive Cohort Studies*

Introduction

Symptom control for people with cancer improves quality of life. Haloperidol is a key drug in palliative care and is frequently used for the treatment of delirium, nausea, and vomiting.[1] Haloperidol, a butyrophenone, is a more potent D2 receptor antagonist than other antiemetics, such as prochlorperazine, olanzapine, or chlorpromazine.

The adverse events associated with haloperidol are like those of the phenothiazines, except that haloperidol potentially causes less sedation and hypotension. However, haloperidol is more strongly associated with extrapyramidal symptoms especially compared with newer drugs such as quetiapine or risperidone, and patients with Parkinson disease or Lewy body dementia may be more sensitive to its adverse events.[2] Haloperidol is inexpensive and has several routes of administration. Only a few studies focus on patients with life-limiting illnesses. The aim of this study was to determine whether the doses of haloperidol used in palliative care cause immediate and short-term harms and, if so, what is their severity?

Material and Methods

This study was a *post hoc* analysis conducted on three randomized controlled trials (studies 1, 2 [nausea], and 3 [delirium])[3–5] and two international collaborative Phase IV consecutive cohort studies (studies 4 [nausea] and 5 [delirium]),[6,7] which have been described previously. Severity of immediate and short-term harms were assessed using the National Institutes of Health Common Terminology Criteria for Adverse Events.[8,9] Nausea was graded by clinicians using verbal descriptors (none, mild, moderate, or severe). Items and evaluation times for harms differed between studies. Most frequently, routine data were collected at baseline and days 1, 2, and 7.

This study reports the number and percentage of participants with severity ≥3 grade and symptom deterioration ≥1 point from baseline in symptoms of interest. Harms in all five studies could also be reported on an *ad hoc* basis.

Descriptive statistics are used in this study, with categorical variables summarized as frequency and percentages, and continuous variables with median and interquartile ranges (IQRs).

This study is generated from secondary use of deidentified data that have been aggregated. All participants in studies 1–3 gave written informed consent, and the studies were approved by the relevant Human Research Ethics Committees before recruitment commenced. For studies 4 and 5, these were capturing routine data after the clinician had made the decision to commence haloperidol for the indication being studied. Sites had waivers of consent for collection of these deidentified clinical data and ethics approvals or waivers depending on the country in which the data were collected to publish the analyses.

Results

Patients' Characteristics

The clinical and demographic data of the 494 subjects are shown in Table 1. In the present study, the most subjects (90%) had advanced metastatic cancer (94% in studies 1–3 [Phase III] and 87% in Phase IV studies, respectively). The median age was 73 years (IQR: 64.5–81), and median Australia-modified Karnofsky Performance Scale score[10] was 40 (IQR: 30–50), indicating that many subjects required "considerable assistance and frequent medical care." AKPS in Phase III studies was better than the Phase IV studies. The median daily dose of haloperidol was 1.5 mg (day 1), 2.0 mg (day 2), 1.5 mg (day 7) in oral, or parenterally preparations.

Harms

Potential harms from treatment with haloperidol and the clinical responses to address those symptoms are shown in Table 1. Harm in this study was defined as a one-point deterioration from baseline in the National Institutes of Health Common Terminology Criteria for Adverse Events for the relevant symptom.