

**Original Article**

# Symptoms and Problem Clusters in Cancer and Non-Cancer Patients in Specialized Palliative Care—Is There a Difference?

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**Abstract**

**Context.** In clinical practice, some symptoms and problems frequently occur in combination, which may have consequences for symptom management.

**Objectives.** Facing a growing number of non-cancer patients in palliative care, this study aimed to differentiate symptom clusters in the non-cancer population from those in cancer patients.

**Methods.** Inpatient data from the German Hospice and Palliative Care Evaluation between 2007 and 2011 were used for a cluster analysis of a 16-item symptom and problem checklist. An agglomerative hierarchical method was chosen. Coefficients from distance matrix ranging between 0 and 1 were calculated to indicate the interrelationship of clustered symptoms.

**Results.** The analysis identified five clusters in cancer patients: 1) nausea and vomiting ( $d = 0.000$ ); 2) anxiety, tension, and feeling depressed ( $d = 0.125$ ); 3) wound care and disorientation/confusion ( $d = 0.229$ ); 4) organization of care and overburdening of family ( $d = 0.202$ ); and 5) weakness, tiredness, need for assistance with activities of daily living, and loss of appetite ( $d = 0.207$ ). Five comparable clusters were identified in non-cancer patients: 1) nausea and vomiting ( $d = 0.000$ ); 2) anxiety, tension, and feeling depressed ( $d = 0.166$ ); 3) organization of care and overburdening of family ( $d = 0.187$ ); 4) weakness and need for assistance with activities of daily living ( $d = 0.139$ ); and 5) tiredness and loss of appetite ( $d = 0.182$ ).

**Conclusion.** As symptom clusters do not significantly differ between cancer and non-cancer patients, specific frequent symptoms in non-cancer patients should be assessed. Identification of symptom clusters may help to target therapies and focus the use of medications to improve patients' quality of

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### Key Words

Cluster analysis, symptoms, problems, cancer, non-cancer, palliative care

## Introduction

The majority of patients receiving specialized inpatient palliative care suffer from numerous and complex symptoms and problems caused by their advanced terminal illness. The relief of these symptoms is one key target of palliative and hospice care.<sup>1</sup> Although patient symptoms should be considered individually, single symptoms may be not only seen as isolated problems but integrated into groups of symptoms, the so-called clusters.<sup>2</sup> There has been a growing interest in the method of clustering symptoms during the last decades. Whereas 777 citations on the search term *cluster analysis* are found in PubMed in 1990, at least 7882 citations may be found in 2012. Clusters are defined as at least two or more related symptoms forming a stable and independent group from other symptom clusters.<sup>3</sup>

The existence of symptom clusters is clearly reflected in clinical practice, where some symptoms do often appear together, and these symptoms seem to have a special interdependence regarding their incidence. Statistically defined symptom clusters are identified using cluster analysis from large data sets. These data sets are obtained by systematic assessment of multiple symptoms.

Thus far, several experiences with symptom clustering in patients with advanced disease have been reported internationally. These analyses often use data from symptom assessment tools such as the Edmonton Symptom Assessment Scale (ESAS)<sup>4</sup> but have significant drawbacks in identification of valid clusters because of the limited symptom content of the tools. The most common clusters found in cancer patients comprise, for example, fatigue and drowsiness supplemented depending on publication to decreased appetite, dyspnea, pain or nausea.<sup>5–8</sup> Anxiety and depression were clustered and completed by pain or sleep problems/insomnia.<sup>5–11</sup> Another cluster was found for pain and fatigue,<sup>9,12</sup> and depression

and pain (complemented by anxiety).<sup>6,7,9</sup> In addition, nausea and vomiting were allocated to clusters empirically<sup>9–11,13,14</sup> and, in some research attempts, complemented by appetite loss.<sup>14</sup> Comparable symptom clusters were found in a first analysis of patients suffering from non-cancer diseases.<sup>15,16</sup> Within these clusters, there may be differences caused by methodological aspects<sup>9</sup> such as study design, number of assessed symptoms, and definition of clusters<sup>17</sup>; different care settings of different countries<sup>18</sup>; or other factors. These statistically identified, but common, symptom clusters can be recognized easily from clinical practice in palliative and hospice care.

Caregivers of any profession might consider the whole set of symptoms and their adequate evaluation, diagnosis, and treatment if a patient currently suffers from just one of the representatives of the symptom cluster. Nevertheless, in clinical practice, a subgroup of patients will not have additional symptoms or only some of the symptoms within a cluster. Single symptoms do not function as sentinel symptoms within a specific cluster, as presence of one symptom does not necessarily mean that the other symptoms will be present.

The consideration of symptom clusters in individual patients is known to supplement information on quality of life and even patient prognosis<sup>15</sup>; for example, there is a correlation between lower quality of life and the incidence of the symptom cluster pain, depression, and anxiety.<sup>7</sup> This indeed emphasizes the importance of analyzing common symptom clusters.

In research, using symptom clustering might help discover associations of different symptoms, although not causation, which also could be important for clinical practice and attempts to standardize treatment strategies for single symptoms and symptom clusters.

Until now, relevant end-of-life studies dealing with symptom clustering have concentrated on patients with advanced cancer in the very late

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