Original article

Risk of disability pension in patients following rectal cancer treatment and surgery

L. Chen[1], I. Glimelius[1,4], M. Neovius[1], S. Eloranta[1], S. Ekberg[1,2], A. Martling[3] and K. E. Smedby[1]

[1]Clinical Epidemiology Unit, Department of Medicine Solna, [2]Department of Medical Epidemiology and Biostatistics, and [3]Department of Molecular Medicine and Surgery, Karolinska Institute, Stockholm, and [4]Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden
Correspondence to: Dr L. Chen, Clinical Epidemiology Unit, Department of Medicine, Eugeniahemmet T2 Karolinska Hospital, 171 76 Stockholm, Sweden (e-mail: lingjing.chen@ki.se)

Background: **Aspects of survivorship, such as long-term ability to work, are increasingly relevant owing to the improved survival of patients with rectal cancer. The aim of this study was to assess risk and determinants of disability pension (DP) in this patient group.**

Methods: **Using Swedish national clinical and population-based registers, patients with stage I–III rectal cancer aged 18–61 years in 1995–2009 were identified at diagnosis and matched with population comparators. Prospectively registered records of DP during follow-up were retrieved up to 2013. Non-proportional and proportional hazards models were used to estimate the incidence rate ratio (IRR) for DP annually and overall. Potential variations in risk by demographic and clinical factors were calculated, with relapse as a time-varying exposure.**

Results: **A total of 2815 patients were identified and compared with 13 465 population comparators. During a median follow-up of 6·0 (range 0–10) years, 23·3 per cent of the relapse-free patients and 10·3 per cent of the population comparators received DP (IRR 2·40, 95 per cent c.i. 2·17 to 2·65). An increased annual risk of DP was evident almost every year until the tenth year of follow-up. Abdominoperineal resection was associated with an increased DP risk compared with anterior resection (IRR 1·44, 1·19 to 1·75). Surgical complications (IRR 1·33, 1·10 to 1·62) and reoperation (IRR 1·42, 1·09 to 1·84), but not radiotherapy or chemotherapy, were associated with risk of DP.**

Conclusion: **Relapse-free patients with rectal cancer of working age are at risk of disability pension.**

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Introduction

The number of patients with newly diagnosed rectal cancer per year exceeds 40 000 in the USA and 100 000 in the European Union[1–3]. With improvements in diagnosis and treatment, the 5-year survival rate of patients with rectal cancer is now higher than 50 per cent[4]. The high incidence and improved survival contribute to a growing number of disease-free patients, and increased attention to aspects of survivorship, such as return to work[5].

The primary treatment for rectal cancer is surgery, often combined with preoperative radiotherapy with or without concomitant chemotherapy, and there may be postoperative adjuvant chemotherapy[6]. Surgery is essential for cure, but morbidity risks are high with extensive surgery[7]. Knowledge of the late consequences of surgery and oncological treatment on ability to work provides a basis for refinement of treatment protocols and rehabilitation.

Previous studies of long-term work ability and employment status among rectal cancer survivors are scarce. The few that exist have investigated patients with colorectal cancer as a whole[8–12], or patients with rectal cancer as a minority group (fewer than 200 patients) among patients with multiple other types of cancer[13–15]. Existing studies have reported a reduced ability to work among patients with rectal cancer during the first year[14] or for up to 5 years[15] after diagnosis, and have sometimes indicated higher risks for patients with rectal cancer than for those with colonic cancer[8,14]. Importantly, none of these previous studies has investigated work ability in relation to clinical factors including treatment, or considered probable effects

on ability to work by cancer relapse. Thus, the extent to which the increased risk of lost work-days in previous studies was driven by cancer relapse or by treatment side-effects among patients in remission is not known. The aim of the present study was to evaluate the influence of cancer stage, surgical procedures, and neoadjuvant and adjuvant treatments on the risk of disability pension (DP) in patients following rectal cancer treatment.

Methods

In a matched cohort design, multiple Swedish national healthcare registers were used to compare DP status among working-age rectal cancer survivors and matched general population comparators for up to 10 years after diagnosis (or match date for comparators). Patients and comparators were selected between 1995 and 2009, and followed through 2013. Linkage between the registers was performed using the unique personal identity number assigned to all Swedish residents[16]. The study was approved by the regional ethics board in Stockholm, Sweden.

In 2009, Sweden had approximately 5·3 million inhabitants aged 18–61 years (total 9·1 million). The Swedish healthcare system is tax-funded, with universal access nationwide. As a means of work loss compensation, partial or complete DP is provided through the Swedish Social Insurance Agency (Försäkringskassan). Retirement usually takes place at the age of 65 years, but employees can choose to retire at age 61 years, or work until aged 67 years.

Study population

Identification of rectal cancer survivors

Patients with rectal cancer were identified from the Swedish Rectal Cancer Register, initiated in 1995 (from 2007 called the Swedish Colorectal Cancer Register). The vast majority (an estimated 98 per cent) of patients operated on during 1995–2009 underwent an open procedure. The register includes detailed clinical information for at least 5 years after diagnosis via specific registration forms (coverage is greater than 98 per cent of all invasive rectal adenocarcinomas; $n = 5058$)[17,18].

Identification of general population comparators

Population comparators were identified from a subset of the Total Population Register kept at Statistics Sweden[19]. This register includes all Swedish residents and holds information such as county of residence, vital status and migration. Comparators were sampled randomly (with replacement) from residents in Sweden who were alive and free from rectal cancer and DP at the beginning of the year of diagnosis of the patients. The population comparators were matched individually to the patients by sex, age, geographical region of residence and educational level.

Clinical characteristics and treatment

Clinical information included TNM stage at diagnosis (I–III), operation type (anterior resection, abdominoperineal resection (APR), Hartmann's procedure), treatment modality (abdominal surgery only, preoperative (chemo) radiotherapy, and postoperative chemotherapy with or without preoperative treatment), complications including reoperation within 30 days of surgery (yes or no), types of complication (surgical, infectious, other), recurrence (yes or no), and dates of locoregional and/or distant relapse during follow-up. Hospitals providing the primary surgical treatment were classified according to number of procedures as high (more than 50 per year), medium (25–50 per year) and low (fewer than 25 per year) volume.

Co-variables

Sick-leave episodes longer than 14 days in the year starting 2 years before the diagnosis of rectal cancers (or match date for the comparators) were registered from the first day, using data from the MiDAS database kept by the Swedish Social Insurance Agency[20]. Unemployment status in the year before diagnosis (or match date for the comparators) was available from the Longitudinal Integrated Database for Health Insurance and Labour Market Studies (LISA) held at Statistics Sweden[21]. People without employment are also eligible for DP in Sweden. The highest attained educational level before diagnosis (less than 10, 10–12, or more than 12 years) was retrieved from the LISA database as a proxy for socioeconomic status.

Outcome assessment

Disability pension

Information about DP was retrieved from the MiDAS database. DP can be granted at 25, 50 or 100 per cent, as described previously[22].

Follow-up

Patients with rectal cancer were followed from date of diagnosis to the date of first emigration, death, retirement (age 65 years), administrative censoring (31 December 2013) or a maximum of 10 years after diagnosis, whichever occurred first. Dates of death were retrieved from the Cause-of-Death Register[19,22]. The matched comparators accrued risk time from the date of diagnosis of the patient with rectal cancer, and were additionally censored if diagnosed with rectal cancer.

Statistical analysis

Differences in the distribution of demographic characteristics between patients with rectal cancer and comparators were tested with χ^2 tests. Using complete-case Cox proportional hazards and Poisson regression models, the DP rate between the two cohorts was compared by estimating the incidence rate ratio (IRR) with 95 per cent c.i., with time from diagnosis as the timescale. Adjustment was made for previous sick leave, unemployment, relapse status and matching variables. Relapse was treated as a time-varying co-variable, where all patients were classified as unexposed until their first relapse. Incidence rates of DP among demographic and clinical subgroups of the patients were compared with the rates in the comparators. In addition, demographic and clinical characteristics were assumed to interact with relapse status, to enable estimation of a separate set of rate ratios for relapse-free follow-up time. Poisson regression was used to estimate the annual IRR for DP throughout the relapse-free follow-up interval. Tests for interaction were carried out by comparing models including interaction terms with models with only main effects using likelihood ratio tests. The proportional hazards assumption was tested formally, based on the Schoenfeld residuals obtained from the Cox model.

Kaplan–Meier survival functions and cumulative incidence functions (treating death and retirement as competing events) were estimated to demonstrate the absolute risks of DP. All statistical analyses were performed with SAS® version 9.3 (SAS Institute, Cary, North Carolina, USA) and STATA® release 12.0 (StataCorp LP, College Station, Texas, USA).

Results

As the aim of the study was to investigate DP with a focus on relapse-free patients, individuals who were not eligible for treatment with curative intent (stage IV disease, ineligible for primary surgery; 1395 patients), patients with other previous primary cancer diagnoses (except non-melanoma skin cancer; 210) and those with DP already at diagnosis (497 patients) were excluded. Patients treated by local excision only (77) were also excluded, resulting in 2815 patients remaining in the study cohort (*Fig. S1*, supporting information). In the study population of working-age rectal cancer survivors, 59·9 per cent were men and 40·1 per cent were women. Median age at diagnosis was 55 years, and 23·1 per cent were diagnosed below the age of 50 years. Patients were followed up for a median of 6·0 (range 0–10) years overall, and for a relapse-free median of 5·7 years (*Table S1*, supporting information). Some 12·2 per cent of the patients and 13·0 per cent of the comparators had had at least one episode of sick leave 1–2 years before diagnosis. Anterior resection was the most commonly used surgical approach, and the majority of the patients had been treated with preoperative (chemo)radiotherapy (*Table 1*). Surgical complications, such as wound infection, anastomotic leakage, bleeding or stoma complications during the postoperative period, occurred in one-quarter of the patients; of these, about one-third needed reoperation. Some 24·9 per cent of the patients experienced a locoregional (5·2 per cent) or distant (20·7 per cent) relapse during follow-up, almost all of which occurred within the first 5 years.

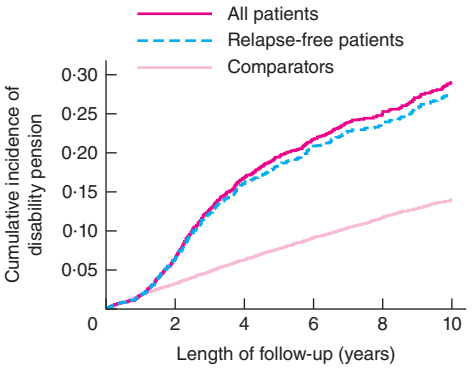
Risk of disability pension in patients with rectal cancer *versus* comparators

The net incidence of DP was plotted during the entire follow-up (including time after relapse) as well as during relapse-free follow-up (*Fig. 1*). The bulk of the DP

Table 1 Clinical characteristics among working-age rectal cancer survivors in Sweden

	Patients with rectal cancer ($n = 2815$)
Tumour stage	
I	738 (26·2)
II	919 (32·6)
III	1158 (41·1)
Type of operation	
Anterior resection	1875 (66·6)
Abdominoperineal resection	826 (29·3)
Hartmann's procedure	86 (3·1)
Missing	28 (1·0)
Treatment	
Abdominal surgery only	289 (10·3)
Preoperative (chemo)radiotherapy	1566 (55·6)
Postoperative chemotherapy*	736 (26·1)
Missing	224 (8·0)
Postoperative complications (within 30 days)	
Surgical	731 (26·0)
Infectious	174 (6·2)
Other†	215 (7·6)
Reoperation‡	291 (10·3)
Relapse	
Overall relapse	702 (24·9)
Within 5 years	677 (24·0)
Local relapse	147 (5·2)
Within 5 years	139 (4·9)
Distant metastasis	584 (20·7)
Within 5 years	565 (20·1)
Hospital volume	
High	1227 (43·6)
Moderate	604 (21·5)
Low	387 (13·7)
Missing	597 (21·2)

Values in parentheses are percentages. *Includes postoperative chemotherapy only or in combination with preoperative treatment. †Includes 45 patients (1·6 per cent) with cardiovascular complication and 170 (6·0 per cent) with other complications. ‡Number of patients having a secondary surgical procedure during the same hospital stay.



No. at risk						
All patients	2815	2504	1879	1146	701	398
Relapse-free patients	2815	2234	1640	1027	655	382
Comparators	13465	12885	11337	7659	4988	3014

Fig. 1 Kaplan–Meier curves showing the cumulative incidence of disability pension in all patients with rectal cancer, relapse-free patients and population comparators

incidence occurred among relapse-free patients, and the incidence increased only marginally when time after relapse was added. During relapse-free follow-up, patients had a greater than twofold increased risk of DP compared with comparators (IRR 2·40, 95 per cent c.i. 2·17 to 2·65) (*Fig. 2*), whereas the IRR was 2·59 (2·35 to 2·85) when relapse was included. The risk increase was not significantly modified by age, sex, educational level, employment status or calendar period. However, survivors with previous sick leave were at an eightfold increased risk (IRR 8·30, 6·90 to 9·97) compared with population comparators with no previous sick leave ($P_{interaction} < 0·001$).

The cumulative incidence of DP at 10 years after diagnosis, accounting for competing events, was 23·3 per cent among rectal cancer survivors compared with 10·3 per cent in the comparators (*Fig. S2a*, supporting information). Men and women with rectal cancer had a similar cumulative incidence of DP at 10 years, but the incidence among female comparators was higher than among male comparators (*Fig. S2b*, supporting information). The annual risk of DP was statistically significantly greater in patients with rectal cancer from the second to the tenth year of follow-up (IRR year 2: 3·25, 95 per cent c.i. 2·58 to 4·09; IRR year 10: 2·30, 1·21 to 4·35), except in the eighth year (*Fig. 3*).

	DP cases per person-years at risk			
	Patients with rectal cancer	Population comparators	IRR for DP*	IRR for DP‡
All patients	512 of 14291	1393 of 90072	2·40 (2·17, 2·65)	
Sex				
M	279 of 8420	752 of 54249	2·55 (2·22, 2·92)	
F	233 of 5871	641 of 35823	2·24 (1·92, 2·60)	
Age (years)				
≤40	17 of 1073	41 of 5787	2·17 (1·23, 3·82)	
41–50	81 of 3653	251 of 23549	2·12 (1·65, 2·72)	
51–60	375 of 8907	1023 of 57009	2·47 (2·19, 2·78)	
>60	39 of 658	78 of 3727	2·58 (1·75, 3·79)	
Educational level (years)				
≤ 9	172 of 3434	525 of 21908	2·16 (1·81, 2·56)	
10–12	236 of 6314	621 of 40699	2·54 (2·18, 2·95)	
> 12	103 of 4523	246 of 27438	2·54 (1·02, 3·20)	
Calendar period				
1995–2002	363 of 7555	1044 of 49467	2·28 (2·02, 2·57)	
2003–2009	149 of 6736	349 of 40605	2·67 (2·20, 3·24)	
Previous sick leave (1–2 years before diagnosis)				
No	332 of 12115	801 of 75749	2·70 (2·38, 3·07)	
Yes†	137 of 1440		8·30 (6·90, 9·97)	
Unemployment (0–1 years before diagnosis)				
No	412 of 12625	1116 of 79602	2·43 (2·17, 2·72)	
Yes†	100 of 1666		3·23 (2·62, 3·97)	

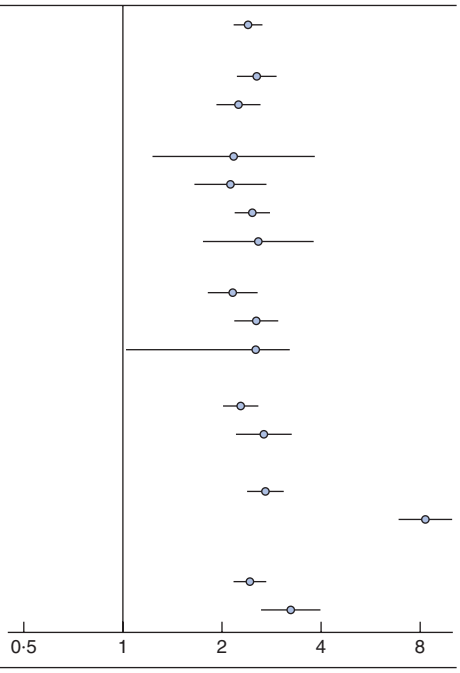


Fig. 2 Incidence rate ratios (IRRs) with 95 per cent c.i. for disability pension (DP) among relapse-free patients following diagnosis of rectal cancer compared with population comparators. *Adjusted for sex, age at diagnosis, calendar period, educational level, region, sick leave before and unemployment 1 year before diagnosis. Follow-up time was censored at death, retirement, migration or end of 10-year follow-up, whichever came first. Relapse was included as a time-varying exposure. †The comparison group for this subgroup was still the general comparators who had not had previous sick leave, as in the previous subgroups. ‡The graph is plotted on a logarithmic scale

	DP cases per person-years at risk			
	Patients with rectal cancer	Population comparators	IRR for DP*	IRR for DP†
Any disability pension				
1st year after disability	47 of 2815	232 of 13465	0·98 (0·72, 1·34)	
2nd year after disability	116 of 2608	192 of 13146	3·25 (2·58, 4·09)	
3rd year after disability	136 of 2234	207 of 12885	4·13 (3·33, 5·14)	
4th year after disability	80 of 1965	194 of 12477	2·91 (2·24, 3·78)	
5th year after disability	39 of 1640	159 of 11337	1·87 (1·32, 2·66)	
6th year after disability	36 of 1289	129 of 9327	2·25 (1·56, 3·26)	
7th year after disability	22 of 1027	96 of 7659	1·93 (1·21, 3·07)	
8th year after disability	8 of 822	83 of 6249	0·81 (0·39, 1·67)	
9th year after disability	16 of 655	57 of 4988	2·32 (1·33, 4·04)	
10th year after disability	24 of 489	110 of 3850	2·30 (1·21, 4·35)	

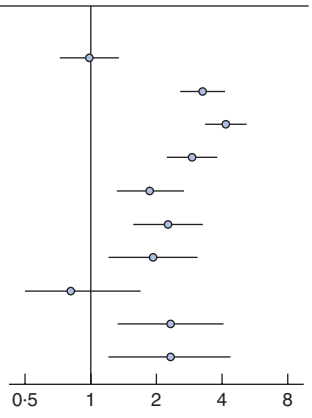


Fig. 3 Annual incidence rate ratio (IRR) with 95 per cent c.i. for disability pension (DP) among relapse-free patients following diagnosis of rectal cancer compared with population comparators. *Adjusted for sex, age at diagnosis, calendar period, educational level, region, sick leave before and unemployment 1 year before diagnosis. Follow-up time was censored at death, retirement, migration or end of 10-year follow-up, whichever came first. Relapse was included as a time-varying exposure. †The graph is plotted on a logarithmic scale

Risk of disability pension by cancer stage, operation, treatment and complications

When investigating clinical determinants among patients with rectal cancer only, operation with APR conferred an increased risk of DP (IRR 1·44, 95 per cent c.i. 1·19 to 1·75) compared with anterior resection (*Table 2*). This higher risk was also found among patients with any postoperative complication (within 30 days) (IRR 1·37, 1·14 to 1·65). Specifically, patients who had surgical complications (IRR 1·33, 1·10 to 1·62) or reoperation (IRR 1·42, 1·09 to 1·84) were at increased risk compared with patients without such complications. Risk of DP did not vary significantly by tumour stage, preoperative or postoperative treatment, non-surgical complications or hospital volume. The association with APR remained after adjusting for complications (IRR 1·45, 1·19 to 1·76), suggesting that the operation-associated risk was not mediated through complications. All groups were at increased DP risk compared with the population comparators (*Table S2*, supporting information).

Table 2 Incidence rate ratio for disability pension among relapse-free patients with rectal cancer, by clinical characteristics

	DP cases per person-years at risk	IRR for DP*
Tumour stage		
I	135 of 3824	1·00 (reference)
II	175 of 4475	1·09 (0·87, 1·37)
III	177 of 4728	1·11 (0·88, 1·39)
Type of operation		
Anterior resection	309 of 8988	1·00 (reference)
Abdominoperineal resection	164 of 3733	1·44 (1·19, 1·75)
Hartmann's procedure	14 of 305	1·22 (0·71, 2·09)
Treatment		
Abdominal surgery	70 of 1744	1·00 (reference)
Preoperative (chemo)radiotherapy	307 of 8082	1·22 (0·93, 1·61)
Postoperative chemotherapy†	110 of 3201	1·09 (0·80, 1·49)
Complications‡		
No	291 of 8661	1·00 (reference)
Yes	196 of 4365	1·37 (1·14, 1·65)
Surgical complications		
No	336 of 9764	1·00 (reference)
Yes	151 of 3263	1·33 (1·10, 1·62)
Non-surgical complications		
No	442 of 11924	1·00 (reference)
Yes	45 of 1103	1·13 (0·81, 1·57)
Reoperation‡		
No	420 of 11750	1·00 (reference)
Yes	67 of 1277	1·42 (1·09, 1·84)
Hospital volume		
High	209 of 5729	1·00 (reference)
Moderate	107 of 2789	0·89 (0·68, 1·17)
Low	71 of 1995	0·88 (0·68, 1·16)

Values in parentheses are 95 per cent c.i. DP, disability pension; IRR, incidence rate ratio. *Adjusted for sex, age at diagnosis, calendar period, educational level, region, sick leave before and unemployment 1 year before diagnosis. Follow-up was censored at death, retirement, migration or end of 10-year follow-up, whichever occurred first. Relapse was included as a time-varying exposure. †Includes postoperative chemotherapy only or in combination with preoperative treatment. ‡Within 30 days of primary surgery.

Discussion

In this large population-based study of prospectively recorded clinical data and DP listings, relapse-free rectal cancer survivors had, on average, more than double the risk of DP up to 10 years after diagnosis compared with population comparators. In absolute terms, this translated into one in four of the patients still alive and of working

age being on DP at 10 years after diagnosis, compared with one in ten of the comparators. Sick leave before diagnosis significantly modified the risk of DP, although a twofold increased risk was still evident among patients without previous sick leave. Surgical factors including operation type (APR) and severe surgical complications, rather than additional oncological treatment, were associated with higher DP risk.

Previous studies on work ability and DP risk among patients with colorectal cancer[8] or with different cancer types including rectal cancer[14] have shown an increased risk of DP following a rectal cancer diagnosis, in line with the present overall findings. However, no previous study has estimated the degree of influence of cancer relapse, or investigated potential variation in risk by detailed clinical factors and treatment. In a Norwegian study[8], DP risk was increased twofold among survivors with localized cancer at diagnosis, threefold among patients with regional cancer spread, and tenfold in those with distant cancer over 14 years of follow-up. The twofold to threefold increased risk associated with locoregional disease[8] is in line with the increased risk observed among patients with stage I–III disease in the present study. The higher risk in patients with distant cancer in the Norwegian study probably reflects the palliative stage of the vast majority of these patients, and indirectly supports the present findings of a higher risk among all patients, including those with relapse. A previous register-based Swedish study[14] further showed that rectal cancer survivors had 1·7 times more DP days 1 year after diagnosis than a matched population sample.

Importantly, most of the increased DP risk remained for patients who did not experience relapse. Thus, the observed excess risk likely reflects longstanding treatment side-effects and late effects from the initial disease, leading to lower productivity. The treatment most strongly associated with DP risk was the operation type APR, which is used for patients with distal tumours. APR is associated with short- and long-term complications such as intra-abdominal or pelvic abscesses, nerve and urological injury, perineal wounds and stoma[23]. Quality of life after APR has been considered worse than that following low anterior resection[24], although one small comparative study[25] indicated the opposite. DP risk was also associated with short-term surgical complications, especially reoperation within 30 days of operation, in line with a Danish study[12] of transition from work to sick leave and DP among patients with colorectal cancer. Previously described long-term effects of rectal cancer treatments include mainly oxaliplatin-induced peripheral neuropathy, bowel dysfunction, pelvic insufficiency fractures after radiation, and urogenital dysfunction[26]. Whether these or other late complications explain the increased risk of DP is unclear. Studies of reasons for altered work ability and quality of life following rectal cancer treatments are needed to clarify the underlying association.

Previous sick leave, a proxy for co-morbidity, strongly modified the risk of DP in the present study. Similarly, prediagnostic sick leave (and unemployment) at diagnosis were shown to be risk factors for long-term DP among colorectal cancer survivors in two previous studies[8,12]. In addition, in a Canadian study[10] older age and low income level increased the likelihood of colorectal cancer survivors having to leave the workforce. Taken together, socioeconomic factors and previous sick leave should clearly be considered as predictors of DP risk in the clinical setting in addition to treatment-related factors, although the increase was also evident among patients with no previous sick leave and in those with a high educational level.

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Supporting information

Additional supporting information may be found in the online version of this article:

Fig. S1 Flow chart for identification of the study population (Word document)

Fig. S2 Cumulative incidence of disability pension in relapse-free patients following diagnosis of rectal cancer compared with population comparators, overall and stratified by sex (Word document)

Table S1 Demographic characteristics of working-age rectal cancer survivors and population comparators in Sweden (Word document)

Table S2 Incidence rate ratios for disability pension among relapse-free patients following diagnosis of rectal cancer compared with comparators, by clinical characteristics (Word document)