Defining the Symptom Cluster: How Far Have We Come?

Andrea Barsevick

Objectives: *To examine the evolution of the concept of the symptom cluster through literature synthesis and identify knowledge gaps.*

Data Sources: *Published literature.*

Conclusion: *A robust body of research has developed showing that clusters of symptoms can be identified empirically with modest evidence of convergence across methods. The science would benefit from a coordinated effort of qualitative studies to ensure that appropriate symptoms are evaluated; empirical symptom cluster identification studies building upon qualitative work; and subgroup identification studies based on empirically defined symptom clusters.*

Implications for Nursing Practice: *Work is needed to demonstrate the value of symptom cluster identification in guiding symptom assessment and management for cancer patients and survivors.*

Key Words: *symptom cluster, cancer, cancer-related symptoms.*

Following the University of California, San Francisco (UCSF) Symptom Management Group challenge to consider the concept of the "symptom cluster,"[1] and a state-of-the-science lecture and paper on the symptom cluster in cancer,[2] more recent publica-

Andrea Barsevick, PhD, RN, AOCN®, FAAN: *Professor, Thomas Jefferson University, Department of Medical Oncology, Sidney Kimmel Cancer Center, Philadelphia, PA.*

Address correspondence to Andrea Barsevick, PhD, RN, AOCN®, FAAN, 834 Chestnut Street, Suite 314, Philadelphia, PA 19107. e-mail: *andrea.barsevick@ jefferson.edu*

tions have examined conceptual and methodological issues in defining symptom clusters.[3-12] For this article, a literature search of PubMed from 2008 to 2015 was conducted and reference lists of relevant publications were also scanned for additional publications. This article examines the evolution over the past 10 years of the concept of the symptom cluster, including its definition, related theoretical concepts, and methods of identification. The literature is synthesized and knowledge gaps are assessed as a basis for future research.

Definition of a Symptom Cluster

A symptom cluster has been defined as a stable group of concurrent symptoms that are related to

one another and distinct from other symptom clusters.[13] Symptoms in a cluster may be related through a common etiology or mechanism, shared variance, or a common outcome.[3] Stability of clusters could relate to the consistency of results across clustering techniques, consistency within cancer populations, or stability over time. To date, no firm conclusions have been drawn about the minimum number of symptoms required to form a cluster; two[1,14] or three symptoms[13] have been proposed. The dictionary defines a cluster as "a number of similar thing that occur together."[15] The actual number of things required is not specified; however, the use of the word "group" carries the implication that it is more than two.

However, there are arguments in favor of including symptom pairs in the definition of a symptom cluster. In two clinical studies in advanced cancer patients, a gastrointestinal (GI) symptom cluster was determined to be made up of two symptoms, nausea and vomiting.[16,17] In a large sample of advanced cancer patients, anxiety-depression was identified as a cluster across three different methods of analysis.[18,19] Given the presence of clinically and statistically meaningful symptom pairs and the potential for others, it makes sense to include symptom pairs in the definition of a symptom cluster. Another reason to consider symptom pairs as clusters is that the number and type of symptoms observed in a cluster is reflective of the number and type of symptoms that were measured. Measuring a larger number of related symptoms is likely to increase the number of symptoms included in a particular cluster. When fewer symptoms are measured, a symptom pair could be a proxy for a cluster with more symptoms. Including symptom pairs in the definition of a cluster provides an opportunity for a more complete description of symptom clusters in a specific context.

On the other side of this issue are questions about when a symptom cluster should be considered complete. As noted above, one determinant of the number of symptoms comprising a cluster is the number and relevance of the symptoms that are measured. Other determinants include characteristics of specific cancers (such as, cough and breathlessness associated with lung cancer),[20,21] treatment modalities (neuropathy related to neurotoxic chemotherapy), and demographics (a body image cluster in women with gynecologic cancers).[22] Acknowledging these influences, experts have begun to advocate for agreement about a core set of symptoms to be measured across all patients,[23,24] as well as consideration of symptom clusters specific to disease[25,26] and treatment types.[27] This topic is described more fully in the article on assessment of multiple co-occurring symptoms by Cooley and Siefert elsewhere in this issue.

RELATED THEORETICAL CONCEPTS

Across symptom management theories and models, the addition of the concepts of interaction,[28] time,[29] and mechanism[30] have proven to be important constructs guiding our scientific understanding of the symptom cluster. As the science of symptom management has developed, the theories and models used to describe symptom clusters have expanded to incorporate explicit components. The Theory of Symptom Management originally proposed three components: the symptoms experience (addressing single or multiple symptoms); symptom management; and outcomes.[1] This theory later was expanded to include personal, health-illness, and environmental contexts of symptoms.[31] The Theory of Unpleasant Symptoms explicitly described the potential for interaction and/or synergy among multiple symptoms.[28] Through a linear presentation of antecedents, symptoms, and outcomes, it suggested but did not explicitly identify a time component. Later theoretical models expanded the time component, recognizing that symptoms can vary considerably over time and that variability in one symptom can influence other symptoms.[32,33] One model, The Symptom Interaction Framework, explicitly identified underlying symptom "mechanisms" to describe alterations in process or function that could explain the presence of a group of symptoms;[30] mechanisms could be biological, psychological, social, or behavioral.

METHODS OF IDENTIFICATION OF SYMPTOM CLUSTERS

Qualitative methods allow for the exploration of the breadth and complexity of related symptoms. Four qualitative studies identified symptom clusters (Table 1).[20-22,34] Women with gynecologic cancers identified the symptoms of tiredness, sleeplessness, pain, depression, and weakness as the most common cluster experienced by all participants over 1 year, irrespective of treatment.[22] Three other