

Common and Co-Occurring Symptoms Experienced by Patients With Gastric Cancer

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PROBLEM IDENTIFICATION: Patients with gastric cancer experience multiple disease- and treatment-related symptoms. The purpose of this review was to describe the common and co-occurring symptoms experienced by patients with gastric cancer.

LITERATURE SEARCH: Search terms, such as *gastric cancer*, *symptoms*, and *experience*, were used to search PubMed®, CINAHL®, and PsycINFO® for empirical papers published from January 1990 to July 2019.

DATA EVALUATION: The search yielded 1,259 articles; 25 studies (21 observational and 4 interventional) were included in this review. Each study was systematically evaluated.

SYNTHESIS: The most common symptoms were categorized into physical and affective/cognitive domains. Three to 17 (median = 7) symptoms occurred concurrently. The severity of most symptoms was reported as mild to moderate. However, patients experienced varying levels of symptom severity following treatment trajectories. Older age, female gender, advanced cancer stage, low socioeconomic status, and total gastrectomy were associated with a greater number and severity of symptoms.

IMPLICATIONS FOR PRACTICE: Future research of symptom clusters may clarify the phenotypes and relationship between multiple co-occurring symptoms in patients with gastric cancer to develop targeted interventions that support symptom self-management for this population.

KEYWORDS gastric cancer; symptom; symptom experience; integrative review

ONF, 47(2), 187-202.

DOI 10.1188/20.ONF.187-202

Gastric (stomach) cancer was the fifth most frequently diagnosed cancer and the third leading cause of cancer deaths worldwide, with an estimated 1 million new cases and 783,000 deaths in 2018 (Bray et al., 2018). In the United States, an estimated 97,915 people were living with gastric cancer in 2015, with more than 26,240 estimated new cases and 10,800 estimated deaths in 2018 (Siegel et al., 2018). Patients diagnosed with gastric cancer have low five-year survival rates (10%–50%) because of advanced staging of disease at the time of diagnosis and the lack of effective treatments (Axon, 2006; Karimi et al., 2014; Venerito et al., 2018). People with gastric cancer experience multiple synergistic disease- and treatment-related symptoms. Investigators found that, on average, 10–15 of these symptoms occurred concurrently and included abdominal pain, weight loss, nausea, vomiting, dysphagia, dyspepsia, fatigue, and depression (Kim et al., 2016; Lee et al., 2016; Rausei et al., 2013). The undertreated symptoms can negatively influence patients' health outcomes, such as functional performance, psychological status, quality of life, and survival rate (Kim et al., 2017; Konishi et al., 2016; Maconi et al., 2003; Rausei et al., 2013).

Symptom science is one of the four identified themes in the National Institute of Nursing Research (NINR, 2016) Strategic Plan, and it is an essential component of the research programs that are supported by NINR and the National Cancer Institute. Scientists and clinicians emphasized the importance of symptom management in cancer survivorship as a future cancer research priority in the United States (Jaffee et al., 2017). In addition, a new *Symptom Science Center: A Resource for Precision Health* was established by NINR (2019) in June; it emphasized the underlying mechanisms of multiple symptoms and developed personalized approaches for symptom management.

Understanding patients' experience with co-occurring symptoms and their trajectories and predictors is critical to ensure appropriate assessment, education, and symptom management (Hockenberry et al., 2017; Miaskowski et al., 2004; National Institutes of Health State-of-the-Science Panel, 2004). For example, pain, fatigue, and sleep disturbance were experienced concurrently by breast cancer survivors and managed effectively through a mind-body intervention (Kwekkeboom et al., 2010).

Multiple co-occurring symptoms have been identified in patients with breast (Bower, 2008; Tchen et al., 2003), lung (Cooley, 2000; Wong et al., 2017), prostate (Talcott et al., 2003), colorectal (Pettersson et al., 2014), and pancreatic (Burrell et al., 2018a, 2018b) cancers, and leukemia (Albrecht, 2014). However, there is limited evidence of the common symptoms (symptoms frequently occur) and co-occurring symptoms (symptoms occur at the same time) experienced by patients with gastric cancer, which is required to build symptom science in gastric cancer.

The purposes of this literature review were to describe the common and co-occurring symptoms experienced by patients with gastric cancer, and to synthesize symptom profiles (i.e., measurement, predictors, trajectories, and management) to create a comprehensive understanding of the state of the science on symptoms in patients with gastric cancer and inform future nursing research and practice for this population.

Methods

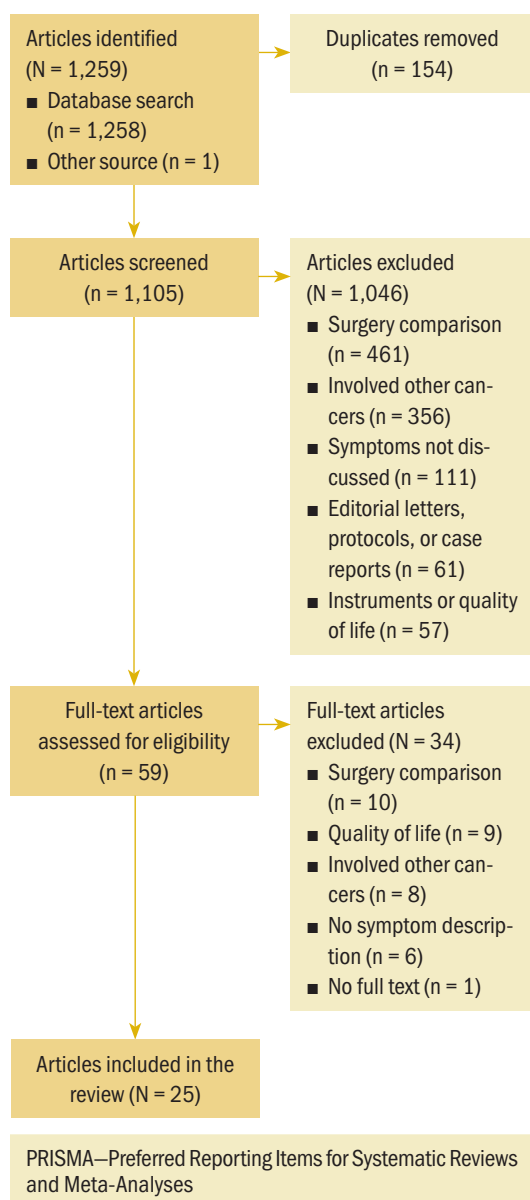
Literature Search

To understand the complexity of symptom science in patients with gastric cancer, the first author (Y.L.) conducted a comprehensive search of PubMed® (MEDLINE®), CINAHL®, and PsycINFO® for empirical papers published from January 1990 to July 2019. This date range was chosen because symptom-related studies in gastric cancer began to appear in 1990. Search terms *stomach neoplasms*, *stomach*, *gastric cancer*, *neoplasm*, *tumor*, and *tumour* were combined with *symptoms*, *symptoms and signs*, *symptom assessment*, *quality of life*, and *experience* to elicit relevant literature. The article selection process is shown in Figure 1.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: studies involving symptoms experienced by people with gastric cancer; studies that considered the measurement, predictors, trajectories, and management of symptoms; reviews, systematic reviews, and meta-analyses; and published in English. The following were the exclusion criteria: editorial letters, comments, unpublished manuscripts, research protocols, and case reports; studies that did not report symptoms in their findings; studies that involved other cancer populations; studies that discussed only quality of life; and studies in which symptoms were a secondary outcome to a surgical procedure or medication trial (because these studies did not specifically describe patients'

FIGURE 1. PRISMA Flowchart of Search Strategy and Selection



experience with symptoms). The search yielded 1,259 primary research studies; 25 studies were included.

Data Evaluation

Data were evaluated using the hierarchy of evidence described by Melnyk and Fineout-Overholt (2011). The levels of evidence for this review consist of level II (high quality) to level VI (low quality); level II is evidence from well-designed randomized controlled trials, level III is evidence from well-designed controlled trials without randomization, level IV is evidence from well-designed case-control and cohort studies, and level VI is evidence from single descriptive or qualitative studies. For the included studies, the majority of studies ($n = 20$, 80%) were level VI, three were level II, one was level III, and one was level IV (see Table 1). The level of evidence for the body of literature was low quality. Data were extracted using the matrix method, which involves reading the documents, listing important issues, and selecting and adding column topics (Garrard, 2014).

Results

Characteristics of the Studies

Twenty-five articles were included in this integrative review. All articles used quantitative methodologies; four articles were interventional studies, and the remainder ($n = 21$) were observational studies. Among the 20 quantitative descriptive studies, 16 reported cross-sectional data and 4 reported longitudinal data. One study used a cohort study design (Hu et al., 2018). The sample sizes ranged from 19 to 28,753 (median = 124). Studies originated from 11 countries or districts, including Korea ($n = 10$), Japan ($n = 4$), China ($n = 3$), Sweden ($n = 1$), Norway ($n = 1$), Spain ($n = 1$), United Kingdom ($n = 1$), Iran ($n = 1$), India ($n = 1$), Israel ($n = 1$), and Taiwan ($n = 1$). More than half (52%) of these studies were published in the past five years. Ten studies reported individual symptoms, and 15 reported multiple co-occurring symptoms.

Common and Co-Occurring Symptoms

The most frequent symptoms were categorized into physical symptoms (i.e., gastrointestinal [GI], fatigue, weight loss, and sleep disturbance), and affective/cognitive symptoms (i.e., anxiety, depression, post-traumatic stress disorder, and delirium). Patients with gastric cancer experienced multiple co-occurring symptoms at varying points before, during, and after treatment. Three to 17 symptoms (median = 7) were reported to occur concurrently in 15 studies.

Based on the Symptoms Experience Model (Armstrong, 2003), the studies were conceptually organized into four dimensions: occurrence, severity, frequency, and distress. All articles reported the occurrence of symptoms; seven studies reported symptom severity using different measures (Cho, 2004; Gunji et al., 2013; Han et al., 2013; Haugstvedt et al., 1991; Nikbakhsh et al., 2016; Park et al., 2015; Yu et al., 2016); three studies reported symptom frequency (Maeda et al., 2006; Maeda & Munakata, 2008; Zhou et al., 2017); and two articles assessed symptom distress (Hong et al., 2015; Kim et al., 2017). Not all study reports of common symptoms described all four dimensions of symptom experience; most reported one to two dimensions.

GI symptoms: GI symptoms were the most frequently occurring symptoms among gastric cancer survivors. Eight studies reported that patients experienced a wide range of GI symptoms. A retrospective study in a sample of 158 gastric cancer survivors showed that abdominal pain (61%) was the most common GI symptom reported by patients, followed by nausea (40%), early satiety and poor appetite (35%), vomiting (21%), dysphagia (18%), and melaena (16%) (Barad et al., 2014). Mine et al. (2010) conducted a cross-sectional study among 1,153 patients with gastric cancer and found that the occurrence of GI symptoms included abdominal pain or fullness (47%), diarrhea (38%), and nausea/vomiting (20%). Together, these results indicate that abdominal pain is the most prevalent of GI symptoms. Other common GI symptoms include nausea, vomiting, diarrhea, constipation, dysphagia, and reflux (Anderson & MacIntyre, 1995; Maeda et al., 2006; Maeda & Munakata, 2008; Oh et al., 2018; Zhou et al., 2017).

Fatigue: Three studies described fatigue among patients with gastric cancer. The prevalence ranged from 21% (Park et al., 2015) to 51% (Hwang et al., 2014). Park et al. (2015) reported that the mean fatigue severity score was 2.728 (SD = 1.441), as measured by the Fatigue Severity Scale (score range = 1–7), which indicated a moderate level of fatigue. In a study of 254 patients who underwent gastrectomy, Yu et al. (2016) reported mild levels of fatigue severity at baseline and five years after surgery. Therefore, the occurrence of fatigue was moderate and the severity was mild among patients with gastric cancer.

Weight loss: Weight loss was prevalent in patients with gastric cancer. The occurrence of weight loss was described in three studies as ranging from 60% (Barad et al., 2014; Climent et al., 2017) to 70% (Haugstvedt et

TABLE 1. Main Findings of the Included Studies for Integrative Review (N = 25)

Study and Location	Sample	Design and Level of Evidence	Measurement	Findings (Symptom Profiles)
Anderson & MacIntyre, 1995 (United Kingdom)	57 consecutive patients undergoing standard resection	Prospective cross-sectional study; level VI	Checklist of symptoms	<ul style="list-style-type: none"> ■ Number: 6 ■ Occurrence: abdominal pain, nausea, vomiting, dyspepsia, fullness, and dysphagia
Barad et al., 2014 (India)	158 patients with primary GC (age range = 28–91 years) undergoing surgery	Retrospective cross-sectional study; level VI	Checklist of symptoms	<ul style="list-style-type: none"> ■ Number: 7 ■ Occurrence: vague abdominal discomfort (61%), WL (60%), nausea (40%), early satiety and poor appetite (35%), vomiting (21%), dysphagia (18%), and melena (16%)
Cho, 2004 (Korea)	103 paired samples of patients with GC (\bar{X} age = 52.29 years, SD = 10.07) receiving chemotherapy and their family caregivers	Prospective cross-sectional study; level VI	PSQI, CES-D, Lee Fatigue Scale, Brief Pain Inventory, and Quality of Life–Cancer	<ul style="list-style-type: none"> ■ Number: 4 ■ Occurrence: sleep disturbance (50%), depression (53%), pain (28%), and fatigue ■ Severity: Average sleep quality = 2.6 (fair); mean global PSQI = 6.92 (SD = 1.45); mean falling asleep time = 22.96 minutes (SD = 19.98); average hours of sleep = 6.74 (SD = 1.45); mean fatigue score = 4.6 (SD = 1.94); mean depression score = 16.57 (SD = 9.12) ■ Predictors: Depression was associated with sleep disturbance ($p < 0.05$); fatigue was not ($p > 0.05$).
Climent et al., 2017 (Spain)	76 patients undergoing curative GC resection without recurrence	Prospective longitudinal study; level VI	WL, EORTC QLQ-C30, and EORTC QLQ-STO22	<ul style="list-style-type: none"> ■ Occurrence: WL $\geq 10\%$ at 2 years ($n = 51, 67\%$) ■ Predictors: Persistent pain, diarrhea, and N/V were associated with WL at 2 years after surgery ($p < 0.05$); lower quality of life was also associated with WL at 2 years after surgery ($p < 0.05$).
Gunji et al., 2013 (Japan)	19 patients with stage I–II cancer; proximal gastrectomy at least 6 months prior; median age = 73 years (range = 59–79)	Quasiexperimental study of 4-week rikkunshito after surgery; level III	GSRS and VAS	<ul style="list-style-type: none"> ■ Number: 7 ■ Occurrence: GI symptoms (reflux, abdominal pain, ingestion, diarrhea, and constipation), WL, and appetite loss ■ Severity: body weight (56.8 kg versus 57.2 kg, $p < 0.05$), GI symptoms scores (2.2 versus 2.1, $p > 0.05$) at baseline and after treatment, respectively ■ Management: rikkunshito (Japanese medicine)
Guo & Wang, 2018 (China)	124 patients with advanced GC receiving chemotherapy	Randomized controlled trial of NES for chemotherapy-induced N/V; level II	VAS, MD Anderson Symptom Inventory, and KPS	<ul style="list-style-type: none"> ■ Number: 3 ■ Occurrence: nausea, vomiting, and loss of appetite ■ Management: NES reduced nausea ($p = 0.02$) and vomiting ($p = 0.04$) severity and improved appetite loss ($p = 0.02$) compared to the control group.
Han et al., 2013 (Korea)	391 disease-free stage I–III GC survivors with a mean age of 55 years (SD = 10.6); at least 1 year after surgery	Prospective cross-sectional study; level VI	Beck Depression Inventory (0–63), EORTC QLQ-C30, and EORTC QLQ-STO22	<ul style="list-style-type: none"> ■ Number: 4 ■ Occurrence: depression ($n = 172, 44\%$), fatigue, dyspnea, and sleep disturbance ■ Severity: mean depression score = 13.3 (SD = 8.7) ■ Predictors: Lower income (OR = 2.49, 95% CI [1.64, 3.78]); problems with care pretreatment (OR = 1.92, 95% CI [1.23, 2.98]); body image change (OR = 2.23, 95% CI [1.41, 3.53]); and fatigue, dyspnea, and sleep disturbance were associated with depression.

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TABLE 1. Main Findings of the Included Studies for Integrative Review (N = 25) (Continued)

Study and Location	Sample	Design and Level of Evidence	Measurement	Findings (Symptom Profiles)
Haugstvedt et al., 1991 (Norway)	855 patients with GC in 51 surgical units; undergoing surgery, chemotherapy, or RT	Prospective cross-sectional multicenter study; level VI	WL	<ul style="list-style-type: none"> ■ Occurrence: WL from diagnosis to admission (n = 596, 70%) ■ Severity: 11-pound median loss (range = 0–79), 3-pound median loss per month (range = 0–26) ■ Predictors: Older age, advanced stage, lower functional status, tumor type (diffused), and tumor location (cardia) were associated with increased WL (p < 0.05).
Hong et al., 2015 (China)	165 patients with GC without recurrence and metastasis with a mean age of 62 years (SD = 8.82); no treatment within 3 months after diagnosis	Prospective cross-sectional correlational study; level VI	DT, EORTC QLQ-STO22 (revised Chinese version), and Cancer Coping Modes Questionnaire	<ul style="list-style-type: none"> ■ Number: 10 ■ Occurrence: The top five symptoms were pain (62%), worry (61%), indigestion (59%), fatigue (58%), and eating restriction (58%). ■ Distress: psychological distress (scored ≥ 4, n = 127, 77%); \bar{X} DT score = 5.13 (SD = 2.39, range = 0–10) ■ Predictors: Psychological distress was correlated with abdominal pain, eating restrictions, and anxiety (p < 0.05).
Hu et al., 2018 (Taiwan)	28,753 patients newly diagnosed with GC (median age = 69 years, range = 55–77) undergoing surgery, chemotherapy, or RT; 28,753 matched patients	Retrospective cohort study; level IV	International Classification of Diseases, 9th Revision, Clinical Modification codes	<ul style="list-style-type: none"> ■ Occurrence: depression (n = 670, 9.1 per 1,000 person-years) in the GC cohort higher compared to the matched cohort (aOR = 1.54, 95% CI [1.39, 1.7]) ■ Predictors: Female gender (HR = 1.46, 95% CI [1.25, 1.7], p < 0.01) and hypertension (HR = 1.27, 95% CI [1.07, 1.52], p < 0.01) were associated with depression.
Hwang et al., 2014 (Korea)	374 patients with stage I–III GC undergoing surgery, chemotherapy, or RT	Prospective cross-sectional study; level VI	Brief Fatigue Inventory, EORTC QLQ-C30, EORTC QLQ-STO22, and Beck Depression Inventory	<ul style="list-style-type: none"> ■ Occurrence: fatigue (n = 192, 51%) ■ Predictors: Female gender, low economic status, rural residence, current smoker, lower functional status, depression, early cancer stage, and TG were associated with fatigue (p < 0.05).
Hwang et al., 2018 (Korea)	163 patients with GC who were scheduled for curative resection; measured preoperatively and at 1, 2, 3, and 7 days after surgery	Prospective longitudinal study; level VI	DRS-R-98, Mini-Mental State Examination, HADS, and PSQI	<ul style="list-style-type: none"> ■ Occurrence: delirium (n = 1, 0.6%) and subsyndromal delirium (n = 19, 12%) ■ Trajectories: DRS-R-98 scores were generally highest the first day after surgery then gradually decreased. ■ Predictors: Older age (OR = 3.85, 95% CI [1.36, 10.92], p < 0.05) and low education level (OR = 3.98, 95% CI [1.39, 11.41], p < 0.05) were risk factors of subsyndromal delirium.
Jeong & An, 2017 (Korea)	52 pairs of patients with GC and their family caregivers; at least 1 month after surgery	Prospective cross-sectional study; level VI	HADS and Duke-University of North Carolina Functional Social Support Questionnaire	<ul style="list-style-type: none"> ■ Occurrence: depression and anxiety ■ Predictors: Socioeconomic status and social support were associated with depression and anxiety (p < 0.05).

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TABLE 1. Main Findings of the Included Studies for Integrative Review (N = 25) (Continued)

Study and Location	Sample	Design and Level of Evidence	Measurement	Findings (Symptom Profiles)
Kim et al., 2017 (Korea)	229 patients with GC; median age of 56 years (range = 20–86); undergoing surgery, chemotherapy, or RT	Prospective cross-sectional study; level VI	HADS and CES-D	<ul style="list-style-type: none"> ■ Number: 3 ■ Occurrence: sleep disturbance (22%), anxiety (30%), and depression (30%) ■ Distress: PD (n = 77, 34%) ■ Predictors: Lower education level (p < 0.05) and advanced stage (p < 0.01) were associated with PD.
Liedman et al., 2001 (Sweden)	32 patients undergoing gastric resection	Prospective cross-sectional study; level VI	GSRS, Sick Impact Profile, Body Symptom Scale, Comprehensive Psychopathological Rating Scale, Mood Adjective Check List, and KPS	<ul style="list-style-type: none"> ■ Number: 7 ■ Occurrence: GI symptoms (abdominal pain, reflux, indigestion, diarrhea, and constipation), WL, and loss of appetite ■ Predictors: Patients with good appetite had fewer GI symptoms (p < 0.05) and less fatigue and anxiety (p < 0.05). Those who had reconstruction had fewer GI symptoms (p < 0.05) in the long term.
Maeda et al., 2006 (Japan)	82 patients receiving gastrectomy with a mean age of 64 years (SD = 10.2) with no indication of recurrence; had surgery within the past 3 years	Prospective cross-sectional correlational study; level VI	Checklist of symptoms, SDS, self-repression scale, interpersonal dependency scale, self-esteem scale, and emotional support scale	<ul style="list-style-type: none"> ■ Number: more than 8 ■ Occurrence: depression, GI symptoms (heartburn, abdominal pain, nausea, diarrhea, bloating, belching), and others ■ Frequency: postoperative symptoms frequency, mainly sometimes (48%) ■ Predictors: Interpersonal dependency, emotional support, and marital status had indirect effect on depression; self-esteem had direct effect (p < 0.001).
Maeda & Munakata, 2008 (Japan)	82 patients receiving gastrectomy with a mean age of 64 years (SD = 10.2) with no indication of recurrence; had surgery within the past 3 years	Prospective cross-sectional correlational study; level VI	Checklist of symptoms, checklist of eating habits, emotional support scale, and SDS	<ul style="list-style-type: none"> ■ Number: more than 8 ■ Occurrence: postoperative symptoms (e.g., diarrhea [30%], belching [28%], heartburn [15%]), depression, and others ■ Frequency: postoperative symptoms frequency: rare (29%), sometimes (48%), often (10%), and very often (13%) ■ Predictors: Marital status ($\beta = -0.32$) and depression ($\beta = 0.21$) were associated with frequency (p < 0.05). Health status and eating habits were not associated with occurrence (p > 0.05).
Mine et al., 2010 (Japan)	1,153 patients who had undergone gastrectomy without a sign of recurrence or metastasis after surgery; 6–66 months after surgery	Prospective cross-sectional study; level VI	VAS and dumping syndrome questionnaire (13 symptoms)	<ul style="list-style-type: none"> ■ Number: 13 ■ Occurrence: EDS symptoms: abdominal pain or fullness (47%), diarrhea (38%), faintness (22%), N/V (20%), palpitations (16%), cold sweats (13%), and flushing (8%); LDS symptoms: hunger (21%), faintness (21%), dizziness (14%), cold sweats (10%), tremors (10%), and loss of consciousness (2%); occurrences of EDS and LDS: 68% and 38%, respectively. ■ Predictors: EDS was associated with WL, younger age, and TG (p < 0.05). LDS was associated with WL, female gender, and TG (p < 0.05).

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TABLE 1. Main Findings of the Included Studies for Integrative Review (N = 25) (Continued)

Study and Location	Sample	Design and Level of Evidence	Measurement	Findings (Symptom Profiles)
Nikbaksh et al., 2016 (Iran)	30 (15 experimental, 15 control) patients with GC receiving chemotherapy (measured at the 4th and 8th week after treatment)	Randomized clinical trial of olanzapine in GC survivors receiving chemotherapy; level II	HADS, World Health Organization Quality of Life–Brief, Rhodes index	<ul style="list-style-type: none"> ■ Number: 5 ■ Occurrence: nausea, vomiting, loss of appetite, anxiety, and depression ■ Severity: anxiety (\bar{X} = 6.73, SD = 2.76 versus \bar{X} = 12.2, SD = 5.43) and depression (\bar{X} = 6.53, SD = 3.92 versus 10, SD = 5.38) in the experimental and control groups, respectively ($p < 0.05$). ■ Trajectories: Anxiety and depression had a rising trend from beginning to 8th week in the control group and a decreasing trend in the experimental group. ■ Management: olanzapine
Oh et al., 2018 (Korea)	100 patients who underwent gastrectomy for GC with an average age of 58.5 years (range = 52.3–67)	Prospective cross-sectional study; level VI	Laboratory examinations: endoscopic examination, messenger RNA expression, and polymerase chain reaction	<ul style="list-style-type: none"> ■ Occurrence: GI symptoms (esophageal reflux symptom [47%], early satiety, bloating, abdominal discomfort) ■ Predictors: postoperative duration, H+/K+-ATPase mRNA expression level and gastroesophageal flap valve disruption were associated with esophageal reflux symptom ($p < 0.05$).
Palgi et al., 2011 (Israel)	123 outpatients with stage I–IV GC; mean age of 57 years (SD = 12.7); undergoing surgery, chemotherapy, or RT	Prospective cross-sectional study; level VI	The short CES-D and the Post-Traumatic Stress Disorder Checklist–Civilian Version	<ul style="list-style-type: none"> ■ Occurrence: PTSD symptoms ■ Predictors: female gender, married status, and less social support were related to higher PTSD symptoms ($p < 0.05$). Risk of clinical level of PTSD increased the risk of clinical level of depression by 15 times (OR = 15.73, 95% CI [3.16, 78.32], $p < 0.01$).
Park et al., 2015 (Korea)	199 GC survivors without recurrence; mean age of 58 years (SD = 10.9); undergoing surgery, chemotherapy, or RT	Retrospective cross-sectional study; level VI	FSS and self-administered symptoms questionnaire (13 symptoms)	<ul style="list-style-type: none"> ■ Occurrence: fatigue (FSS ≥ 4, $n = 42$, 21%) ■ Severity: $\bar{X} = 2.728$, SD = 1.441 ■ Predictors: Arthralgia (aOR = 12.95, 95% CI [3.21, 52.34]), dyspnea (aOR = 10.54, 95% CI [2.94, 37.8]), dyspepsia (aOR = 8.25, 95% CI [2.63, 25.96]), changed bowel habits (aOR = 4.56, 95% CI [1.09, 19.11], and anemia (aOR = 3.18, 95% CI [1.26, 8.05]) were associated with fatigue. Regular exercise (aOR = 0.31, 95% CI [0.12, 0.77]) and advanced GC (aOR = 0.34, 95% CI [0.13, 0.89]) were associated with lower fatigue.
Shim et al., 2019 (Korea)	242 patients with GC admitted for resection surgery with a mean age of 62.05 years (SD = 10.6)	Prospective longitudinal study; level VI	DRS-R-98, FACT-Cog, Korean version of the Mini-Mental State Examination, and HADS; measured before and 1, 2, 3, and 7 days after surgery	<ul style="list-style-type: none"> ■ Occurrence: subsyndromal delirium, 22 patients (9%) at POD 1, 9 (4%) at POD 2, 7 (3%) at POD 3, and 5 (2%) at POD 7 ■ Trajectories: Delirium symptom severity declined over 3 days after surgery ($p < 0.001$). ■ Predictors: Older age and longer anesthesia time were associated with the higher initial level of delirium symptom severity ($p < 0.05$); a medication history for memory complaints and using propofol as an anesthetic agent were risk factors.

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TABLE 1. Main Findings of the Included Studies for Integrative Review (N = 25) (Continued)

Study and Location	Sample	Design and Level of Evidence	Measurement	Findings (Symptom Profiles)
Yu et al., 2016 (Korea)	254 patients who underwent a curative gastrectomy for primary GC with a mean age of 55 years (SD = 10.7)	Prospective longitudinal study; level VI	EORTC QLQ-C30 and EORTC QLQ-STO22; measured preoperatively and 1, 2, 3, 4, and 5 years after surgery	<ul style="list-style-type: none"> ■ Number: 17 ■ Occurrence: fatigue, nausea, vomiting, pain, dyspnea, sleep disturbance, appetite loss, constipation, diarrhea, dysphagia, reflux, eating restriction, anxiety, dry mouth, taste, body image, and hair loss ■ Severity: The severity score of these symptoms ranged from 6.2–38.2 at 5 years after surgery. ■ Trajectories: Fatigue and anxiety increased significantly 1 year after surgery and then decreased gradually ($p < 0.001$). Dysphagia and eating restrictions increased 1 year after surgery ($p < 0.001$).
Zhou et al., 2017 (China)	56 (28 control, 28 experimental) patients with advanced GC with an average age of 57 years (range = 41–68); receiving standard chemotherapeutic regimen	Randomized controlled trial of 2-week acupuncture therapy during chemotherapy; level II	Self-reported symptoms questionnaire and World Health Organization Quality of Life questionnaire–100	<ul style="list-style-type: none"> ■ Number: 4 ■ Occurrence: nausea, vomiting, abdominal pain, and diarrhea ■ Frequency: nausea ($\bar{X} = 11$ minutes, SD = 3 versus $\bar{X} = 32$ minutes, SD = 5), vomiting ($\bar{X} = 2$ times, SD = 1 versus $\bar{X} = 4$ times, SD = 1), abdominal pain ($\bar{X} = 7$ minutes, SD = 2 versus $\bar{X} = 16$ minutes, SD = 5), and diarrhea ($\bar{X} = 1$ time, SD = 1, versus $\bar{X} = 3$, SD = 1) were in the experimental and control groups, respectively ($p < 0.05$). ■ Management: acupuncture therapy

aOR—adjusted odds ratio; CES-D—Center for Epidemiologic Studies–Depression; CI—confidence interval; DRS-R-98—Delirium Rating Scale–Revised–98; DT—distress thermometer; EDS—early dumping syndrome; EORTC QLQ-C30—European Organisation for the Research and Treatment of Cancer Quality-of-Life Questionnaire–Core 30; EORTC QLQ-STO22—European Organisation for the Research and Treatment of Cancer Quality-of-Life Questionnaire gastric module; FACT-Cog—Functional Assessment of Cancer Therapy–Cognitive; FSS—Fatigue Severity Scale; GC—gastric cancer; GI—gastrointestinal; GRS—Gastrointestinal Symptom Rating Scale; HADS—Hospital Anxiety and Depression Scale; HR—hazard ratio; KPS—Karnofsky Performance Status; LDS—late dumping syndrome; NES—Nerve Electrical Stimulation; N/V—nausea and vomiting; OR—odds ratio; PD—psychological distress; POD—postoperative day; PSQI—Pittsburgh Sleep Quality Index; PTSD—post-traumatic stress disorder; RT—radiation therapy; SDS—Self-Rating Depression Scale; TG—total gastrectomy; VAS—visual analog scale; WL—weight loss

Note. The number of symptoms is provided only for studies that described multiple co-occurring symptoms.

al., 1991). In addition, Haugstvedt et al. (1991) reported a median weight loss of 11 pounds (range = 0–79) from the time of diagnosis through admission, and the median loss of weight was 3 pounds per month following treatment (range = 0–26). These studies indicate a high level of weight loss occurrence and severity in patients with gastric cancer.

Sleep disturbance: Disturbance in sleep was found to be problematic in two studies of patients with gastric cancer. The rate of sleep disturbance was reported as 22% in a sample of 229 patients with gastric cancer (Kim et al., 2017). In a study by Nikbakhsh et al. (2016), using the Pittsburgh Sleep Quality Index (PSQI), the average sleep quality was rated as 2.6 (fair sleep), the average hours slept were 6.74 hours (SD = 1.45), and the average time to fall asleep was 22.96

minutes (SD = 19.98). This suggests that patients with gastric cancer experienced sleep disturbance, with lower than the nationally recommended seven to nine hours of sleep and a longer time to fall asleep (Hirshkowitz et al., 2015).

Anxiety and depression: Anxiety and depression were the most prevalent affective symptoms experienced by patients with gastric cancer. Four studies described anxiety and depression. Hu et al. (2018) conducted a large-scale cohort study of 28,753 patients who were newly diagnosed with gastric cancer and found that depression among the gastric cancer cohort was 1.5 times higher than the matched control cohort (adjusted odds ratio [OR] = 1.54, 95% confidence interval [CI] [1.39, 1.7], $p < 0.05$). In a cross-sectional study of 229 gastric cancer survivors,

Kim et al. (2017) reported anxiety (30%) and depression (30%) using a modified distress thermometer. The mean severity score of depression, assessed using the Beck Depression Inventory, was 13.3 (SD = 8.7), which indicated a mild level of severity (Han et al., 2013). Distress levels of anxiety and depression were reported to be as high as 77% in a study by Hong et al. (2015). In summary, these studies suggest that patients with gastric cancer experience anxiety and depression that is mild in severity but high in occurrence and distress.

PTSD: Cancer-related PTSD symptoms include feeling emotionally numb and feeling distant from other people (Palgi et al., 2011). In a cross-sectional study of 123 outpatients with stage I to III gastric cancer, investigators found an association between PTSD symptoms and depressive symptoms ($r = 0.474$, $p = 0.001$) (Palgi et al., 2011).

Delirium: Delirium was a neurocognitive symptom reported in two articles published by the same Korean research team. Hwang et al. (2018) reported that 19 patients (12%) with a mean age of 70.11 years (SD = 7.49) experienced postoperative subsyndromal delirium, measured by the Delirium Rating Scale-Revised-98 (DRS-R-98 = 8–14), and one patient (1%) experienced delirium (DRS-R-98 ≥ 15) in a sample of 163 participants; the severity of subsyndromal delirium was the highest on the first day after surgery and then gradually decreased. Shim et al. (2019) found that the occurrence of subsyndromal delirium was 9%, 4%, 3%, and 2% at 1, 2, 3, and 7 days after surgery, respectively, among 242 patients with gastric cancer (\bar{X} age = 62.05 years, SD = 10.6). The severity of subsyndromal delirium decreased at three days after surgery. Taken together, these results suggest that delirium is prevalent in those undergoing gastrectomy; its severity gradually decreased after surgery.

Synthesis of Symptom Profiles

The authors organized descriptions of the symptom profiles into four themes: symptom measurement, symptom predictors, symptom trajectories, and symptom management.

Symptom measurement: A range of instruments, with established validity and reliability, were used to measure symptoms in patients with gastric cancer. The most commonly used instruments for multiple co-occurring symptoms included the European Organisation for the Research and Treatment of Cancer Quality-of-Life Questionnaire-Core 30 (EORTC QLQ-C30) and its gastric module (EORTC QLQ-STO22), and the Gastrointestinal Symptom

Rating Scale. The use of self-designed questionnaires, which lacked established validity and reliability, was reported in a small number of studies (Anderson & MacIntyre, 1995; Park et al., 2015; Zhou et al., 2017). The remaining studies used non-disease-specific symptom instruments (i.e., PSQI and DRS-R-98) with established validity and reliability to evaluate a single symptom experienced by patients with gastric cancer (Hwang et al., 2018; Kim et al., 2017).

Symptom predictors: Predictors of symptoms varied by studies and types of symptoms. Table 2 summarizes associations between different symptoms among patients with gastric cancer. Older age, female gender, low socioeconomic status (SES), low social support, advanced cancer stage, and total gastrectomy were associated with a higher number and severity of symptoms. Older age was associated with weight loss (Haugstvedt et al., 1991) and subsyndromal delirium (Hwang et al., 2018), whereas female gender was related to fatigue (Hwang et al., 2014), anxiety and depression (Hu et al., 2018), and PTSD symptoms (Palgi et al., 2011). Four studies reported that lower SES was associated with depression and anxiety (Han et al., 2013; Jeong & An, 2017; Kim et al., 2017) and fatigue (Hwang et al., 2014). In addition, Liedman et al. (2001) and Hwang et al. (2014) both found that patients who had undergone total gastrectomy had more symptoms (i.e., GI symptoms and fatigue) than patients who had other types of surgery ($p < 0.05$). Advanced cancer stage was a risk factor that was associated with increased weight loss (Haugstvedt et al., 1991) and psychological distress (Kim et al., 2017). However, Hwang et al. (2014) and Park et al. (2015) found that advanced cancer stage was related to lower levels of fatigue. Therefore, it is difficult to draw a conclusion on predictors of a variety of symptoms.

Symptom trajectories: Symptoms experienced by patients with gastric cancer were found to change over time. Four prospective longitudinal studies reported findings related to the trajectories of symptoms (Hwang et al., 2018; Nikbakhsh et al., 2016; Shim et al., 2019; Yu et al., 2016). For example, Yu et al. (2016) measured symptoms yearly for five years after surgery and found that fatigue increased significantly at year 1 and then decreased gradually ($p < 0.001$). This study also reported that dysphagia and eating restrictions worsened at year 1 ($p < 0.001$) and were at higher levels at year 5 than preoperatively ($p < 0.001$). In addition, Hwang et al. (2018) reported that subsyndromal delirium severity was highest on the first day after surgery and then gradually

decreased in the following week ($p < 0.05$), whereas another study (Shim et al., 2019) found that the severity of subsyndromal delirium decreased over three days after surgery. Nikbakhsh et al. (2016) found that the severity of anxiety and depression increased from the beginning to the eighth week in the control group and decreased in the experimental group ($p < 0.05$). Together, these findings provide important insights into trajectories of common

symptoms with short-term (days) and long-term (years) observation.

Symptom management: Interventions have been developed and tested to help patients with gastric cancer self-manage their symptoms. Four studies examined the effects of complementary and alternative approaches and pharmaceutical therapy for the management of multiple symptoms in gastric cancer, and evaluated the feasibility and efficacy of

TABLE 2. Common and Co-Occurring Symptoms by Domain in Patients With Gastric Cancer

Symptom	Measurement	Predictor
Affective/cognitive symptoms		
Delirium/subsyndromal delirium	Delirium Rating Scale	Older age, low SES, longer anesthesia time, memory loss history, and using propofol
Depression/anxiety	Hospital Anxiety and Depression Scale and Distress Thermometer	Female gender, low SES, advanced cancer stage, hypertension, low social support, married status, and negative self-esteem; other symptoms (fatigue, dyspnea, sleep disturbance, body image change, abdominal pain, and eating restriction)
PTSD symptoms	PTSD Checklist	Female gender, married status, and low social support; depression
Physical symptoms		
GI symptoms: abdominal pain, nausea, vomiting, diarrhea, constipation, reflux, dysphagia, and loss of appetite	EORTC QLQ-C30, EORTC QLQ-STO22, and Gastrointestinal Symptom Rating Scale	Total gastrectomy and weight loss
Fatigue	Brief Fatigue Inventory and Fatigue Severity Scale	Female gender, low SES, rural residence, current smoker, early cancer stage, depression, total gastrectomy, and lack of regular exercise; other symptoms (arthralgia, dyspnea, dyspepsia, changed bowel habits, and anemia)
Sleep disturbance	Pittsburgh Sleep Quality Index	Depression
Weight loss	Body weight loss	Older age, advanced cancer stage, tumor type (diffuse), tumors location (cardia), and lower physical function; other symptoms (persistent pain, diarrhea, and nausea/vomiting)
EORTC QLQ-C30—European Organisation for the Research and Treatment of Cancer Quality-of-Life Questionnaire—Core 30; EORTC QLQ-STO22—European Organisation for the Research and Treatment of Cancer Quality-of-Life Questionnaire gastric module; PTSD—post-traumatic stress disorder; SES—socioeconomic status		

the interventions (Gunji et al., 2013; Guo & Wang, 2018; Nikbakhsh et al., 2016; Zhou et al., 2017). In a randomized controlled trial of nerve electrical stimulation treatment for chemotherapy-induced nausea and vomiting, Guo and Wang (2018) reported that the severity of nausea and vomiting decreased and loss of appetite improved significantly in 124 patients with advanced gastric cancer ($p < 0.05$). Similarly, another randomized controlled trial of acupuncture conducted by Zhou et al. (2017) found that the duration of nausea and abdominal pain and the frequency of vomiting and diarrhea were lower in the experimental group than in the control group ($p < 0.05$). In a quasiexperimental study of four-week rikkunshito (Japanese herbal therapy) administered after surgery, Gunji et al. (2013) found that the severity of abdominal pain, reflux, diarrhea, and constipation experienced by participants significantly decreased ($p < 0.01$). These results suggested that alternative therapies can decrease the severity and frequency of symptoms. In addition, in a randomized clinical trial of olanzapine among 30 patients with gastric cancer receiving chemotherapy (Nikbakhsh et al., 2016), the severity of anxiety and depression was lower in the experimental group compared to the control group ($p < 0.05$). In summary, three of four studies used different alternative therapies for GI symptom management, and one study effectively treated anxiety and depression using a pharmaceutical therapy.

Discussion

The purpose of this integrative review was to describe common and co-occurring symptoms and their symptom profiles, including measurement, predictors, trajectories, and management in patients with gastric cancer, and to address the state of symptom science in gastric cancer. The studies in this review were mainly conducted with Asian patients (21 of 25, 84%), perhaps because of higher rates of gastric cancer within this population. The latest global cancer statistics show that incidence rates of gastric cancer are highest in East Asia (particularly in Korea, Japan, and China) (Bray et al., 2018). However, the incidence of cancers of the lower stomach has been increasing among Americans aged younger than 50 years, according to a National Cancer Institute (NCI, 2018)-led study. To date, no studies have been conducted in the United States regarding symptoms in patients with gastric cancer. Therefore, more attention must be given to issues related to symptoms experienced by this population.

A number of instruments was used to assess common and co-occurring symptoms. However,

KNOWLEDGE TRANSLATION

- Common and co-occurring symptoms in patients with gastric cancer include physical symptoms (gastrointestinal symptoms, fatigue, weight loss, sleep disturbance) and affective/cognitive symptoms (depression, anxiety, post-traumatic stress disorder symptoms, delirium).
 - Older age, female gender, advanced cancer stage, low socioeconomic status, and total gastrectomy are associated with a greater number and severity of symptoms among patients with gastric cancer.
 - Given the prevalence, range, and severity of symptoms in patients with gastric cancer, oncology nurses should provide patients with appropriate assessment, education, and management for multiple co-occurring symptoms.
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no standard instrument was identified to measure multiple co-occurring symptoms in patients with gastric cancer, which set difficulties for comparison studies. The EORTC QLQ-C30 and EORTC QLQ-STO22 scales were the instruments used most frequently to measure symptoms in gastric cancer survivors. Although these two scales provide a simple and rapid assessment, they have some disadvantages. They may only allow for the evaluation of the occurrence and severity of symptoms and may not reflect other dimensions (e.g., distress, meaning), and they do not measure affective/cognitive symptoms. Several investigator-designed instruments were used, but these lacked reliability and validity indices (Park et al., 2015; Zhou et al., 2017), which may lead to inaccurate assessment of symptoms among patients with gastric cancer. In a literature review summarizing measurement tools for patient-reported outcomes in advanced gastric cancer, three additional instruments were widely used: the Functional Assessment of Cancer Therapy (FACT)-General, FACT-Gastric, and MD Anderson Symptom Inventory for GI cancer (Xu et al., 2013). In addition, two leading patient-reported outcomes (PROs) measures, the PROs version of the Common Terminology Criteria for Adverse Events and PROs Measurement Information System, developed by the National Institutes of Health, are quickly becoming the standard in patient-reported health measurement (Basch et al., 2014; Lee et al., 2020; Reeve et al., 2007). These systematically and rigorously tested instruments may provide a more comprehensive measure of multiple aspects of co-occurring symptoms in patients with gastric cancer.

The current review reported that 3–17 symptoms (median = 7) were experienced concurrently by patients with gastric cancer. Similarly, researchers have acknowledged the multiple co-occurring symptoms in patients with gastric cancer (Kawamura et al., 2014; Tey et al., 2014). In 2001, Dodd et al. first introduced the concept of symptom clusters. A symptom cluster has been defined as two or more symptoms occurring concurrently with or without sharing a common etiology (Aktas, 2013; Barsevick, 2016). It has been proposed that symptom clusters may have common underlying mechanisms that could benefit cancer symptom management (Miaskowski et al., 2017). In the past two decades, research on symptom clusters has continued to grow. To date, the authors found only one paper identifying symptom clusters in GI cancers (Han et al., 2019). However, the authors did not find any studies focused on symptom clusters in patients with gastric cancer, suggesting that symptom clusters research in this population is at an early stage of development. Future research is needed that focuses on symptom clusters to identify the phenotypes of groups of symptoms. This will enhance more efficient symptom assessment and management.

In this integrative review of 25 studies, GI symptoms (e.g., abdominal pain, dysphagia, constipation, nausea, vomiting) were among the most frequent, bothersome, and co-occurring symptoms experienced by patients with gastric cancer. This is consistent with previous findings (Cherwin, 2012; Cherwin et al., 2019) of GI symptoms being prevalent among patients with cancer. Other previous studies partially explained the etiology of this set of symptoms. For example, abdominal pain, nausea, and diarrhea are prominent issues that could be explained by bloating and abnormal movement of remnant stomach or intestine (Hejazi et al., 2010), and vomiting was because of a lower ability to store food (Kawamura et al., 2014). Increasing the need for effectively assessing and managing GI symptoms is crucial for gastric cancer survivors.

Symptom experience is a multidimensional concept with four components (Armstrong, 2003); however, very few studies have examined symptom frequency and symptom distress, and no studies have explored symptom meaning for patients with gastric cancer. These oversights are critical in the understanding of symptoms that are of particular importance, such as those based on patients' concomitant meanings (Maguire et al., 2014). Also, the most severe or frequently occurring symptoms are not always the most distressing or meaningful to patients with cancer (Boehmke & Dickerson, 2005). These

issues should be considered when systematically and comprehensively describing symptom experience in patients with gastric cancer.

Research on symptom trajectories is limited. Understanding how symptoms and symptom clusters change over time is critical to ensure appropriate symptom self-management (Dodd et al., 2001). Therefore, it is crucial to conduct longitudinal studies of symptoms in the gastric cancer population. In addition, the science behind predictors of symptoms (e.g., advanced cancer stage) reports conflicting or inconsistent results. Symptom trajectories and predictors of symptom clusters are also absent in the literature. Further investigation is needed in those areas.

Developing and testing effective symptom interventions is critical for managing co-occurring symptoms and improving quality of life for patients with cancer (Kwekkeboom, 2016). Complementary and alternative therapies have been tested for their efficacy at relieving symptoms for patients with gastric cancer. For example, herbal therapy was found to relieve the symptoms of fatigue, nausea and vomiting, pain, loss of appetite, and constipation (Xu et al., 2017). Acupuncture was also found to minimize GI symptoms after gastrectomy (Lu & Rosenthal, 2013). However, key design issues in this set of studies prevent understanding of their efficacy; these issues include small samples (19–56) and lack of well-designed randomized controlled trial designs. Therefore, further research is needed to understand the impact of alternative therapies among patients with gastric cancer who experience multiple co-occurring symptoms.

Limitations

The generalizability of the results of this literature review may be limited by several characteristics of the studies. More than half (21 of 25) of the studies are from Asian countries where gastric cancer rates are the highest globally, and the review was limited to articles written in English. Therefore, it may omit relevant articles published in other languages, particularly in Asian. There also was a very wide variability in stage of gastric cancer and stage of treatment. Studies included participants who were newly diagnosed, patients with advanced cancer, patients diagnosed with a range of earlier-stage disease (e.g., I, II), patients undergoing chemotherapy, and those who underwent gastrectomy. This variability may result in different symptoms experienced by patients with gastric cancer and, consequently, inaccurate findings on symptom profiles.

Implications for Practice and Research

The study of symptoms in patients with gastric cancer and their application to practice is vital to nursing research and practice. Three implications were identified to guide researchers and nurse clinicians in the future. First, nurses and researchers should identify common data elements (defined as variables that are operationalized and measured in identical ways across studies) for symptoms in patients with gastric cancer (Redeker et al., 2015). This would be helpful for advancing symptom science in gastric cancer and comparison across studies and populations (e.g., cancer, heart disease). Second, evidence indicates that people living with gastric cancer experience a wide range of symptoms. Healthcare providers should be directed to strengthen awareness of assessing co-occurring symptoms and symptom clusters in this population and discover potential symptoms with common etiology. Third, clinicians and researchers should partner to develop innovative interventions to support self-management of symptoms, including targeting the symptom clusters instead of individual symptoms. Further exploration of symptom clusters will provide a foundation for developing future interventions for efficient, effective symptom management in patients with gastric cancer.

Conclusion

The authors reviewed relevant studies on symptom experience, measurement, predictors, trajectories, and management in patients with gastric cancer. This area of science remains in its infancy because robust evidence related to these symptoms is not available. Symptom predictors and trajectories have yet to be fully studied and described in patients with gastric cancer. Identification of symptom clusters may help to determine how symptoms are related to one another and how they influence patients' outcomes. This emphasizes the need for further research to establish the science. Interventions targeted to symptom clusters may help to improve the efficacy of symptom management in patients with gastric cancer.

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No financial relationships to disclose.

All authors contributed to the conceptualization and design and manuscript preparation. Lin and Bailey completed the data collection, evaluation, and analysis.

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