Published in final edited form as:
J Natl Compr Canc Netw. 2009 September ; 7(8): 883–894.

The Challenges of Colorectal Cancer Survivorship

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Abstract

With advances in treatment, colorectal cancer is being transformed from a deadly disease to an illness that is increasingly curable. With this transformation has come increased interest in the unique problems, risks, needs, and concerns of survivors who have completed treatment and are cancer-free. Research has shown that physical and mental quality of life for colorectal cancer survivors was inferior when compared with age-matched individuals without cancer. Although issues and symptoms were most prominent during the first three years, long-term effects of treatment can persist and include fatigue, sleep difficulty, fear of recurrence, anxiety, depression, negative body image, sensory neuropathy, gastrointestinal problems, urinary incontinence, and sexual dysfunction. The unique challenges and issues of colorectal cancer survivors can and should be addressed by health care providers and the research community to ensure effective interventions and models of care to manage these problems. In this review, we discuss what is known about the long-term effects of colorectal cancer treatment on quality of life, the care of survivors, and existing models of survivorship care.

Keywords

Colorectal cancer; survivorship; quality of life; late effects; long-term effects

With advances in cancer prevention, early detection, and treatment, the population of cancer survivors in the United States is over 11 million and growing(1). However, colorectal cancer (CRC) remains the third most common cause of cancer and cancer death in both men and women, with an estimated 108,070 new cases of colon cancer and 40,740 new cases of rectal cancer, and an estimated 49,960 deaths attributed to colorectal cancer in 2008 (2). Over 90% of invasive colorectal cancers are diagnosed in patients over the age of 50, with 67% being diagnosed in patients over age 65, and CRC is the most common cancer diagnosis in patients over age 75 (3, 4).

Fortunately, the majority of patients will be diagnosed with local or regional disease, and may be candidates for curative therapy (3). Five-year survival rates for all stages of disease currently are 65% and 66% for colon and rectal cancer, respectively (2). This improvement in survival is likely due to earlier detection of tumors and improved therapy (5). The use of

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Conflicts of Interest: Dr. Denlinger receives research support from Merrimack Pharmaceuticals and Genentech, Inc. Dr. Barsevick has no conflicts of interest or financial disclosures.

adjuvant 5-fluorouracil has resulted in an improvement in survival of approximately 30%, with an additional 20% improvement with the addition of oxaliplatin in stage III colon cancer (6, 7). The use of chemoradiotherapy in rectal cancer has resulted in improved survival and local control (8, 9).

With improved treatment comes the potential for late and long-term side effects that can affect quality of life. Long-term follow-up, health maintenance, and lifestyle modifications remain important components of the care of CRC survivors. Recommendations from the Institute of Medicine (Table 1) can shape a high quality approach to the care of cancer survivors (10). Because a significant proportion of individuals treated for CRC are likely to be cancer-free for longer intervals and potentially for the rest of their lives, this manuscript will focus on the survivor experience of those patients with stage I–III CRC who have completed primary treatment and have no evidence of disease. In this review, we will discuss quality of life after treatment, the late and long-term effects of treatment, lifestyle interventions, and models for the long-term care of CRC survivors.

Quality of Life and Psychosocial Issues

Quality of life (QOL), the subjective evaluation of one's personal satisfaction with overall health and well-being, is an important outcome of cancer survivorship that includes physical, functional, psychological, and social functioning (11). Most reports of survivor QOL have focused on mixed groups of cancer diagnoses including CRC survivors. Mental and physical QOL was poorer for these mixed groups compared to age-matched individuals without cancer (12). The most prevalent concerns reported one year after diagnosis and treatment were fear of recurrence (68%), fatigue (67%), and sleep difficulties (48%) (13). When evaluated six and 12 months after diagnosis, more than 8% of survivors experienced distress that was severe enough to require follow-up (14). Long-term adult survivors had more physical limitations in sustained activities such as shopping, sports, and social events than individuals without cancer (53% versus 21%) (15). Gastrointestinal cancer survivors, including CRC, were found to be at higher risk for unemployment than healthy adults (48.8% versus 33.4%), while cancer survivors as a group had an almost 3-fold higher rate of disability causing unemployment compared to healthy controls (16).

Older adult cancer survivors were distinguished from older adults without cancer by more chronic conditions, poorer physical functioning, and poorer health ratings (17, 18). Older female long-term survivors reported more limitations of physical functioning such as inability to do housework, walk a half-mile, or walk up and down stairs compared to an age-matched group without cancer (19). Age, low income, symptom severity, and comorbidities were predictive of poorer physical functioning, perhaps due to cancer diagnosis, age, or some other combination of factors (12, 15, 18, 20–24). Although elderly long-term survivors generally reported low levels of anxiety and depression overall, they had worse psychological outcomes and used more mental health services than individuals without cancer (24–27). Thus, issues of CRC survivorship may be complicated by advancing age, as the age-adjusted rate of CRC for individuals over 65 years of age is more than three times higher than for persons aged 50–64 (3).

In contrast to other disease-based survivor populations, some studies have shown that CRC survivors report fewer physical problems and concerns (12, 28–30) and that problems reported in the short-term generally improved within three years of diagnosis, with two thirds of survivors reporting no symptoms and less than 10% reporting more than two symptoms by four years after diagnosis (31, 32). The most commonly reported symptoms were fatigue (23%) and physical discomfort (19%), while stomachache was more frequent for survivors treated with chemotherapy (11% versus 3%), diarrhea more common after

radiotherapy (24% versus 10%), and pain and cramping more prominent in those with ostomies (17% versus 5%) (32). Matched for age, long-term CRC survivors did not differ from their healthy counterparts with regard to physical functioning (15, 33). However, within the group of CRC survivors, increased age and number of comorbid conditions was associated with lower physical functioning (15).

A major limitation of research that includes both colon and rectal cancer survivor groups is that symptoms and problems averaged across groups with differences in diagnosis and treatment could lead to incorrect conclusions. For example, bowel symptoms tend to be more prominent for survivors of rectal rather than colon cancer due to more surgical techniques and therapies with long-term effects. The prevalence of rectal cancer is lower so averaging across both diagnoses could mask the severity of problems of rectal cancer survivors. Therefore, conclusions about symptom severity or quality of life are limited by differences in diagnosis and treatment between the two sites.

In a cross-sectional study of older CRC survivors, cohorts that were less than three years from diagnosis had lower overall QOL than cohorts that had been diagnosed more than three years previously; in all groups, QOL varied substantially across stages of disease (31). There was a trend for declining QOL in those with stage IV disease. Low income was associated with higher pain levels, difficulty ambulating, and lower social and emotional well-being. Pain remained a substantial problem that did not improve with time in this population. This population also had a high prevelance of comorbidities: 77% had one comorbid condition; 38% had two and 19% had three comorbid conditions. In another cross-sectional study of CRC survivors five or more years after diagnosis, a higher number of comorbid conditions was associated with poorer QOL (18). These results suggest that the physical and functional aspects of QOL improve three or more years after a CRC diagnosis for most survivors, but a small percentage continue to report distressing symptoms (Tables 2 and 3).

With regard to emotional status, depressive symptoms (measured by the CES-Depression Scale) of CRC survivors were not especially high at diagnosis and improved over the course of the first year after treatment (24). Survivors with more limitations of their daily social activities tended to be more depressed than those without limitations (24); those with better social networks consisting of more close friends and relatives as well as community involvement had better mental health outcomes (34). Despite low levels of depressive symptoms, 26–44% of long-term CRC survivors continued to worry about cancer recurrence, symptoms as cancer indicators, getting a second malignancy, or future diagnostic tests. Cancer-related health worries were associated with anxiety and depression, with 24% of the survivors reporting depression scores that were high enough to need evaluation for clinical depression (29). Thus, screening for psychological distress, depression, fatigue, and pain is warranted in all CRC survivors and may identify issues requiring intervention to improve their QOL after treatment (35).

The presence of a permanent stoma may affect QOL. Survivors with a permanent stoma who had been treated with radiotherapy followed by surgery for locally advanced rectal cancer reported improved bowel symptoms, fatigue, and pain compared to pretreatment levels (36). However, the presence of a stoma has also been associated with diminished body image and increased financial worries although global QOL was not affected (37, 38). Four years after treatment, survivors with a stoma were more likely to report negative feelings about body appearance at four years compared to non-stoma survivors (25% vs. 12% p=0.02) (32). Although social functioning one year after diagnosis was negatively impacted by the presence of a stoma (37, 39), follow-up over two years suggests that a permanent stoma did not have a durable impact on social functioning or activities of daily living (40, 41).

Late and Long-Term Effects of Treatment

Oxaliplatin-induced Peripheral Neuropathy

Recent studies of long-term CRC survivors have begun to address the late- and long-term effects of newer treatment regimens (Tables 3 and 4). Oxaliplatin-induced peripheral neuropathy has become a common and occasionally dose-limiting toxicity in the CRC survivor population, usually manifesting as sensory impairment of the peripheral nerves in a stocking-glove distribution. Symptoms of numbness, pain, paresthesias, dysesthesias, and changes in proprioception may affect fine motor skills such as writing, holding objects, buttoning shirts, picking up coins, and walking. Rarely, urinary retention and Lhermitte's sign (electric-shock sensation shooting down spine with neck flexion) can occur (42–44). Symptoms most commonly appear after cumulative doses of oxaliplatin exceeding 780 mg/m2, and are most likely due to oxaliplatin accumulation in the dorsal root ganglia with interference of calcium-dependent voltage-gated sodium channels by oxalate, a metabolite of oxaliplatin (42, 43, 45–48).

In the adjuvant setting, up to 92% of survivors treated with oxaliplatin and infusional 5-fluororuacil (FOLFOX) or bolus 5-fluorouracil (FLOX) developed some degree of sensory neuropathy, with 8 to 12% developing severe neuropathy interfering with function (Grade 3) and 22% requiring premature discontinuation of oxaliplation for severe neuropathy (49, 50). While the majority of survivors have improvement or recovery of nerve function within 1 month of discontinuation of treatment, the median time to resolution of symptoms was approximately 9 months(51). Furthermore, 20% of survivors may experienced a worsening of their symptoms after treatment discontinuation and up to 12% had persistent symptoms four years after completion of adjuvant treatment (7, 51). Therefore, persistent numbess, tingling, and cold-induced pain may be a long-term problem in a small subset of survivors (52).

Measures to prevent or treat oxaliplatin-induced neuropathy are needed. In the metastatic setting, there is limited evidence that glutamine, reduced glutathione, alpha-lipoic acid, and oxycarbazepine may reduce the incidence and severity of sensory neuropathy while gabapentin and carbamazepine have not been shown to be effective (53–58). A retrospective evaluation of calcium and magnesium infusions before and after oxaliplatin infusion suggested a reduction in chronic neuropathy without compromising chemotherapy efficacy, although randomized prospective studies have yet to confirm this (59, 60). In the adjuvant setting, the use of intravenous calcium gluconate and magnesium sulfate pre- and post-oxaliplatin infusion decreased the incidence of grade 2 neurotoxicity compared with placebo (28% vs. 58% p=0.01) (61), although the study was stopped prematurely due to initial concerns regarding lower tumor response with the same intervention in the metastatic setting (62). Non-steroidal anti-inflammatory medications, opioids, and referral to neurology or pain management for persistent symptoms may be useful, although their efficacy is unknown (44).

Bowel Dysfunction

Chronic diarrhea is reported by 13–50% of patients up to 10 years after treatment, with rectal cancer patients more likely than colon cancer patients to report diarrhea (24% vs. 10% p=0.04) (18, 32, 63). Diarrhea has been associated with limitations in activity and can negatively affect QOL (18, 32). Survivors who underwent an anterior resection reported a median of three bowel movements per day, frequency, urgency, evacuatory difficulties, and inability to differentiate stool and gas. These symptoms were most problematic during the first year after resection and were associated with fear, poor body image, and low self-confidence (38, 64).

Both preoperative and postoperative radiation for rectal cancer increases the risk of long-term bowel dysfunction. Preoperative short course radiation (5 Gray in 5 fractions) has been associated with a 2.5-fold higher rate of small bowel obstruction and 2-fold higher incidence of abdominal pain compared to those not treated in this manner (65) as well as increased bowel frequency and limitations in activities of daily living and social activities up to 5 years after treatment (41, 66). Postoperative radiation also results in frequent bowel movements similar to survivors who receive preoperative radiation and is associated up to five years after treatment with clustering of bowel movements (42%), increase in nighttime bowel movements (46%), incontinence (39%), pad wearing (41%), and inability to defer defecation (78%) (67, 68). Long-term anorectal dysfunction after radiation, including reduced reservoir capacity, can persist at 10 years (69).

Treatment for bowel problems after treatment for CRC typically includes anti-diarrheal medications, bulk-forming agents, use of undergarment pads, and diet manipulation (64). Elimination of specific foods (fats and oils, meat, milk products, raw vegetables, or fibrous foods) and the use of probiotic supplements has had limited benefit (63, 70). Attention to this issue is imperative as survivors may assume abnormal bowel symptoms are an inevitable consequence of treatment and may not address persistent symptoms at follow-up appointments (63, 71).

Pelvic Insufficiency Fractures after Radiation

Bone damage and risk of fractures may be increased after radiotherapy for rectal cancer. A large retrospective study of older women diagnosed with anal, cervical, or rectal cancer demonstrated a 65% increase in the cumulative incidence of pelvic fractures in rectal cancer survivors after radiation compared to nonirradiated patients (11.2% vs. 8.7% $p<0.001$), resulting in a possible increase in the absolute lifetime risk of fracture from 17% to 27%. The effect of radiation remained significant after controlling for other risk factors (72). The use of combined modality therapy may heighten the effect of radiation on bone density; medications and estrogen deficiency may further contribute to the risk of osteoporosis (73). Therefore, survivors who have received prior pelvic radiation should receive long-term monitoring of bone density, appropriate medical treatment of osteopenia and osteoporosis, and be carefully evaluated if symptoms suggesting fractures develop.

Urogenital Dysfunction

Urinary and sexual dysfunction are known complications of rectal cancer treatment, reported in at least 30% of patients undergoing definitive treatment (41, 74–77). In studies of short course radiation followed by total mesorectal excision (TME) versus TME alone, symptoms at five years included urinary incontinence (38%), difficulties in bladder emptying (31%), need to void within two hours of voiding (70%), and need for protective pads (57%) (41, 74). Risk factors for postoperative incontinence included preoperative incontinence, being female, perioperative blood loss, preoperative bladder emptying difficulties, autonomic nerve damage, and presence of a permanent stoma (40, 41, 74). Severity of urinary incontinence increased with time, from 18% at 3 months to 31% at five years, and contributed to a lower overall perception of health status (41, 74).

While preservation of autonomic nerves during TME has been shown to minimize permanent sexual dysfunction, abdominoperineal resection has been associated with lower sexual function at 5 years compared to anterior resection (26% vs. 48% $p=0.001$) (38, 78). Males enrolled in a TME trial reported generalized sexual dysfunction (76.4%), erectile dysfunction (79.8%), and ejaculatory problems (72.2%) after surgery. Risk factors included preoperative radiation, presence of a stoma, perioperative blood loss, anastomotic leak, and autonomic nerve damage. Women reported an increase in generalized sexual dysfunction

(62%), dyspareunia (59%), and vaginal dryness (56.6%) after treatment. Risk factors included preoperative radiation and the presence of a stoma (75). Vaginal stenosis can also occur after pelvic radiation and contribute to dyspareunia (79).

Few intervention trials have targeted urogenital dysfunction in rectal cancer survivors. A study of 32 men undergoing rectal resection for cancer or inflammatory bowel disease demonstrated that 79% of men receiving sildenafil reported reversal or satisfactory improvement in erectile dysfunction versus 13% receiving placebo (p=0.0009) (80). The use of vaginal dilators by women undergoing vaginal brachytherapy for cervical cancer has demonstrated benefit in maintaining vaginal patency, and dilators have been utilized empirically in rectal cancer survivors (79, 81).

Lifestyle and Behavior Interventions

While a careful assessment of QOL and treatment effects is an essential component of follow-up care for CRC, survivors are motivated to seek information on ways they can improve their outcomes, with informed choices especially important at the completion of treatment (82). Cancer survivors present unique opportunities to implement primary, secondary, and tertiary prevention strategies that may result in multiple beneficial outcomes (83). Many long-term survivors do not meet physical activity and dietary recommendations, and physicians can be powerful catalysts for promoting healthy behaviors (84, 85). In a prospective observational study of survivors with stage III colon cancer treated with adjuvant chemotherapy, Meyerhardt et al (86) demonstrated a 47% improvement in disease free survival (DFS) in those who engaged in at least 18 MET-hours per week of physical activity (6 or more hours per week of walking at an average pace) compared to inactive patients (less than 3 MET-hours per week) at a median follow-up of 2.7 years. Relapse-free (RFS) and overall survival (OS) were also improved. This effect was independent of other prognostic factors such as T stage, nodal status, treatment, performance status, age, or gender (86). In the Nurses' Health Study, greater than 18 MET-hours per week of physical activity after a diagnosis of colorectal cancer was associated with reduced cancer-specific mortality and overall mortality. Those women who increased their level of physical activity after diagnosis had a significant improvement in colorectal cancer-specific and overall mortality in both stage I/II and stage III disease (87). Thus, physical activity may improve CRC-specific outcomes and prevent the development of other morbidities such as cardiovascular events and osteoporosis (82).

Body mass index (BMI) may predict outcome in CRC survivors (88–90). Obese women had a significant increase in overall mortality but not in risk of colon cancer recurrence compared to normal weight women at a median follow-up of 9.4 years after adjuvant chemotherapy, a trend not seen in men (89). An evaluation of Dukes B and C colon cancer survivors who received adjuvant chemotherapy detected 27% increase in the risk of colon cancer recurrence or death, with a 38% excess risk of colon cancer events and a 51% excess risk of death before colon cancer or second primary cancer, among very obese (BMI ≥ 35 kg/m2) patients at a median follow-up of 11.2 years. Overall survival was also worse among very obese and underweight survivors (90). BMI and weight change after diagnosis in 1053 colon cancer survivors who received adjuvant chemotherapy was not associated with DFS, RFS or OS at a median follow-up of 5.3 years (91). Obese men with rectal cancer receiving adjuvant 5-FU and radiation were 61% more likely to have a local recurrence and 23% more likely to have an overall cancer recurrence compared to normal-weight men. Increasing BMI was also associated with a higher rate of abdominoperitoneal resection (92).

Visceral adiposity may be a better predictor of DFS, with those survivors exhibiting a visceral to subcutaneous fat ratio of greater than 50% having a significantly lower

cumulative DFS rate compared to those with lower ratios in a small cohort of 161 patients (93). Thus, survivors should be counseled about the importance of weight control and exercise, which may reduce the risk of cancer recurrence and improve overall health status.

The role of diet, nutritional supplements, and tobacco use in preventing cancer recurrence is often a topic of interest to cancer survivors. In a prospective observational study of dietary patterns in 1009 colon cancer survivors who received adjuvant chemotherapy, higher intake of a Western diet pattern (high in meat, fat, refined grains, and dessert) was associated with a more than 3-fold decrease in DFS compared to those with the lowest intake of the same diet, with a similar decrease in relapse-free and overall survival. This association was independent of treatment group or other traditional prognostic factors. A prudent diet (high in fruits, vegetables, poultry, and fish) was not associated with cancer recurrence or mortality (94). Additional prospective cohort studies have shown lower overall and CRC-specific mortality with consistent aspirin use and high circulating levels of 25-hydroxyvitamin D (95, 96). Lifetime tobacco usage may also impact colon cancer recurrence, with trends toward lower DFS in survivors with a 20 pack-year or greater smoking history compared to never smokers (97). These studies provide hypotheses for further prospective investigation and possible interventions to improve outcomes in CRC survivors.

Promoting Quality Survivorship Care

Survivors must contend with risk of cancer recurrence, effects of cancer treatment, and non-cancer comorbidities. The majority of recurrences in stage II or III colon cancer occur within 3 years of diagnosis, with rates of recurrence declining with time (less than 1.5% at 5 years and 0.5% at 8 years) (98, 99). Non-cancer comorbidities may have more influence on overall QOL and long-term survival than the cancer diagnosis (100). Therefore, CRC survivor care should shift from surveillance for recurrence initially to management of comorbidities and receipt of appropriate preventive care long-term. With the majority of long-term survivors reporting at least one symptom attributed to previous cancer diagnosis or treatment and more than 70% of survivors having comorbid conditions, coordination of care is paramount for optimal care of cancer survivors to prevent functional decline and ensure receipt of necessary care for both cancer and non-cancer conditions (20).

Follow-up remains intensive after curative treatment for CRC, with increasing visits to primary care physicians (PCP) and decreasing visits to oncologists over time (101–103). Although survivors followed only by a PCP did not perceive lower quality of care, PCPs reported significant uncertainty about surveillance protocols and side effects of treatments, and dissatisfaction with the transfer of care of survivors (102, 104). CRC survivors may receive less health behavior counseling and care for comorbid conditions compared to adults without cancer, and are more likely to experience an avoidable health outcome (100, 105). In addition, while receipt of preventive care is high in the early years after diagnosis, rates of preventive care received decreased after 5 years in CRC survivors (101). Survivors followed by both a PCP and an oncologist had the highest likelihood of receiving both preventive care (influenza vaccination, bone densitometry, and lipid monitoring), and cancer surveillance (colonoscopy, cervical cancer screening and mammography) (100, 101).

A shared model of care is ideal for survivorship care and may be facilitated by a survivorship care plan (106). In this plan, late effects (those that may occur in the future) and long-term effects (residual effects from treatment not expected to improve) can be delineated. The plan should be completed at the end of primary treatment by oncology providers, and include a summary of treatment received, a description of the plan for surveillance of cancer recurrence, ways to address the chronic physical and psychosocial

effects of cancer, and necessary lifestyle and preventive care measures appropriate for the individual survivor (10, 107).

Conclusion

Survivorship is a distinct phase of colorectal cancer treatment. Goals of care include surveillance for recurrence, management of late and long-term toxicities associated with multimodality treatment, encouragement of healthy diet and lifestyle behaviors, and adherence to recommended preventive care guidelines. Coordination of care, including the use of a survivorship care plan, is paramount to ensuring longevity. Further research evaluating issues specific to CRC survivorship and potential interventions need to be a priority.

Acknowledgments

We would like to thank Drs. Yu-Ning Wong, Roger Cohen, and Paul Engstrom for guidance, review, and editorial comments in the preparation of this manuscript.

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Table 1

Recommendations for the care of cancer survivors by the Institute of Medicine and National Research Council Committee on Cancer Survivorship (10)

1.	Raise awareness of the needs of cancer survivors, establish cancer survivorship as a distinct phase of cancer care, and act to ensure the delivery of appropriate survivor care.
2.	Provide a comprehensive care summary and follow-up plan, written by the providers who coordinated oncology treatment, that is clearly and effectly explained to the patient.
3.	Develop and use evidence-based clinical practice guidelines, assessment tools, and screening instruments to identify and manage late effects of cancer and its treatment.
4.	Develop quality of survivorship care measures and quality assurance programs to monitor and improve care received by survivors.
5.	
6.	
7.	
8.	Cancer survivors with short-term and long-term limitations in ability to work should be supported, while discrimination and adverse effects of cancer on employment should be actively eliminated.
9.	
10.	

Table 2

General Symptoms of Cancer Survivors (Not related to specific cancer or treatment)

Symptom	Short-term (≤ 3 yrs post diagnosis)	Long-term (> 3 yrs)	Intervention
Fatigue	67% (13)	23% (32)	NCCN Fatigue Guidelines (108) ONS PEP Guidelines (109)
Sleep difficulty	48% (13)		ONS PEP Guidelines (110)
Distress			NCCN Distress Guidelines (35)
• Anxiety	7% (14)		
• Depression	7% (14)		
• Negative feelings about body appearance		25% (32)	
• Fear of recurrence	67% (13)		

Table 3

Symptoms Most Common After Treatment of Rectal Cancer

Symptom	Short-term (≤ 3 yrs post diagnosis)	Long-term (> 3 yrs)	Intervention
Stomach ache, cramping, pain		5% (32)	
Bowel Dysfunction			† Antidiarrheal medication, bulk-forming agents (64)
▪ Clustering of BMs	42% (68)		
▪ Night time BM	46% (68)		
▪ Incontinence	39% (68)		† Diet modification: limit fats, meat, milk, raw vegetables, fiber (63, 70)
▪ Pad wearing	41% (68)		
▪ Inability to defer BM	78% (68)		
▪ Diarrhea (Schneider; Ramsey)			
▪ Constipation (Schneider)		14%–49% (18, 32) 7% (32)	
Urinary Incontinence (Surgery +/− Radiotherapy)		38% (74)	† Referral to Genito-urinary specialist
• Difficulty bladder emptying		31% (74)	
• Need to void within 2 hrs		70% (41)	
• Pad wearing		57% (41)	
Male Sexual Dysfunction			* Sildenafil (80)
• Loss of orgasm		50% (77)	
• General dysfunction		76% (75)	† Referral to Genito-urinary specialist
• Erectile dysfunction		80% (75)	
• Ejaculatory problems		72% (75)	
Female Sexual Dysfunction			
• General dysfunction		62% (75)	* Vaginal Dilators (79, 81)
• Dyspareunia		59% (75)	
• Vaginal dryness		57% (75)	† Referral to Genito-urinary specialist or Gynecologist

* One or more positive small studies;

† Efficacy not known

Table 4

Symptoms Due to Chemotherapy for Colorectal Cancer

Symptom	Short-term (≤ 3 yrs post diagnosis)	Long-term (> 3 yrs)	Intervention
Sensory neuropathy (5FU & Oxaliplatin)	92% (49, 50)	12% (7)	† NSAIDs, opiods, referral to neurology (44)

*One or more positive small studies;

†Efficacy not known