Analyzing Symptom Management Trials: The Value of Both Intention-to-Treat and Per-Protocol Approaches

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Purpose/Objectives: Two analytical approaches are described for a randomized trial testing interventions for symptom management.

Design: To compare an intention-to-treat with a per-protocol approach.

Setting: Patients were accrued from six cancer centers.

Sample: 94 men and 140 women with solid tumors were accrued.

Methods: An intention-to-treat approach (as randomized) and per-protocol analyses (at least one symptom reaching threshold and one follow-up intervention) were compared. The analysis determines how each approach affects results. A two-arm, six-contact, eight-week trial was implemented. In one arm, nurses followed a cognitive behavioral protocol. In the second arm, a non-nurse coach referred patients to a symptom management guide.

Main Research Variables: Trial arm; summed severity scores; interference-based severity categories at intake, 10 weeks, and 16 weeks; site; and stage of cancer.

Findings: Each arm produced a reduction in severity at 10 and 16 weeks with no differences between arms. In the per-protocol analyses, symptoms reported at the first contact required more time to resolve. Older patients exposed to the nurse arm resolved in fewer contacts.

Conclusions: The intention-to-treat analyses indicated that both arms were successful but offered few insights into how symptoms or patients influenced severity. Per-protocol analyses (intervention and dose), when, and which strategies affected symptoms.

Implications for Nursing: Each analytical strategy serves a purpose. Intention-to-treat defines the success of a trial. Per-protocol analyses allow nurses to pose clinical questions about response and dose of the intervention. Nurses should participate in analyses of interventions to understand the conditions where interventions are successful.

Among patients with cancer undergoing chemotherapy, the occurrence and severity of symptoms are important indicators of adverse events as well as of compromises in the quality of patients' lives. National cooperative groups and community clinical oncology programs have focused on pharmacologic approaches to symptom management, whereas support for nonpharmacologic trials has been confined largely to the National Institutes of Health (NIH) R01 and R21 research project grant mechanisms (Buchanan, O'Mara, Kelaghan, & Minasian, 2005; Minasian et al., 2007; Sloan, Cella, & Hays, 2005). Cleeland (2007) defined cancer symptom burden as the sum of all symptoms reported by patients. He argued that reducing symptom burden is important, even if improved overall quality of life cannot be achieved.

The goals of this article are to present data from a two-arm trial to determine whether a nurse-directed cognitive behavioral approach to symptom management that tailored intervention strategies to patients around education, counseling, support, reframing, and rehearsal produced significant reductions in symptom severity, compared with an education information arm delivered by a non-nurse coach prepared with a master's degree in the social sciences.

In previous work, elaborate cognitive behavioral models proved significantly more effective in reducing symptom severity compared with conventional care alone (Given et al., 2004b; Miaskowski, Dodd, & Lee, 2004). However, when compared with alternative approaches, most notably education information strategies, cognitive behavioral models appeared no more effective (Jacobsen et al., 2002; Newell, Sanson-Fisher, & Savolainen, 2002; Yates et al., 2005). Therefore, a comparison of two approaches guided the design, implementation, and analysis of this trial.

To establish that a novel intervention reduces total symptom severity burden, a summary measure of symptom severity is required, and analysis must follow an intention-to-treat approach. However, a composite measure of symptom burden summarized as a single