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A Review of the Literature on Multiple Co-Occurring Symptoms in Patients with Colorectal Cancer Who Received Chemotherapy Alone or Chemotherapy With Targeted Therapies

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Abstract

Background—Patients with colorectal cancer (CRC) rarely experience a single symptom associated with their disease and its treatment.

Objective—Purpose of this literature review was to summarize the current state of knowledge of multiple co-occurring symptoms in CRC patients who received chemotherapy alone or chemotherapy with targeted therapies.

Methods—Comprehensive literature search was conducted from 1990 to 2014. These studies were evaluated in terms of the occurrence of multiple, co-occurring symptoms in CRC patients who received CTX alone or CTX with targeted therapies; the most common symptom assessment and quality of life (QOL) instruments used; and the associations identified between select demographic and treatment characteristics, QOL, and multiple co-occurring symptoms.

Results—Only five studies met this review's inclusion criteria. Two studies compared symptoms in patients who received CTX alone or CTX with targeted therapies and only one study reported on symptom occurrence. Of the five studies identified, only two used the same instrument to assess symptoms and only two studies evaluated for associations between demographic and treatment characteristics and symptom burden, as well as QOL outcomes.

Conclusions—Given the larger number of patients with CRC, as well as the increased number of CRC patients who will receive targeted therapies with or without CTX, future studies need to describe the occurrence, severity, and distress of multiple co-occurring symptoms and their impact on CRC patients' QOL.

Implications for Practice—To deliver effective symptom management interventions, the most common, severe, and distressing symptoms that CRC patients experience need to be identified.

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INTRODUCTION

Colorectal cancer (CRC) is the third most frequently diagnosed cancer and the third leading cause of cancer deaths in the United States.[1] Despite an increased awareness of CRC screening, the American Cancer Society estimates that 132,700 new cases of CRC will be diagnosed in 2015.[1] Today, patients with CRC are treated with surgery, radiation therapy (RT), chemotherapy (CTX), and/or targeted therapies depending on the stage of their disease at the time of diagnosis.[2] Because targeted therapies were developed to block the key regulators of a cancer's growth and development, they have become an effective treatment strategy for patients with CRC. Of note, several reviews suggest that the use of targeted therapies has improved the toxicity profile of treatments for CRC as compared to CTX alone.[3–5] In addition, some evidence suggests that patients tolerate targeted therapies better than traditional CTX and that survival rates increase in patients on targeted therapies.[6]

Patients with CRC rarely experience a single symptom associated with their disease and its treatment. Over the past decade, our group[7–9] and others[10–12] have evaluated multiple co-occurring symptoms in patients with cancer, which is more reflective of their experience. However, the majority of this research has focused on a description of the number and severity of symptoms in patients with a variety of cancer diagnosis.[7, 9, 13–15] Additional research is warranted within a specific diagnosis like CRC to determine the co-occurrence and severity of multiple symptoms that are common as well as unique to these oncology patients.

While several studies in patients with a variety of cancer diagnoses suggest that symptoms can occur in clusters,[16] no studies were identified that evaluated for symptom clusters in a homogenous sample of patients with CRC. Therefore, this review focused on studies of multiple co-occurring symptoms in patients with CRC as an initial effort to describe these patients' symptom experiences. When multiple co-occurring symptoms are not addressed, they can impair patients' ability to carry out activities of daily living (ADLs), reduce their functional status, and decrease their quality of life (QOL).[17] In addition, multiple co-occurring symptoms can complicate treatment outcomes and decrease overall survival.[13] Therefore, the identification of common multiple co-occurring symptoms in CRC patients and their impact on patients' QOL are integral components of effective symptom management.[18]

While advances in treatments for CRC, like targeted therapies, continue to become available, clinical experience and a limited amount of research[19] suggest that multiple co-occurring symptoms continue to be a challenge for CRC patients. However, no comprehensive review has summarized the findings from studies that evaluated multiple, co-occurring symptoms in CRC patients who received CTX alone or CTX with targeted therapies. Therefore, the purposes of this review are to: 1) describe the most common symptom assessment and QOL instruments that were used in these studies; 2) describe the occurrence and severity of multiple, co-occurring symptoms in CRC patients who received CTX alone or CTX with targeted therapies; 3) summarize the associations identified between select demographic and treatment characteristics and multiple co-occurring symptoms; and 4) summarize the associations between multiple co-occurring symptoms and QOL outcomes. We hypothesized

that compared to patients who received only CTX, patients who received CTX and targeted therapy would have fewer and less severe, multiple co-occurring symptoms.

METHODS

For this review, a systematic electronic literature search was conducted using PubMed®, Excerpta Medica Database (EMBASE®), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL®) databases. Key words used when searching the databases were *colorectal cancer* AND *drug therapy* AND *symptom* AND *quality of life*. An additional inclusion criterion was that the paper was published in English between 1990 and 2014 (targeted therapies were not approved until the 1990s.). Studies were included if they met all of the following criteria: 1) evaluated the prevalence of multiple, co-occurring symptoms; 2) included CRC patients who received CTX alone or CTX with targeted therapies; and 3) used a valid and reliable instrument (e.g., M. D. Anderson Symptom Inventory [MDASI],[20] Memorial Symptom Assessment Scale [MSAS][21]) to evaluate multiple co-occurring symptoms. Studies were excluded if symptom clusters were identified for evaluation and if current active treatment regimens included only surgery, RT, or chemo-radiotherapy.

The search strategy yielded 246 studies identified in PubMed®, 204 studies in EMBASE®, and 28 studies in CINAHL®. A total of 473 studies were removed from the analysis because the majority of these studies did not evaluate multiple co-occurring symptoms in CRC patients. In addition, duplicate articles across the databases were eliminated. Based on the pre-specified search criteria, a total of five studies were identified.[20–24]

Two tables were generated to summarize the three studies of multiple co-occurring symptoms in patients with CRC who received CTX alone[20, 22, 24] (Table 1) and the two studies of patients with CRC who received CTX with targeted therapies[21, 23] (Table 2). Both tables are organized using the following evaluation criteria: author, year, purpose, study design (i.e., cross-sectional, longitudinal), sample characteristics (i.e., sample size, age, gender, diagnosis, setting, time since diagnosis, previous treatments, current treatments, use of targeted therapy), symptom assessments (i.e., instruments, number of symptoms assessed, dimensions of symptoms assessed), major findings, strengths, and limitations. Because only five studies were identified, the results and discussion sections of this paper summarize the findings across these five studies.

RESULTS

Description of the studies

Four of the five studies that evaluated for multiple co-occurring symptoms in patients with CRC used a descriptive, cross-sectional design.[20–22, 24] The fifth study used a descriptive, longitudinal, repeated-measures design.[23] Across these five studies, retrospective data were used in four.[20–22, 24] The sample sizes ranged from 104[21] to 5442[22] patients and three of the five studies had less than 250 patients.[21, 23, 24] Across the 5 studies, the weighted grand mean age was 59.5 years and gender distribution was approximately equal. In three of the five studies,[21, 23, 24] 100% of the patients had CRC and in one study,[20] 49.6% of the patients

had colon cancer and 50.4% had rectal cancer. In a fifth study,[22] 55.5% of the patients had CRC and 44.5% had lung cancer.

All five studies were conducted in outpatient settings. Only one out of the five studies reported the patients' previous treatment regimens.[20] All five studies reported that patients received CTX as one of their current treatment modalities. Only two studies reported symptom data on patients with and without targeted therapies.[21, 23] In terms of geographic locations, two studies were conducted in the United States,[22, 23] one in Turkey,[24] one in Sweden,[21] and one in China.[20]

Symptom assessment and QOL instruments

Symptom assessment instruments—A number of instruments were used to evaluate multiple, co-occurring symptoms. All five studies used a multidimensional symptom assessment instrument (i.e., European Organization for Research and Treatment of Cancer Quality of Life Questionnaire [EORTC-QLQ],[22, 24] Patient Care Monitor [PCM],[23] MSAS,[21] MDASI[20]). Two of the studies used the EORTC-QLQ,[22, 24] one used the PCM,[23] one used the MDASI,[20] and one used the MSAS.[21] In addition, two studies[22, 24] utilized single symptom assessment instruments to evaluate additional symptoms (e.g., anxiety [i.e., State Trait Anxiety Inventory],[24] depression [i.e., Beck Depression Index,[24] Center for Epidemiological Studies-Depression Scale[22]]).

Number and dimensions of symptoms assessed—The number of symptoms assessed ranged from a minimum of seven[22] to a maximum of 32.[21] The one symptom dimension that was assessed across all five studies was severity. In one study,[21] occurrence, frequency, severity, and distress were assessed. While in another study,[20] interference from symptoms was assessed.

Functional status and QOL instruments—Generic and disease specific instruments were used to evaluate QOL in three of the five studies. In these studies, one[20] used a functional status instrument (i.e., MDASI) and another study[24] used a cancer specific QOL instrument (i.e., EORTC-QLQ). Only one study[22] utilized both a generic (i.e., SF-36) and a disease specific (i.e., EORTC-QLQ) instrument to evaluate the effects of multiple co-occurring symptoms on patients' QOL.

Occurrence and severity of multiple co-occurring symptoms

Occurrence of multiple co-occurring symptoms—The occurrence of symptoms was evaluated in only one study.[21] In this study, using the MSAS, the mean number of symptoms was 10.3 (range, 0–32; SD, 7.7). Using the MSAS classifications, the most common physical symptoms experienced by more than 40% of the patients were: numbness/tingling in the hands/feet (64%), lack of energy (62%), feeling drowsy (49%), nausea (45%), shortness of breath (43%), and dry mouth (42%). The most common psychological symptoms were difficulty sleeping (46%) and worrying (44%).

Severity of multiple co-occurring symptoms—While the severity of multiple co-occurring was reported in all five studies, the findings were inconsistent. In one study,[22]

51% of patients reported at least one symptom of moderate/severe intensity. While in another study,[23] it was noted that patients experienced moderate to severe symptoms (defined by a PCM item score of ≥4, at some point during second-line therapy) and 67% of patients reported fatigue as the most common symptom occurring at moderate to severe levels. In one study that evaluated 32 symptoms using the MSAS,[21] for almost all of the symptoms, patients reported higher scores for frequency than for severity or distress. Of the five studies, only one study reported the range of severity scores for seven symptoms.[23] Compared to patients who received CTX with targeted therapies, patients who received CTX alone had a higher rate of moderate to severe nausea. In addition, compared to patients who received Cetuximab, patients who received Bevacizumab had significantly ($p < .0001$) lower (i.e., better) rash scores than patients in the CTX only group.[23]

Associations between patient characteristics and multiple co-occurring symptoms

Associations between demographic characteristics and the severity of multiple co-occurring symptoms were evaluated in two studies.[20, 22] In one study,[20] patients with more severe symptoms were ≥60 years of age, more likely to be female, had a lower BMI, were single or divorced, were living in a suburban area, and had stage III colon cancer. In the second study,[22] moderate or severe symptoms were significantly more likely to be associated with younger age; Hispanic or Latino ethnicity; being female; unmarried; and less educated; having a lower income; being uninsured; having more comorbidities; being diagnosed with late stage cancer; as well as having received treatment more recently.

Association between multiple co-occurring symptoms and QOL outcomes

The associations between multiple co-occurring symptoms and functional status or QOL outcomes were evaluated in three of the five studies.[20, 22, 24] In one study,[24] global QOL scores were significantly lower in patients with higher anxiety scores (STAI ≥45) and higher depressive symptom (BDI ≥17) scores. In the second study,[20] the authors reported that results from their study were consistent with other studies that demonstrated that higher self efficacy scores were associated with lower symptom severity and less symptom interference with daily life. Although one study utilized the EORTC-QLQ to evaluate multiple co-occurring symptoms,[22] the investigators did not describe the relationships among these symptoms and QOL outcomes.

DISCUSSION

This review is the first to summarize the findings from studies that examined multiple co-occurring symptoms in CRC patients who received CTX alone or CTX with targeted therapies. Across the five studies included in this review, only two studies[21, 23] compared symptoms in patients who received CTX with or without targeted therapies. In addition, only one longitudinal study was identified.[23] Given the larger number of patients with CRC, as well as the significant toxicities associated with CTX for CRC, it is surprising that only five studies have systematically evaluated symptom burden in these patients.

Symptom assessment and QOL instruments

Of the five studies identified for this review, only two used the same assessment instrument to assess symptoms in CRC patients (i.e., EORTC-QLQ).[22, 24] This finding is not surprising given the number of valid and reliable instruments that are available to assess multiple co-occurring symptoms in oncology patients.[25, 26] In addition, a question remains about the most appropriate symptoms to assess in CRC patients.[27] Findings from this review suggest that little is known about the frequency, severity, and distress of symptoms in CRC patients and how these symptom dimensions change over time. Of note, across the five studies in this review, the most common instrument was the EORTC-QLQ, which contains a symptom severity scale with only seven symptoms. However, the two studies that used the EORTC-QLQ[22, 24] did not report data on the severity of each symptom.

Occurrence and severity of multiple co-occurring symptoms

In the one study that reported on symptom occurrence, CRC patients reported an average of 10.3 out of 32 symptoms using the MSAS. This finding is consistent with two systematic reviews,[28, 29] as well as findings from our research team[7, 8] and others[30, 31] that regardless of diagnosis, oncology patients receiving active treatment experience a large number of unrelieved symptoms. In terms of the occurrence rates for specific symptoms, only one study reported the occurrence rates for unrelieved symptoms.[21] The five most common symptoms were: numbness/tingling in the hands/feet (64%), lack of energy (62%), feeling drowsy (49%), difficulty sleeping (46%), and nausea (45%).

A surprising finding is the lower occurrence rates for fatigue, which in most studies of patients receiving CTX[32–35] occurs in over 80% of patients. For example, in one study,[32] fatigue was reported as the chief complaint by 51.1% of the patients with occurrence rates that ranged from 34% to 64%. In addition, the relatively high rate of numbness/tingling is consistent with two studies,[36, 37] in which a subset of patients with CRC who received a CTX regimen that contained oxaliplatin reported this symptom. Additional research is warranted to assess the occurrence rates for common symptoms in CRC patients across their disease trajectory. In addition, given the advances in CRC treatments, studies are needed that evaluate for differences in the occurrence rates for common symptoms in patients who do and do not receive targeted therapies.

Associations between demographic and treatment characteristics and multiple co-occurring symptoms

Several demographic and treatment characteristics were associated with increases in symptom burden. For example, in two studies[20, 22] and consistent with previous studies of symptoms in oncology patients receiving CTX,[35, 37] being female was associated with more severe symptoms. However, given that only two studies evaluated for associations between demographic and treatment characteristics and symptom burden in CRC patients, a more detailed evaluation is warranted to identify high-risk patients.

Associations between multiple co-occurring symptoms and QOL outcomes

Only two studies[20, 22] described associations between symptoms and QOL outcomes. While the data reported suggest that higher scores on anxiety and depression instruments were

associated with lower global QOL scores[22] and that positive correlations were found between patients' ability to self-manage their symptoms and their functional status,[20] no studies evaluated associations between multiple co-occurring symptoms and QOL in patients with CRC.

One of the primary purposes of this review was to compare symptom burden in CRC patients who received CTX alone or CTX with targeted therapies. While current estimates suggest that approximately 25% of CRC patients who have metastases at the time of diagnosis receive targeted therapies,[38, 39] only one study addressed this question. In this study, an instrument that evaluated only eight specific symptoms (i.e., rash, dry skin, itching, nail changes, nausea, vomiting, diarrhea, burning sensation in hands or feet) was used. The only difference identified was that compared to patients who received CTX with a targeted therapy, patients who received only CTX reported a higher rate of moderate to severe nausea. Additional research is warranted to determine if a differential symptom burden occurs in CRC patients who do or do not receive targeted therapies with their CTX. Moreover, future studies of multiple co-occurring symptoms need to use comprehensive symptom assessment instruments (i.e., National Institutes of Health-supported advances in measurement science through the Patient Reported Outcomes Measurement Information System network [PROMIS])[40, 41] that evaluate multiple dimensions of the patient's symptom experience.

SUMMARY AND CONCLUSIONS

Given that approximately 5% of Americans will be diagnosed with CRC in their lifetime[1] and more patients with CRC will receive targeted therapies with and without CTX,[42] additional studies of multiple co-occurring symptoms are warranted. Future studies need to describe the occurrence, as well the severity, frequency, and distress of multiple co-occurring symptoms and their impact on QOL in CRC patients. In addition, changes in these symptom dimensions across the patients' disease trajectory are warranted to be able to develop more targeted and effective symptom management interventions for these patients.

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Table 1

Summary of Studies of Multiple Co-Occurring Symptoms in Patients With Colorectal Cancer Who Received Chemotherapy.

Author, Year **Purpose, Study Design**	**Sample Characteristics (sample size, age, gender, diagnosis, setting, time since diagnosis, previous treatments, current treatments, targeted therapy)**	**Symptom Assessment (instruments, number of symptom assessed; dimensions of symptoms assessed)**	**Major Findings**	**Strengths and Limitations**
Author: Alacacioglu et al. (2010) Purpose: Investigate variations in quality of life as a function of depression and anxiety scores of CRC patients with BDI and STAI scoring system. Design: Cross-sectional	N=110 Age: 58 ± 12.7 years Gender: 59% Male Diagnosis: CRC = 100% Setting: Outpatient Previous treatments: NR Current treatments: CTX alone = 73.6% CTX + radiation = 26.4% Targeted therapy: None	Symptom instrument(s): BDI STAI - Trait EORTC-QLQ-C30 Number of symptoms: 10 Symptom dimensions: Severity QOL or FS instrument(s): EORTC-QLQ-C30	•Mean depression score were 11.2 (± 9.0, range 0 – 44). •Mean anxiety score were 41.9 (± 8.8, range 22 – 71). •QOL symptom scale scores were significantly higher in patients who had BDI scores of ≥17. •QOL symptom scale scores were significantly higher in patients who had trait anxiety scores of ≥45. •Patients with BDI scores of ≥17 and patients with trait anxiety scores of ≥45 had lowered functional and QOL scores.	Strengths • Relatively large sample. • Correlated symptom severity for 8 symptoms, as well as QOL with valid and reliable measures of depression and trait anxiety Limitations • Cross-sectional design. • Patients were from a single institution.
Author: Walling et al. (2014) Purpose: Describe the prevalence and severity of symptoms among a large, representative cohort of newly diagnosed cancer patients. Design: Cross-sectional	N= 5,442 Age: ≥21 years Gender: 53.3% Male Diagnosis: CRC = 55.5% Lung = 44.5% Setting: Outpatient Previous treatments: NR Current treatments: Surgery = 4% Radiation = 11.3% CTX = 43.1% Targeted therapy: NR	Symptom instrument(s): EORTC-QLQ CESD-8 BPI Number of symptoms: 7 (nausea/vomiting, pain, fatigue, depressive symptoms, cough, dyspnea, diarrhea) Symptom dimensions: Severity QOL or FS instrument(s): EORTC-QLQ SF-36	•93.5% of patients reported at least one symptom •51% of patients reported at least one symptom of moderate/severe intensity •Lung cancer patients reported more symptoms than CRC patients. •Moderate to severe symptoms were associated with younger age, Hispanic or Latino ethnicity, being female, unmarried, less educated, having a lower income, uninsured, having more comorbidities, diagnosed with late stage cancer, as well as having received treatment more recently. •Patients who received previous treatment or had more comorbidities were more likely to report symptoms.	Strengths • First, large-scale study to report estimates of the prevalence of symptoms in a nationally representative incident cohort of cancer patients. Limitations • Cross-sectional design • Multiple dimensions of symptom experience were not evaluated.

Author, Year Purpose, Study Design	Sample Characteristics (sample size, age, gender, diagnosis, setting, time since diagnosis, previous treatments, current treatments, targeted therapy)	Symptom Assessment (instruments, number of symptom assessed; dimensions of symptoms assessed)	Major Findings	Strengths and Limitations
Author: Zhang et al. (2014) Purpose: Explore the influence of self-efficacy and demographic, disease-related, and psychological factors on symptom distress among Chinese CRC patients receiving postoperative adjuvant CTX. Design: Cross-sectional	N=252 Age: 53.3 ± 10.7 years Gender: 65.5% Male Diagnosis: 49.6% Colon 50.4% Rectum Setting: Outpatient Previous treatments: 49.6% Radical resection 50.4% Transabdominal Current treatments: CTX = 100% Targeted therapy: NR	Symptom instrument(s): MDASI HADS Number of symptoms: 20 (18 symptoms on MDASI and depression and anxiety) Symptom dimensions: Severity Interference QOL or FS instrument(s): Interference	•Patients' overall level of symptom distress was mild. •Anxiety and depression were positively associated with symptom distress. •More severe symptoms were associated with age ≥60 years, female gender, suburban residence, BMI <18.5, and stage III cancer. •Age ≥60 years, female gender, marital status of single or divorced, and suburban residence were associated with greater symptom interference with daily activities •Greater self-efficacy was associated with milder symptoms severity and less symptom interference with daily life.	Strengths • Large sample size. • First study to evaluate the relationship between self-efficacy and symptom severity and symptom interference. • One of the first studies to identify risk factors for higher symptom severity during adjuvant CTX. Limitations Cross-sectional design. • Patients were from a single institution.

Abbreviations: BDI = Beck Depression Index; BMI = body mass index; BPI = Brief Pain Inventory; CES-D = Center for Epidemiological Studies Depression; CRC = colorectal cancer; CTX = chemotherapy; EORTC QLQ = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; FS = functional status; HADS = Hospital Anxiety and Depression Scale; MDASI = MD Anderson Symptom Inventory; NR = not reported; QOL = quality of life; SF-36 = Medical Outcomes Study Short Form 36; STAI = State Trait Anxiety Inventory

Table 2

Summary of Studies of Multiple Co-Occurring Symptoms in Patients With Colorectal Cancer Who Received Chemotherapy and Targeted Therapy.

Author, Year Purpose, Study Design	Sample Characteristics (sample size, age, gender, diagnosis, setting, time since diagnosis, previous treatments, current treatments, targeted therapy)	Symptom Assessment (instruments, number of symptom assessed; dimensions of symptoms assessed)	Major Findings	Strengths and Limitations
Author: Pettersson et al. (2014) Purpose: Describe the prevalence, frequency, and severity of symptoms and the distress they cause during the early treatment of patients with CRC undergoing CTX. Design: Cross-sectional	N = 104 Age: 65 ± 11.2 years Gender: 56% Male Diagnosis: CRC = 100% Setting: Outpatient Previous treatments: NR Current treatments: CTX alone = 91% CTX + targeted therapy = 9% Targeted therapy: Bevacizumab	Symptom instrument(s): MSAS Number of symptoms: 32 Symptom dimensions: Occurrence, frequency, severity, and distress QOL or FS instrument(s): None	•Mean number of symptoms was 10.3 (± 7.7, range 0 – 32). •Most common physical symptoms, experienced by more than 40% of patients were: numbness/tingling in the hands/feet (64%) lack of energy (62%) feeling drowsy (49%) nausea (45%) shortness of breath (43%) dry mouth (42%) •Most common psychological symptoms were: difficulty sleeping (46%) worrying (44%) •For almost all symptoms, patients reported higher scores for frequency than for severity or distress.	Strengths • First study to evaluate multiple dimensions of the symptom experience of CRC patients in the early phase of their treatment. • Used a valid and reliable measurement to assess multiple dimensions of 32 symptoms. Limitations • Cross-sectional design. • No evaluation was done on the differences in the symptom experience of patients who did and did not receive targeted therapies.
Author: Walker et al. (2012) Purpose: Describe symptom burden among patients treated for mCRC in community settings who received second-line regimens that contained bevacizumab, cetuximab or CTX regimens without the addition of a monoclonal antibody. Design: Longitudinal	N = 182 Age: 62 ± 12.6 years Gender: 48.9% Male Diagnosis: CRC = 100% Setting: Outpatient Previous treatment: NR Current treatment: CTX alone = 28.9% CTX + targeted therapy = 79.1% Targeted therapy: Cetuximab N = 38 Bevacizumab N = 106	Symptom instrument(s): PCM Number of symptoms: 8 (rash, dry skin, itching, nail changes, nausea, vomiting, diarrhea, burning sensation in hands or feet). Symptom dimensions: Severity QOL or FS instrument(s): None	•67% of patients reported fatigue as the most common symptom occurring at moderate to severe levels. •Cetuximab group reported a significantly higher rate of moderate to severe dry skin ($p < .0001$), itching ($p = .0028$), and rash ($p < .0001$), compared to the Bevacizumab group. •Patients on CTX had a higher rate of moderate to severe nausea ($p = .0485$) and tended to have a higher rate of physical pain ($p = .0564$) compare to the Bevacizumab group.	Strengths • Evaluated symptom burden among different treatment regimens (including two widely used targeted therapies) compared to CTX alone. • Characterized changes in severity of 8 symptoms from the initiation of second line treatment for CRC to six months after the initiation of treatment. Limitations • Retrospective, cohort study • Convenience sample • Validity and reliability of PCM not reported

Abbreviations: CRC = colorectal cancer; CTX = chemotherapy; FS = functional status; mCRC = metastatic colorectal cancer; MSAS = Memorial Symptom Assessment Scale; NR = not reported; PCM = Patient Care Monitor; QOL = quality of life