

Physical functional limitations and psychological distress in people with and without colorectal cancer: findings from a large Australian study

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Title

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Abstract

Purpose: To quantify physical disability and psychological distress in people with and without colorectal cancer (CRC).

Methods: Questionnaire data (2006-2009) from 267,153 Australian general population members aged ≥ 45 years participating in the 45 and Up Study (n=213,231 following exclusions) were linked to cancer registry and hospital admission data, to ascertain CRC status. Modified Poisson regression estimated adjusted prevalence ratios (PRs) for physical disability and psychological distress in participants with CRC versus those without.

Results: Compared with participants without CRC (n=210,836), CRC survivors (n=2,395) had significantly higher physical disability prevalence (11.9% versus 19.5%, respectively): PR=1.11 (95%CI=1.03-1.20); and a similar prevalence of distress (23.1% versus 20.2%): PR=1.03 (0.94-1.20). Adverse outcomes were associated with certain clinical characteristics. Compared to participants without CRC, CRC survivors diagnosed 5-<10 and ≥ 10 years, with regional spread and without recent cancer treatment had broadly similar outcomes; survivors with metastatic CRC and recent treatment had 30-60% higher prevalence of disability and distress. Compared to participants with neither CRC nor disability, PRs for distress were 4.71 (4.22-5.26) for those with disability and CRC; and 4.22 (4.13-4.31) for those with disability without CRC.

Conclusions: Physical disability is elevated in CRC survivors. Psychological distress is elevated 4- to 5-fold with disability, regardless of CRC diagnosis, with lesser increases around diagnosis and treatment.

Implications for cancer survivors: CRC survivors with less advanced disease and who have not been recently diagnosed or treated have physical disability and psychological distress comparable to the general population. Survivors with disability are at particularly high risk of psychological distress.

Keywords: Colorectal cancer, physical functional limitations, psychological distress, clinical characteristics, joint consideration

Introduction

Colorectal cancer (CRC) is one of the most common cancers worldwide [1], and the third most common cancer in Australia [2]. The 5-year survival for CRC in Australia has increased from 50% to 69% over the past three decades, with a 2013 estimate of almost 200,000 people living with CRC [2].

There is increasing emphasis on gaining a greater understanding of cancer survivorship experience, including “person-centred” outcomes such as physical functioning and psychological wellbeing. Evidence on these outcomes, indicative of the quality of life, is critical to inform policy and practice and the provision of holistic support to CRC survivors.

In general, a diagnosis of cancer is associated with lower levels of physical functioning and a greater likelihood of physical disability [3-9]. Recent diagnosis or advanced disease are associated with higher levels of psychological distress as well [10-12]. Available evidence on cancer survivors also indicates that the risk of psychological distress in long-term cancer survivors relates more strongly to physical disability than to cancer diagnosis per se [13]. However, cancer is a heterogeneous disease, with significant differences in incidence, symptoms, treatment and survival across cancer types [14]. There is a lack of large-scale reliable evidence on physical functional limitations and psychological distress in relation to CRC diagnosis and its clinical characteristics, particularly for long-term CRC survivors. There is also a lack of evidence on how the relationship of CRC diagnosis and psychological distress varies by levels of physical functional limitations.

The aim of this study was to quantify and compare physical functional limitations and psychological distress between people with and without CRC in a large cohort of Australian adults. We also examined this association in relation to different clinical characteristics of CRC and in a range of population subgroups, and investigated the joint relationship between physical functional limitations and psychological distress in people with and without CRC.

Methods

Data resources

Data were from the Sax Institute’s 45 and Up Study, a prospective cohort study that included more than 267,000 people from New South Wales (NSW), Australia. The details of the study methods and characteristics of the cohort are described elsewhere [15]. Briefly, participants were men and women aged ≥ 45 years old randomly sampled from the Medicare Australia database provided by Services Australia (formerly the Australian Department of Human Services). The 45 and Up Study covered around 10% of the aged-matched population in NSW. Individuals joined the study by completing a questionnaire distributed between 2006 and 2009, and giving informed consent for linkage of their data to population health databases. Participants aged ≥ 80 years old and residents of rural areas were oversampled by a factor of two. The baseline questionnaire collected individual self-reported data from participants on demographic factors, smoking, alcohol intake, physical activity, diet, height, weight, surgical history, physical functioning impairment, income, social support, quality of life, self-rated health, falls, mental health and medical history.

Questionnaire data from the study participants were linked probabilistically by the NSW Centre for Health Record Linkage to two population-wide health databases [16]: 1) NSW Cancer Registry (NSWCR; January 1994 to December 2013), which provided records of all diagnosed cancers (except non-melanoma skin cancers), including cancer type, date of diagnosis, cancer stage, and other details of cancer for residents in NSW; 2) NSW Admitted Patient Data Collection (APDC; July 2001 to June 2016), which provided hospital admission data of all

public and private hospitals in NSW, including admission date, primary diagnosis code, and up to 50 more diagnosis codes. Data from 2006-2009 were available in the NSWCR and the APDC datasets.

Study variables

Exposure

The main exposure in this analysis was CRC diagnosis at baseline. An individual was considered to have CRC if they were registered in the NSWCR dataset within 12 years prior to baseline or had a diagnosis in the APDC dataset within 5 years prior to baseline, according to the International Statistical Classification of Disease and Related Health Problems (ICD-10) codes of C18 to C21 [17]. Date of diagnosis from NSWCR or APDC, whichever was the earliest, was used to identify CRC prior to enrolment in the study.

Clinical characteristics of CRC included time since diagnosis, cancer stage at diagnosis, and whether respondents had received any treatment for cancer in the last month before completing the baseline questionnaire. Time since diagnosis was calculated as the date of the baseline 45 and Up Study questionnaire completion minus the date of CRC diagnosis. It was categorised as <1 year, 1 -<2 years, 2 -<5 years, 5 -<10 years, and ≥ 10 years. Stage of CRC was derived from the NSWCR dataset, categorised as localised spread, regional spread, and distant metastases. Recent treatment for cancer was based on self-reported treatment for cancer in the previous month, derived from the baseline questionnaire of the 45 and Up Study.

Outcomes

The two outcomes in this analysis, physical functional limitation and psychological distress, were derived from self-reported data in the baseline questionnaire of the 45 and Up Study.

Physical functional limitation was assessed using the Physical Functioning scale from the Medical Outcomes Study (MOS-PF) [18], which asks participants whether they are limited in their ability to perform vigorous and moderate physical activities and tasks such as lifting, shopping, climbing stairs, walking, bending, kneeling, stooping, bathing or dressing. Scores of MOS-PF ranged from 0 to 100, where higher scores indicated fewer limitations. Physical functional limitation was classified as no limitations (MOS-PF=100); minor limitations ($90 \leq \text{MOS-PF} \leq 99$); moderate limitations ($60 \leq \text{MOS-PF} \leq 89$); and severe limitations ($0 \leq \text{MOS-PF} \leq 59$) [13].

Psychological distress was measured using the Kessler Psychological Distress Scale (K10) [19]. The scale is designed to measure anxiety and depression through a 10-item questionnaire. Each question pertains to an emotional state and has a five-level response scale. Scores of K10 ranged from 10 to 50, where high scores indicated higher levels of distress. Psychological distress was categorised as low distress ($10 \leq \text{K10} \leq 15$); moderate distress ($16 \leq \text{K10} \leq 21$); and high distress ($22 \leq \text{K10} \leq 50$) [20].

Other variables

Socio-demographic characteristics considered to be potential confounding factors in the relationship between the outcomes (physical functional limitations and psychological distress) and CRC diagnosis were: age, sex, education, region of residence, and country of birth. These variables were based on self-reported data from the baseline questionnaire of the 45 and Up Study, except for region of residence, which was derived from the Accessibility Remoteness Index of Australia Plus (ARIA+) [21] score for each participant's postcode as recorded in the Medicare Australia Database.

Study population

After logical imputation and backfilling, proportions of missing data in outcome variables were: physical functioning limitations (n=35,486; 13.3%) and psychological distress (n=30,330; 11.4%). Imputing missing data in outcome does not add materially to beta estimates from regression models, unless the imputation model includes strong predictors of the missing values [22-23], such as comorbidity, which is beyond the scope of this study. Hence, excluding participants with missing outcomes, as was done here, was considered the most appropriate option. Respondents with missing/invalid data on physical functional limitations or psychological distress were excluded from this analysis (n=53,468, 20% of 266,699 participants). Those remaining were grouped into people with and without CRC at baseline. CRC survivors at baseline were identified according to the aforementioned criteria; people without CRC were identified as participants without any record of CRC diagnosis before they completed the baseline questionnaire.

Ethics approval for the 45 and Up Study as a whole was provided by the University of New South Wales Human Research Ethics Committee. Ethics approval for the present study was provided by the NSW Population and Health Services Research Ethics Committee (12/CIPHS/31) and the Australian National University Human Research Ethics Committee (2012/504).

Statistical analysis

Distributions of the MOS-PF and K10 scores by CRC diagnosis in different age groups were presented using histograms. MOS-PF and K10 scores were then categorised as outlined above, respectively. Prevalence of each category of physical functional limitations and psychological distress were calculated according to CRC diagnosis and its clinical characteristics.

A modified Poisson Regression model with robust error variance [24] was used to estimate prevalence ratios (PRs) for outcomes in those with versus without CRC, adjusting for age, sex, education, region of residence, and country of birth. In this study, there were no missing data in the exposure variable (cancer status); proportion of missing data in covariates adjusted for in the models were <2% (no missing data in age or sex; missing 1.1% for education, 1.9% for region of residence and 0.6% for country of birth) and were included as separate categories in regression models. The main analysis included three groups of regression models: 1) PRs and 95% confidence intervals (CIs) of severe limitations and moderate-to-high distress were estimated according to CRC diagnosis and its clinical characteristics. These analyses used people without CRC as the reference group; 2) adjusted PRs and 95%CIs of severe limitations and moderate-to-high distress in participants with and without CRC were estimated within the following subgroups: age groups (45-59, 60-69, 70-79, and ≥80 years), sex (male, female), education (university, certificate/diploma, ≤secondary school), residence (major city, inner regional, and outer regional/remote area), and country of birth (Australian born and not Australian born). interaction terms were included in the model to assess statistical interaction; 3) to jointly consider psychological distress in relation to CRC diagnosis and physical functional limitations, PRs and 95%CIs of moderate-to-high distress were estimated among participants with and without CRC stratified by levels of physical functioning (no limitations, minor limitations, moderate limitations, and severe limitations). This analysis used people with neither CRC diagnosis nor physical functional limitations as the reference group.

Two sensitivity analysis were conducted. First, the prevalence of severe physical functional limitations and moderate-to-high psychological distress were compared between CRC survivors and a restricted comparison group of those without any cancer (as opposed to the

main comparison group, which was those without CRC only). Second, PRs and 95% CIs of alternative outcome measures were examined: moderate-to-severe limitations ($0 \leq \text{MOS-PF} \leq 89$) and high distress ($22 \leq \text{K10} \leq 50$) comparing those with and without CRC.

All statistical analyses were conducted using Stata software, version 14.

Results

At baseline, 2,395 CRC survivors and 210,836 participants without CRC had valid data on physical functional limitations and psychological distress (Supplementary file: Table S1). Compared to people without CRC, CRC survivors were, in general, older, more likely to be male, and of lower educational attainment. Region of residence and country of birth were similarly distributed between participants with and without CRC. Most CRC survivors had their cancers diagnosed within the past 2 to 10 years, had disease with regional spread, and had not received treatment for cancer in the past month (Table 1). Among CRC survivors, 1,539 were diagnosed with colon cancer (ICD-10 codes of C18), 679 were diagnosed with rectal cancer (C20), 234 were diagnosed with cancer of recto-sigmoid junction (C19), and 49 were diagnosed with anal cancer (C21) (Supplementary file: Table S2).

Physical functional limitations in relation to CRC diagnosis

Physical disability, indicated by lower MOS-PF scores, increased markedly with age. The proportion of participants with relatively low MOS-PF scores was higher among CRC survivors compared to people without CRC (Supplementary file: Figure S1).

Overall, 19.3% of participants with CRC had no physical limitations, compared to 35.2% of those without CRC; while 19.5% and 11.9%, respectively, had severe limitations (Supplementary file: Table S3). Compared to people without CRC, severe limitations were more common among CRC survivors with recent diagnosis, with metastatic cancer stage, or who had received treatment for cancer in the last month.

Overall, the PR (95% CI) for severe limitations, adjusting for age, sex, education, region of residence, and country of birth, was 1.11 (1.03-1.20) in people with versus without CRC. CRC survivors diagnosed more than 5 years previously (PR=1.04 (0.90-1.20) for those diagnosed ≥ 10 years; 0.97 (0.75-1.27) for those diagnosed 5-<10 years), with regional spread of cancer (PR=1.05 (0.93-1.19)), and those who had not received treatment for cancer in the last month (PR=0.99 (0.90-1.08)) had similar prevalence of severe limitations to those without CRC (Figure 1). The adjusted PRs (95% CIs) were 1.33 (1.09-1.62), 1.48 (1.12-1.96) and 1.61 (1.39-1.87) for CRC survivors diagnosed within a year, with metastatic disease and who had received treatment for cancer in the past month, respectively, compared to those without CRC (Figure 1).

Of CRC survivors aged 45-59, 11.2% had severe limitations compared to 7.1% of those without CRC in the same age group; 34.9%/38.0% of people with/without CRC aged over 80 had severe limitations. Hence, the relative prevalence of severe limitations was higher in younger compared to older people, with PRs in people with versus without CRC of 1.51 (1.16-1.93) for age 45-59 and 0.95 (0.84-1.08) for age ≥ 80 years ($p_{\text{interaction}}=0.013$). There was no statistically significant variation in the CRC-related PRs according to other examined factors, including sex, education, residence, and country of birth (Figure 2).

In sensitivity analyses, the PRs (95% CIs) of severe limitations in CRC survivors versus people without any cancer did not differ materially from the main analyses comparing CRC survivors with the general population without CRC (Supplementary file: Figure S3). Moderate-to-severe limitations (MOS-PF ≤ 89) was more prevalent among CRC survivors compared to those

without CRC with most clinical characteristics, except in those diagnosed within 1-2 years and more than 10 years previously (Supplementary file: Figure S6).

Psychological distress in relation to CRC diagnosis

The distribution of K10 scores were broadly similar across age groups regardless of CRC diagnosis (Supplementary file: Figure S2).

The crude prevalence of low ($10 \leq K10 \leq 15$), moderate ($16 \leq K10 \leq 21$), and high ($22 \leq K10 \leq 50$) distress were similar in CRC survivors and those without CRC. However, high distress was more common in survivors with metastatic cancer and recent treatment (Supplementary file: Table S4). The prevalence of moderate-to-high psychological distress did not differ between people with and without CRC (adjusted PR (95%CI) 1.03 (0.94-1.11)) (Figure 3), nor did it vary significantly with time since diagnosis. Moderate-to-high distress increased by 46% in CRC survivors with metastatic disease and was 31% higher in those who had received treatment for cancer in the past month, compared to people without CRC (Figure 3).

Compared to people without CRC, there was no significant association between CRC survivorship and moderate to high distress in all subgroups examined, nor was there any significant variation in the CRC-distress relationship according to any of the factors examined (Figure 4).

In sensitivity analyses, the PR of moderate-to-high distress among CRC survivors versus those without cancer remained similar to the PR of moderate-to-high distress among people with versus without CRC (Supplementary file: Figure S4). When high distress ($K10 \geq 22$) was considered, we found no statistically significant difference in the prevalence between people without CRC and CRC survivors according to all clinical characteristics examined (Supplementary file: Figure S7).

Joint consideration of psychological distress in relation to physical functional limitations and CRC diagnosis

Stratification based on participants' CRC diagnosis and physical functional limitations showed that moderate-to-high distress was strongly related to limitations in physical functioning, rather than CRC diagnosis. 10%-15% of participants with no limitations had moderate-to-high distress compared to 40%-50% of those with severe limitations. Compared to participants without a CRC diagnosis or physical functional limitations, the PRs (95% CIs) of moderate-to-high distress were 1.33 (1.30-1.36), 2.28 (2.23-2.33), and 4.22 (4.13-4.31) among non-CRC participants with minor, moderate, and severe limitations, respectively.

There was no statistically significant difference in the prevalence of moderate-to-high distress in CRC survivors with no or minor physical limitations, compared to people without CRC and with no limitation. The PRs (95% CIs) of moderate-to-high distress in CRC survivors with moderate and severe limitations were 2.04 (1.77-2.36) and 4.71 (4.22-5.26), respectively, compared to non-CRC participants with no limitation (Figure 5).

Results from sensitivity analyses showed similar results in the prevalence of moderate-to-high distress among CRC survivors versus participants without any cancer and among CRC survivors versus the general population without CRC (Supplementary file: Figure S5). The crude prevalence of high distress among those with severe limitations was five times that of participants with no limitations, regardless of CRC diagnosis. Compared to participants without CRC and with no limitations, the prevalence of high distress was almost eight times higher in non-CRC participants with severe limitations (PR: 7.98 (7.64-8.34)); and more than seven

times higher in CRC survivors with severe limitations (PR: 7.55 (6.04-9.43)) (Supplementary file: Figure S8).

Discussion

In this large-scale population-based Australian study, people living with CRC experienced greater levels of physical disability than people without CRC. The elevated risks of disability were focused in those who were recently diagnosed, had advanced disease and had undergone recent treatment; long-term survivors, those with less advanced disease and those who had not received treatment for cancer in the previous month had physical functioning levels similar to the general population without CRC. Overall, CRC survivors had levels of psychological distress similar to the general population without CRC. However, CRC survivors with metastatic disease experienced around 50% higher prevalence of moderate-to-high psychological distress than people without CRC. People with severe limitations to physical functioning, regardless of whether or not they had CRC, had markedly increased risks of psychological distress, at least four-fold that of people with no limitations.

Almost one in five CRC survivors experienced physical disability, compared to around one in ten participants without CRC. Accounting for age, sex, and other potential confounding factors, the prevalence of physical disability was around 10% higher in people with versus without CRC. The absolute risk of physical disability increased with increasing age, and the relationship of CRC diagnosis to physical disability was stronger in younger compared to older age groups. Younger CRC survivors were 51% more likely to experience physical disability than the age-matched general population while no difference in physical disability was observed between older participants with and without CRC.

Our study provides new insights on how CRC relates to the important outcomes of physical disability and psychological distress and, to our knowledge, provides the most comprehensive analysis to date on how these vary according to the characteristics of the person and their condition. The results of our analysis are generally consistent with the published evidence to date, despite wide variation in methods and measures used.

Cancer is known to cause physical disability [3, 6-8] or lower levels of physical functioning [25]. Studies focusing on CRC have generally compared outcomes to people without cancer of any type and found lower average levels of physical functioning in people with CRC than people without any cancer [9, 26-29]. Evidence on the prevalence of physical disability in relation to CRC diagnosis is limited. One study found that the prevalence of any self-reported limitation in activity in CRC survivors diagnosed less than 5 years previously was around two-fold (odds ratios 2.25 (1.45-3.51) in females and 2.62 (1.72-3.99) in males) that in people without any cancer [4]. However, this study and another previous study of long-term CRC survivors (diagnosed >5 years) found that levels of self-reported physical limitations were similar to people without any diagnosis of cancer [4, 5]. Since these studies did not generally exclude other cancers from the group with CRC, but excluded them from the comparison group, they may overestimate differences attributable to CRC.

Most previous studies on the association between cancer diagnosis and psychological distress included people with all cancer types combined; these studies found that a diagnosis of cancer in general was associated with an increased risk of psychological distress [3, 9, 13, 30-37]. However, taking time since diagnosis into account, psychological distress in long-term cancer survivors was similar to people without cancer [37, 38]. Among the limited number of studies considering CRC specifically, the average level of psychological distress, reflected in psychological outcome scores, was similar between CRC survivors and people without cancer [26, 39]. The prevalence of serious psychological distress, measured by the Kessler-6, did not

differ significantly between CRC survivors and people without cancer, (6.9% and 4.8%, respectively; $p=0.9043$) [40], consistent with our findings. Psychological distress measured using a single question rather than a specific scale was similar between CRC survivors and those without cancer [41-42]. Depression and anxiety, which are alternative mental health outcome measures, have been reported to be higher in CRC survivors than those without cancer [43, 44]. When comparing CRC survivors with the general population without CRC, the risks of hospitalisation for depression and anxiety were also higher [45]. The few studies which had data on the clinical characteristics of CRC concluded that recent diagnosis [46] and treatment [47] were associated with a higher risk of psychological distress, broadly consistent with our findings.

One previous study, based on an earlier subset of data from the 45 and Up Study, considered the role of physical disability in the relation of cancer diagnosis to psychological distress. Consistent with our findings, this study observed risks of high distress in people with physical disability six to eight times those of people without disability, regardless of cancer diagnosis [13]. Our study is the first to consider the role of physical disability in the relationship of CRC to psychological distress. We have observed a strong relationship of physical disability to both high distress and moderate-to-high distress, regardless of CRC diagnosis, and no significant relationship of CRC to distress in people without disability.

The physical impact of CRC and its treatments varies from person to person. CRC itself can cause a range of potentially disabling symptoms (such as fatigue, pain and weight loss) [48], especially when disease is advanced. Treatments for most CRC, such as surgery and chemotherapy, are invasive and can lead to a range of effects including physical disability [49-54]. Psychological distress is strongly related to physical disability in the general population [55] and, as demonstrated here, in people with CRC. Physical disability has been shown to play a similar role in the relationship between psychological distress and other conditions, such as diabetes, heart disease, and arthritis [56,57].

Physical and psychological outcomes underpin the ability of individuals and communities to have a good quality of life; all of these outcomes have been shown to be of importance to cancer survivors [58]. The US National Cancer Institute has proposed a Facing Forward booklet on how to manage the side effects of treatment and how treatment affects health related quality of life, including physical functioning [59]. Understanding physical functional limitations in relation to CRC diagnosis may be a key step for supporting CRC survivors. These data indicate that significant proportions of CRC survivors are experiencing psychological distress and people with impaired physical functioning are at a particularly high risk. Screening for psychological distress and provision of support among survivors, and specific consideration of those with disability, may be of benefit.

The large-scale, population-based nature and the wide range of health data collected in the 45 and Up Study allowed us to use both the general population without CRC and people without any history of cancer as the reference groups, which further allowed us to consider how CRC is likely to impact physical functional limitations and psychological distress in the general population, rather than in a clinical sample, which has been the focus of most previous research. The large numbers in the 45 and Up Study provide statistical reliability and allowed the examination of the relationship of CRC to the outcomes according to time since diagnosis, stage, and recent treatment for cancer, as well as examining this relationship in various population subgroups. The current study used validated measures of physical functional limitations and psychological distress that ensured the reliability of the data.

As the analysis used data from the baseline questionnaire linked to the cancer registry and hospital admissions datasets, we cannot assess whether physical disability and psychological

distress happened before or after the diagnosis of CRC. Therefore, it is not possible to exclude the potential contribution of differences in physical functioning and psychological distress in CRC survivors occurring prior to diagnosis. However, we compared CRC survivors to other study participants without CRC, adjusting for potential confounding factors. Furthermore, a longitudinal study in US that examined the health related quality of life among CRC survivors pre and post diagnosis showed that CRC diagnosis and treatment is followed by a decrease in the level of physical function [60]. Since psychological distress is unlikely to be a major cause of CRC and the relationship of physical functional limitations and psychological distress is well-established and consistent with other studies [13, 36, 44, 56], we interpret our findings as indicating that physical functional limitations are related to CRC diagnosis, and physical functional limitations further relate to psychological distress. CRC survivors in the 45 and Up Study and the prevalence estimated in this analysis may not be representative of the wider population. However, evidence has shown that representativeness is not necessary for generating reliable estimates of relative risks based on internal comparisons [61, 62] and PRs are based on internal comparisons in this study. Participants with missing data on the outcome variables were excluded from the study. Those missing values on outcome data were, on average, older and less educated than those with data, consistent with experiencing higher levels of morbidity. Missing values were more common among CRC survivors, largely because they were older than people without CRC; once age was accounted for, the difference in the proportions with missing outcome data between people with and without CRC was less than 5% in each age group. This potential bias would generally lead to underestimation of the association between CRC diagnosis and outcomes of physical disability and psychological distress.

The relationship between psychological distress and cancer is likely to vary according to the cancer type. Survivors of other cancers may experience higher levels of psychological distress than the general population [64, 65]; hence including them in the group with CRC but not the reference group may lead to overestimation of the magnitude of the association between CRC and distress. However, sensitivity analysis using people without any cancer as the reference group indicated very similar results to those using the general population without CRC as the reference group, indicating that there were no material changes in effect estimates when those with other cancers were excluded from the reference group. Due to the small numbers of CRC survivors with high distress, we considered moderate-to-high distress in our main analysis and high distress in the sensitivity analysis. The findings for high distress in relation to CRC diagnosis were similar to those with moderate-to-high distress. Additionally, the confidence intervals for high distress are narrow for most results, except for CRC survivors diagnosed more than 10 years previously, which indicate the statistical reliability of most PRs.

Compared to the general population, a significant proportion of people living with CRC experience physical disability, especially immediately following diagnosis and treatment, and with more advanced disease. CRC survivors can be reassured that most should have long-term psychological outcomes similar to other members of the general population and that psychological outcomes are especially good if people have few limitations in physical functioning. Identification of needs and support tailored to needs, especially for those with physical disability, is likely to be of benefit to survivors.

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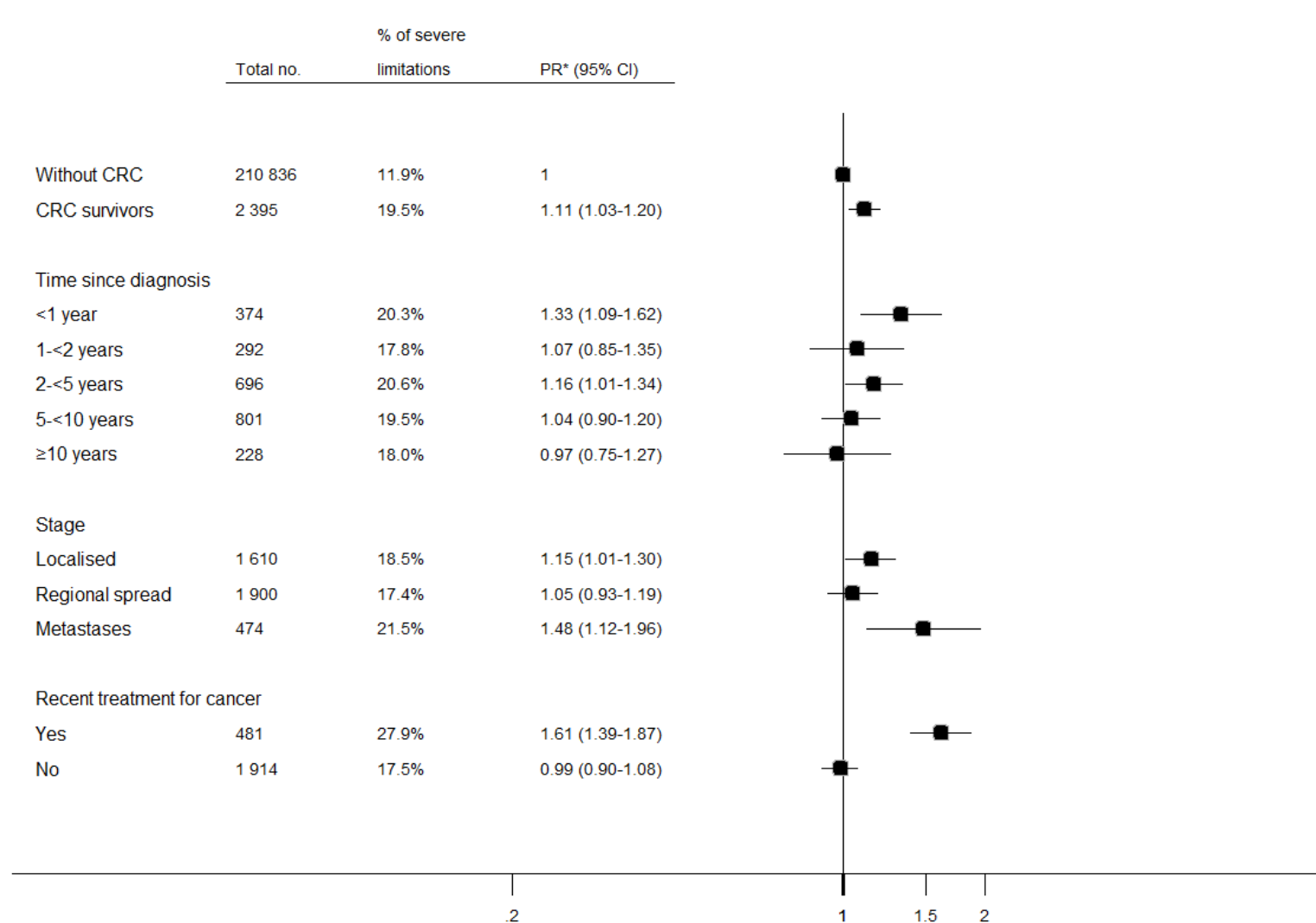
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Table 1 Characteristics of participants with and without CRC in the 45 and Up Study

	With CRC n=2,395	Without CRC n=210,836
	% (No.)	% (No.)
Age group		
45-64	32.0% (767)	67.0% (141,199)
65-79	49.8% (1,192)	25.9% (54,526)
≥80	18.2% (436)	7.2% (15,111)
Sex		
Male	59.2% (1,417)	47.7% (100,504)
Female	40.8% (978)	52.3% (110,332)
Educational levels		
University graduation	36.5% (875)	30.3% (63,931)
Certificate/diploma	9.7% (231)	9.9% (20,953)
Secondary school graduation	34.2% (820)	32.9% (69,251)
<Secondary school	18.1% (434)	25.8% (54,366)
Missing	1.5% (35)	1.1% (2,335)
Region of residence		
Major cities	52.1% (1,247)	52.3% (110,330)
Inner regional areas	35.4% (847)	34.8% (73,381)
Outer regional and remote areas	10.9% (260)	11.0% (23,096)
Missing	1.7% (41)	1.9% (4,029)
Country of birth		
Australia	78.2% (1,872)	75.5% (159,107)
Not Australia	21.2% (507)	24.0% (50,534)
Missing	0.7% (16)	0.6% (1,195)
Time since diagnosis		
Mean	4.78 years	
Median	4.22 years	
Less than 1 year	15.6% (374)	
1 to less than 2 years	12.2% (292)	
2 to less than 5 years	29.1% (696)	
5 to less than 10 years	33.4% (801)	
10 years and more	9.5% (228)	
Stage		
Localised	38.8% (928)	
Regional spread	45.3% (1,085)	
Metastases	6.3% (150)	
Unknown	8.6% (205)	
Treatment for cancer in the last month		
Yes	20.1% (481)	
No	79.9% (1,914)	

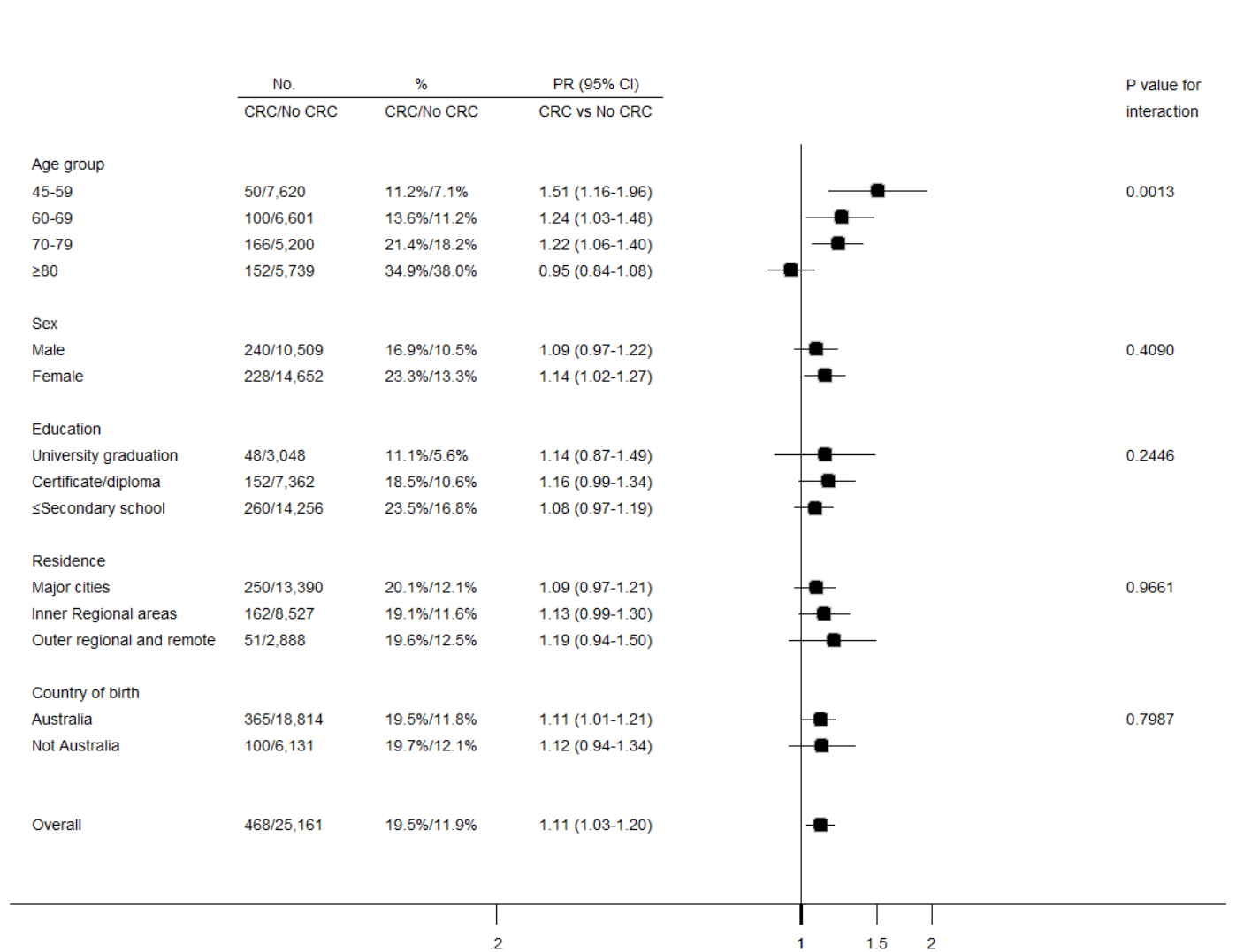
Figure 1 Severe physical functional limitations (MOS-PF¹≤59) in relation to CRC diagnosis and its clinical characteristics



* Adjusted for age, sex, education, residence, and country of birth

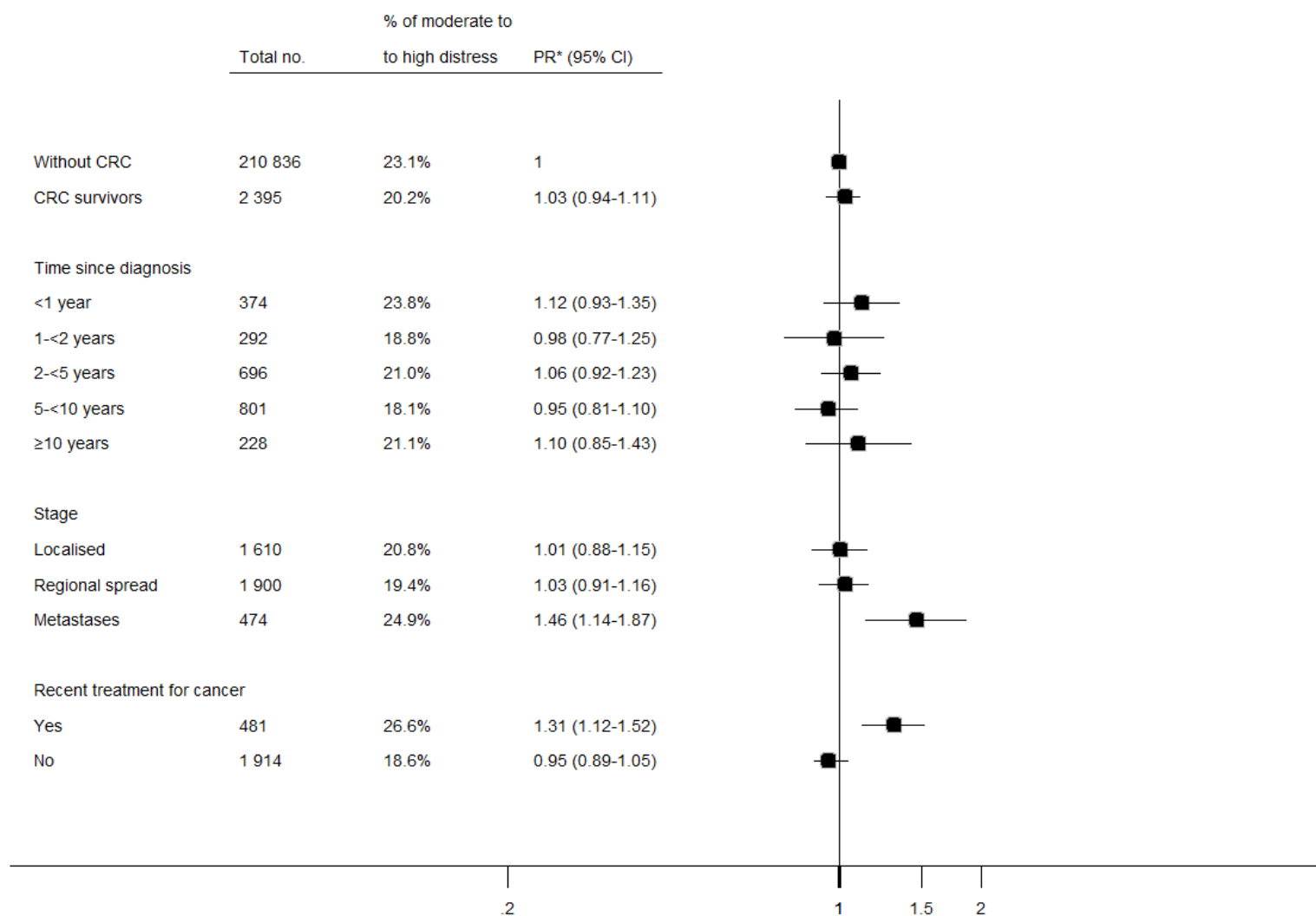
¹Physical functioning scale of Medical Outcome Study

Figure 2 Severe physical functional limitations (MOS-PF¹≤59) in people with versus without CRC, in various population subgroups



¹Physical functioning scale of Medical Outcome Study

Figure 3 Moderate to high distress (Kessler-10 score ≥ 16) in relation to CRC diagnosis and its clinical characteristics



* Adjusted for age, sex, education, residence, and country of birth

Figure 4 Moderate to high distress (Kessler-10 score ≥ 16) in people with versus without CRC, in various population subgroups

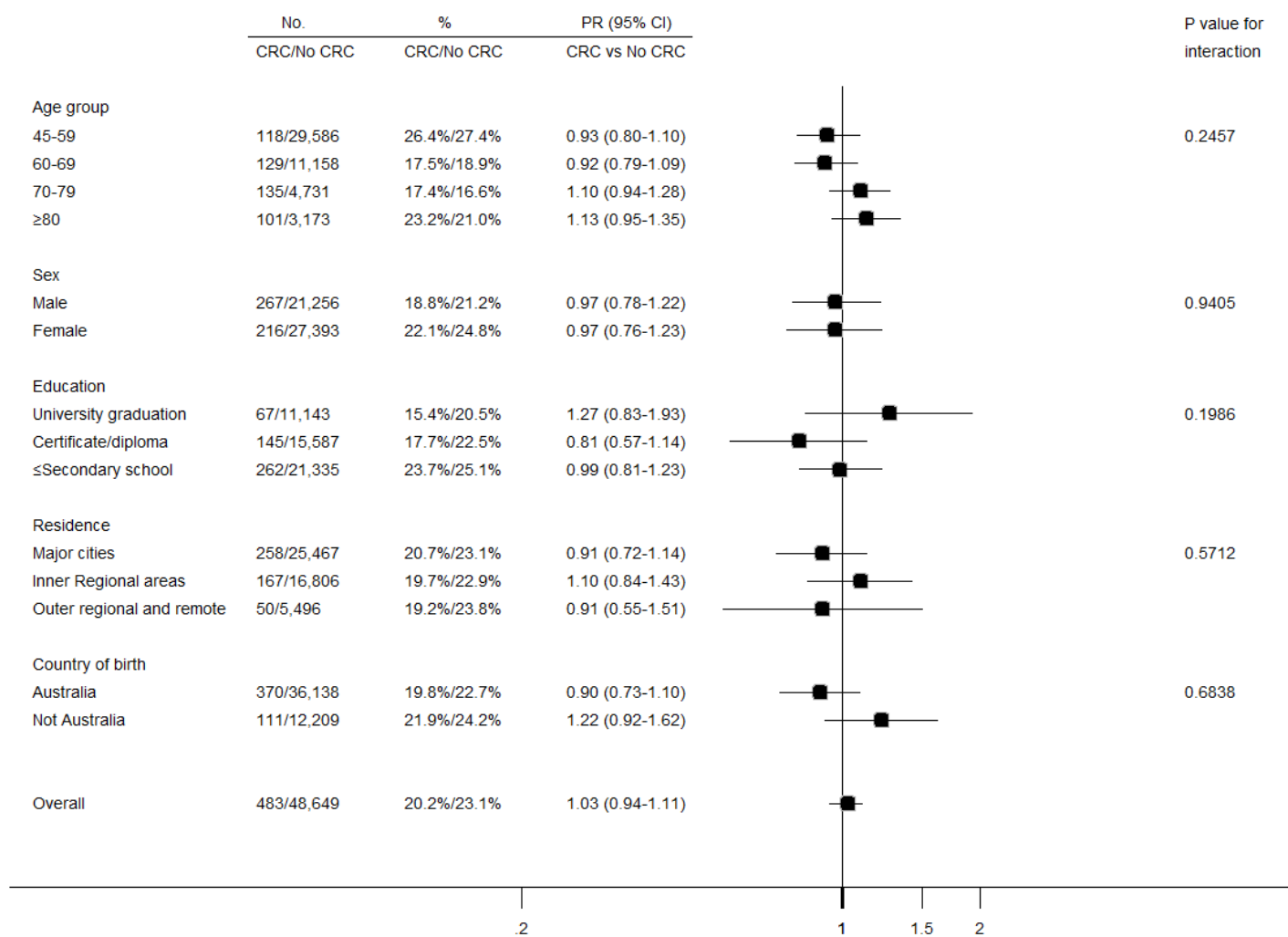
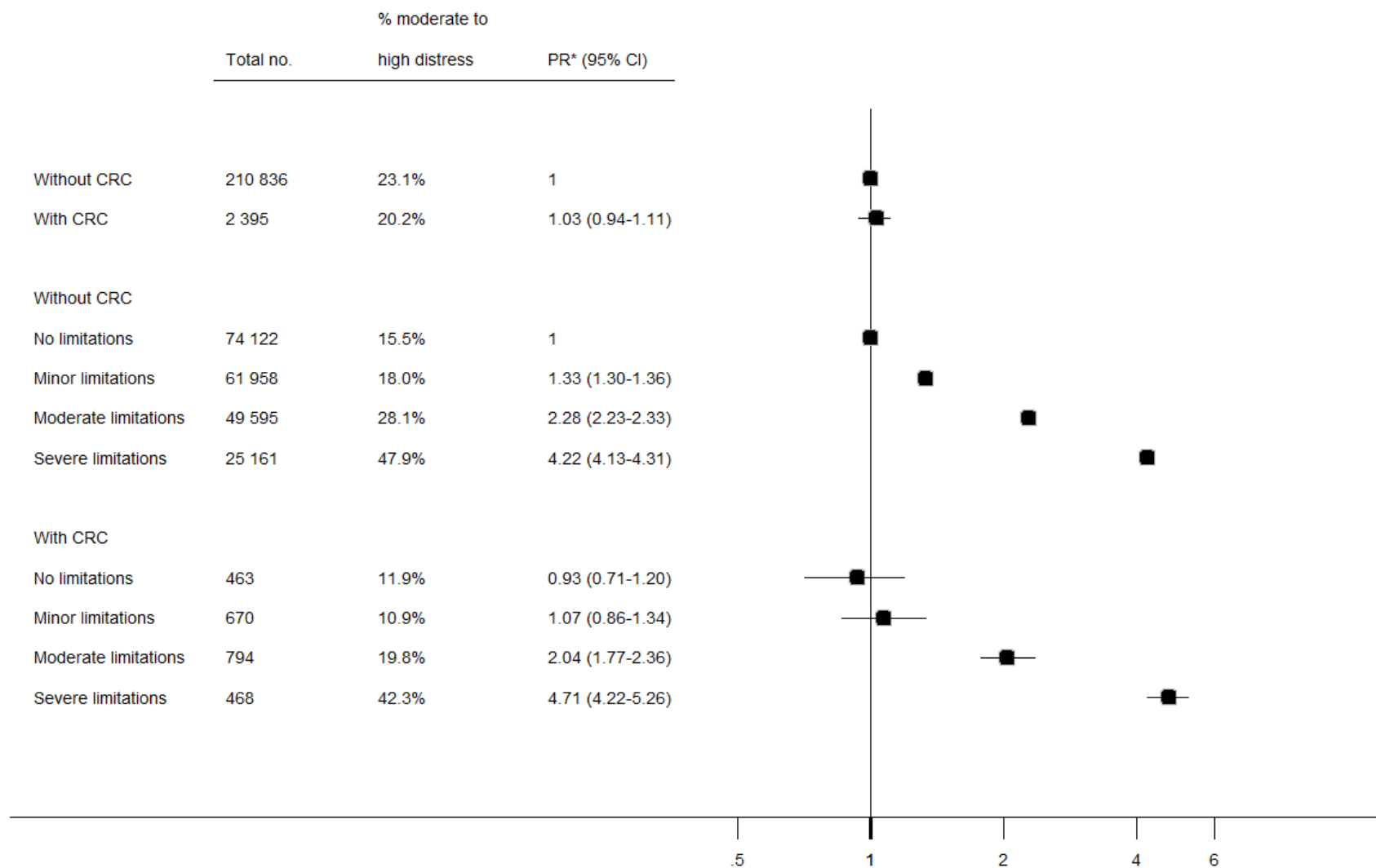


Figure 5 Moderate to high psychological distress (Kessler-10 score ≥ 16) in relation to CRC diagnosis and physical functional limitations



* Adjusted for age, sex, education, residence, and country of birth

Supplementary files

Table S1 Study population

	With record of CRC in Cancer Registry	Without record of CRC in Cancer registry	Total
With record of CRC in APDC	643	27	670
Without record of CRC in APDC	1,725	210,836	212,561
Total	2,368	210,863	213,231

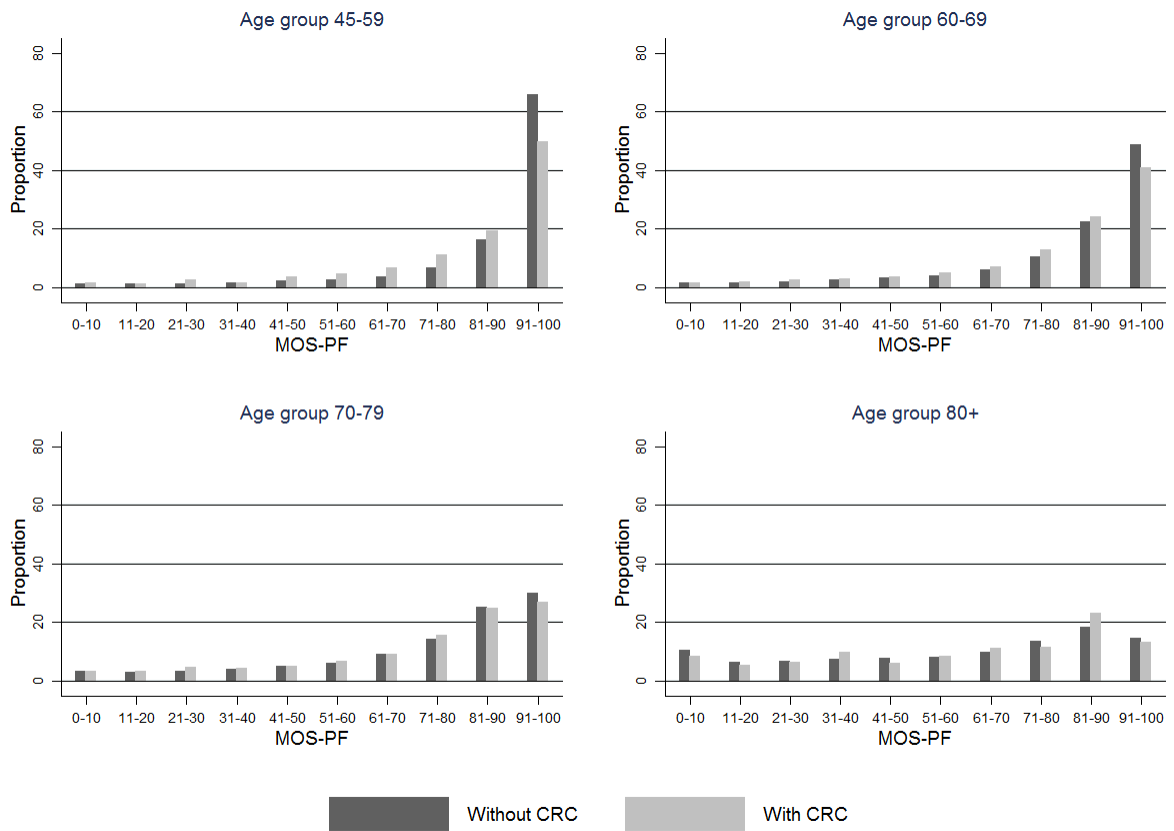
Table S2 ICD-10 codes of CRC survivors

	C18	C19	C20	C21
C18	1,464	37	36	2*
C19	37	166	31	0*
C20	36	31	609	3*
C21	2*	0*	3*	44
Total	1,539	234	679	49

Note: three more participants with C18, C19, and C20

*n ≤5

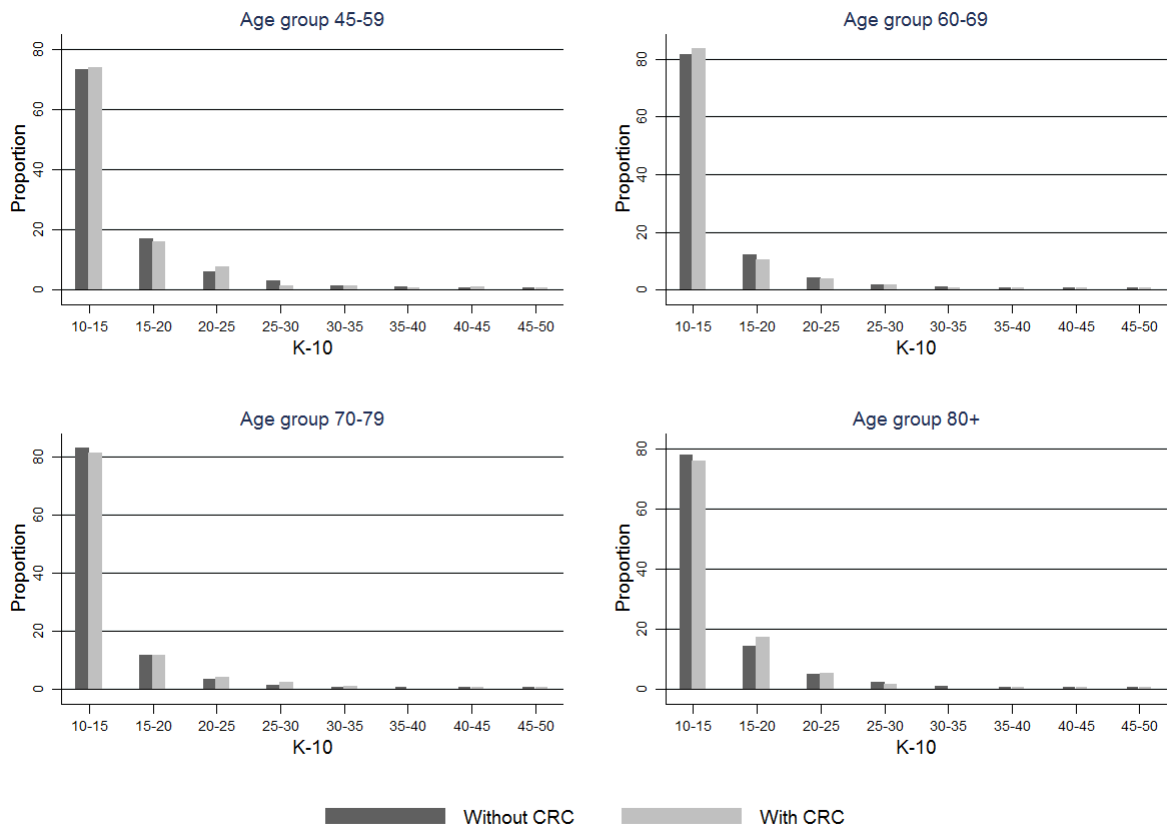
Figure S1 Distributions of MOS-PF^{1,2} scores among participants with and without CRC in different age groups



¹Physical functioning scale of Medical Outcome Study

²Higher scores indicate less limitations in physical function

Figure S2 Distributions of Kessler 10 scores¹ among participants with and without CRC in different age groups



¹Higher scores indicate higher levels of psychological distress

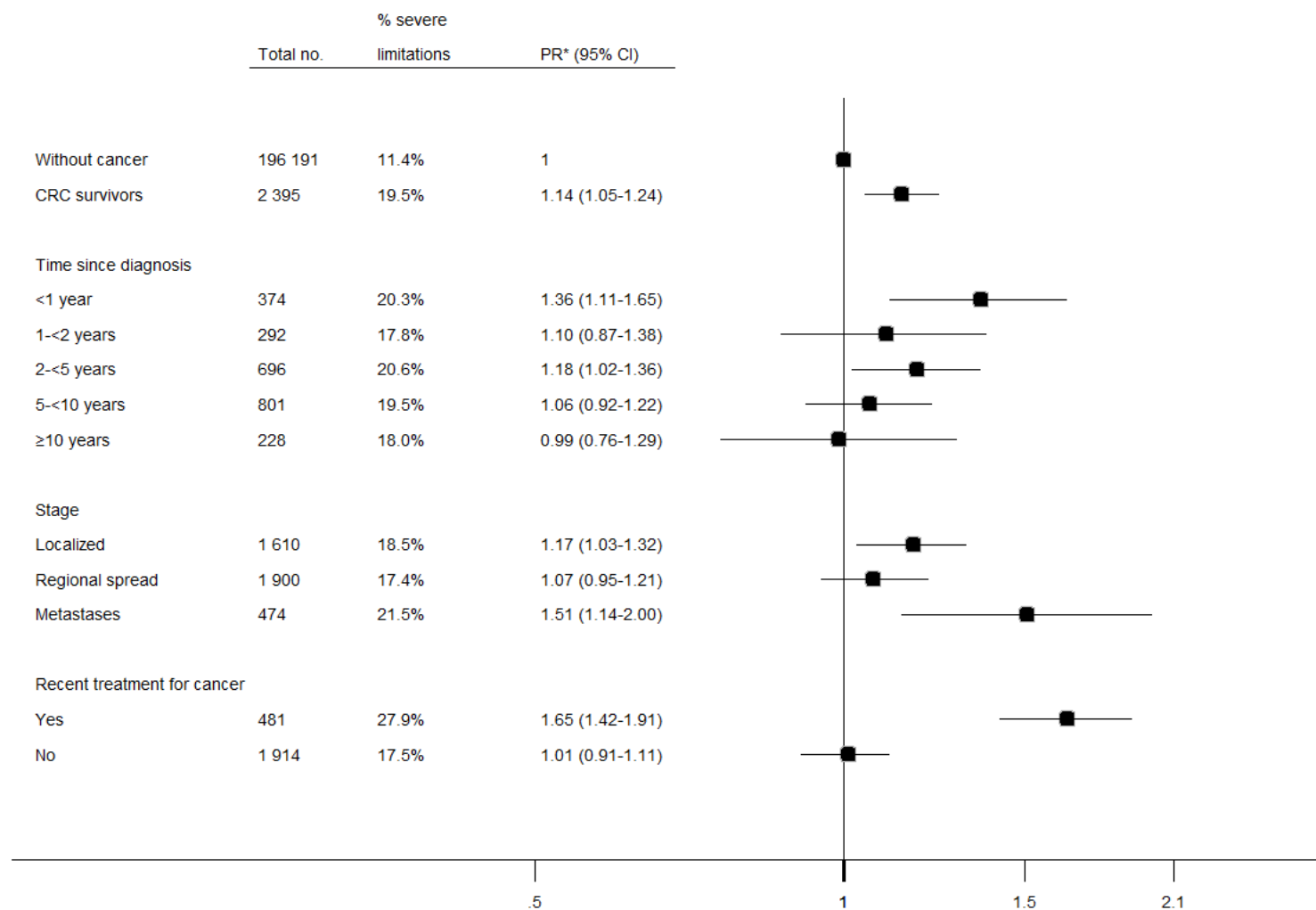
Table S3 Crude prevalence of different categories of physical functional limitations among people with and without CRC

	No limitations %	Minor limitations %	Moderate limitations %	Severe limitations %	Total No.
Without CRC	35.2%	29.4%	23.5%	11.9%	210,836
With CRC	19.3%	28.0%	33.2%	19.5%	2,395
Time since diagnosis					
<1 year	18.7%	28.9%	32.1%	20.3%	374
1-<2 years	20.2%	28.8%	33.2%	17.8%	292
2-<5 years	20.1%	26.9%	32.5%	20.6%	696
5-<10 years	18.2%	28.3%	34.0%	19.5%	801
≥10 years	20.6%	27.2%	34.2%	18.0%	228
Stage					
Localised	22.1%	30.0%	29.4%	18.5%	928
Regional	20.5%	29.3%	32.8%	17.4%	1,085
Metastases	19.0%	26.8%	32.7%	21.5%	150
Recent treatment for cancer					
Yes	12.3%	22.7%	37.2%	27.9%	481
No	21.1%	29.3%	32.1%	17.5%	1,914

Table S4 Crude prevalence of different categories of psychological distress among people with and without CRC

	Low distress %	Moderate distress %	High distress %	Total No.
Without CRC	76.9%	15.7%	7.4%	210,836
With CRC	79.8%	14.3%	5.9%	2,395
Time since diagnosis				
<1 year	76.2%	15.5%	8.3%	374
1-<2 years	81.2%	14.4%	4.5%	292
2-<5 years	79.0%	14.2%	6.8%	696
5-<10 years	81.9%	12.9%	5.2%	801
≥10 years	79.0%	18.0%	3.1%	228
Stage				
Localized	79.3%	14.0%	6.8%	928
Regional	80.6%	14.3%	5.2%	1,085
Metastases	75.1%	17.3%	7.6%	150
Recent treatment for cancer				
Yes	73.4%	18.3%	8.3%	481
No	81.5%	13.3%	5.2%	1,914

Figure S3 Severe limitations (MOS-PF¹≤59) in relation to CRC diagnosis and its clinical characteristics, compared to people without cancer



* Adjusted for age, sex, education, residence, and country of birth

¹Physical functioning scale of Medical Outcome Study

Figure S4 Moderate to high distress (Kessler 10 score ≥ 16) in relation to CRC diagnosis and its clinical characteristics, compared to people without cancer

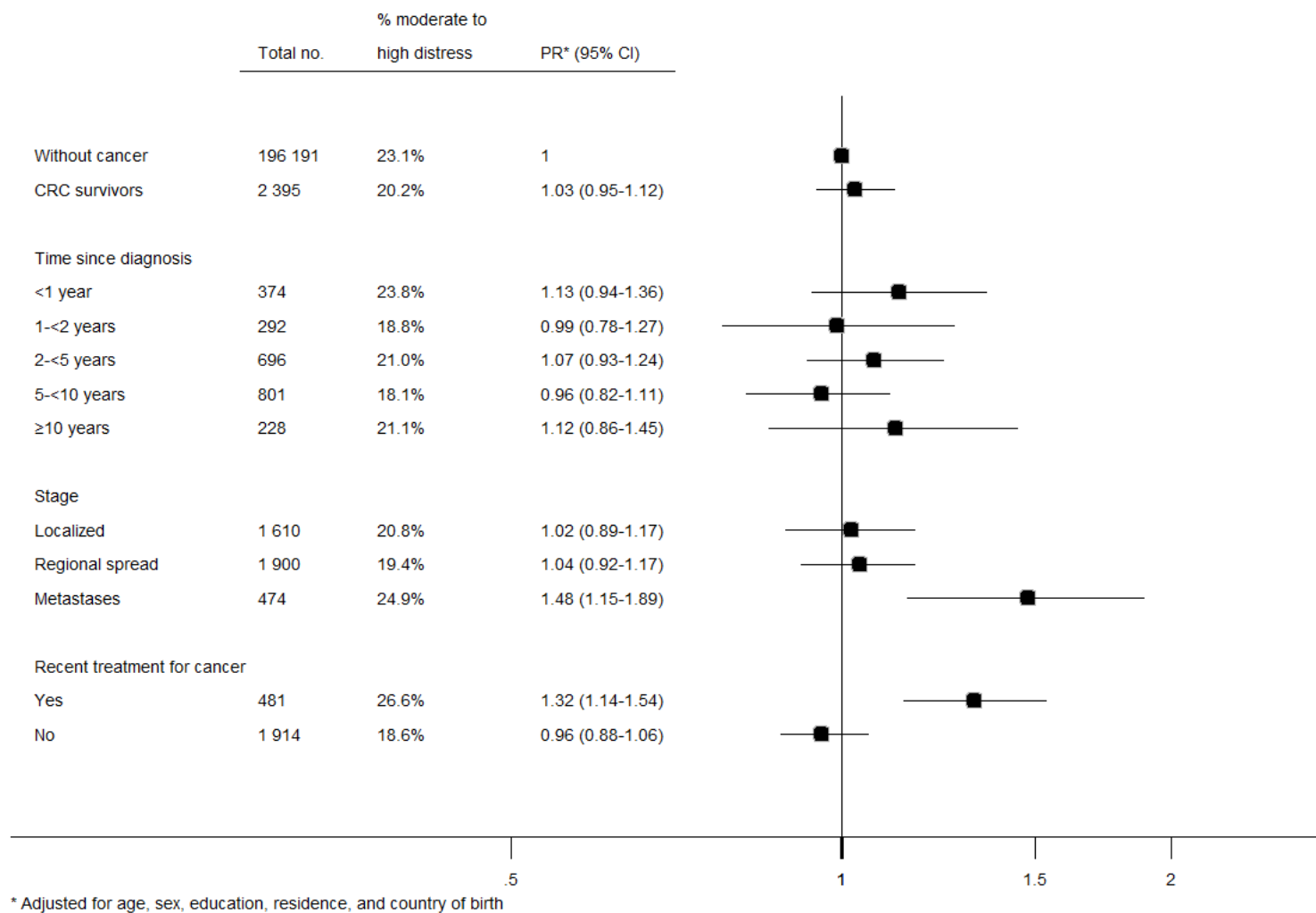


Figure S5 Prevalence ratios of moderate to high distress (Kessler 10 score ≥ 16) according to different physical functional limitations in CRC survivors and people without cancer

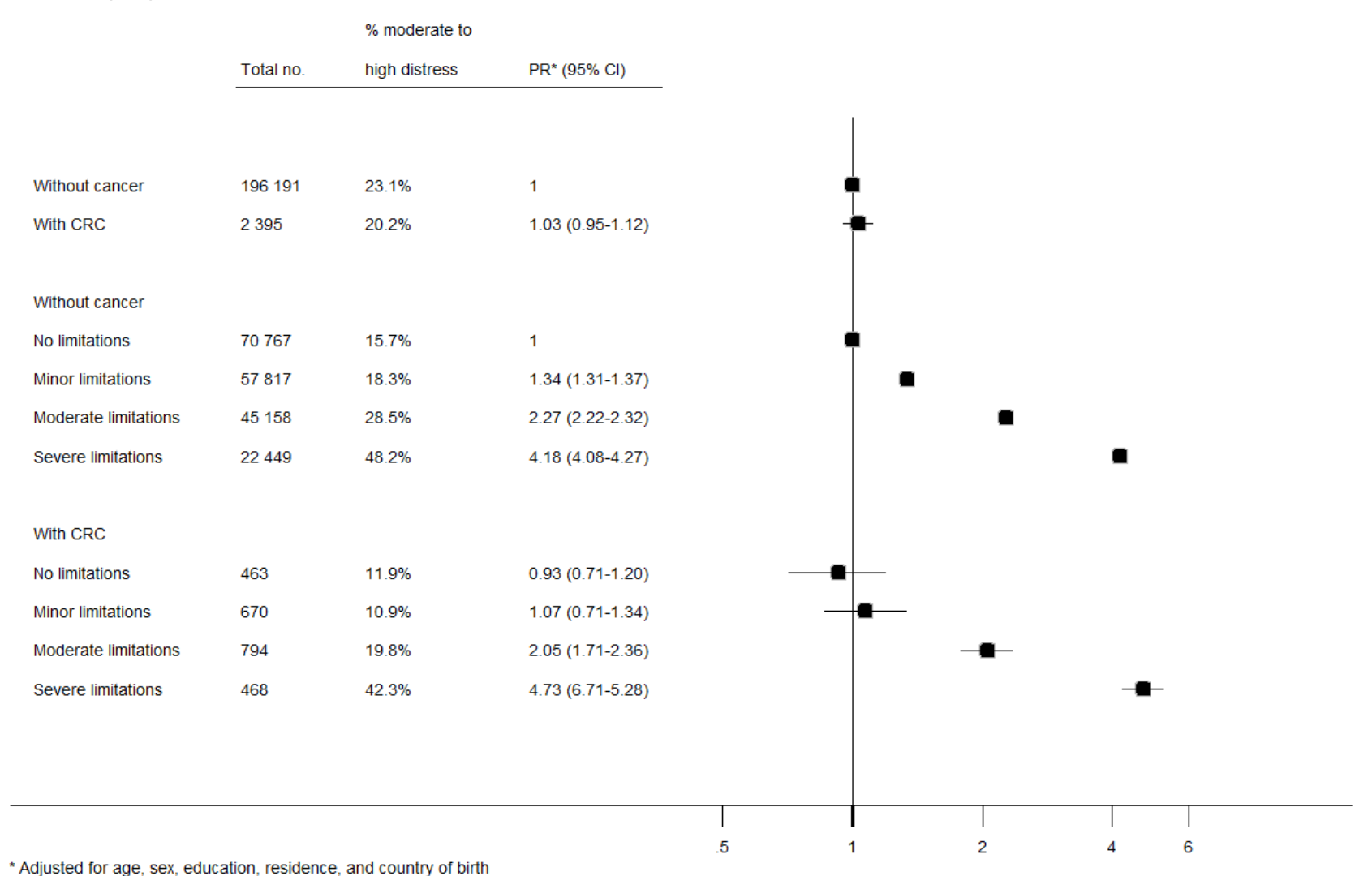
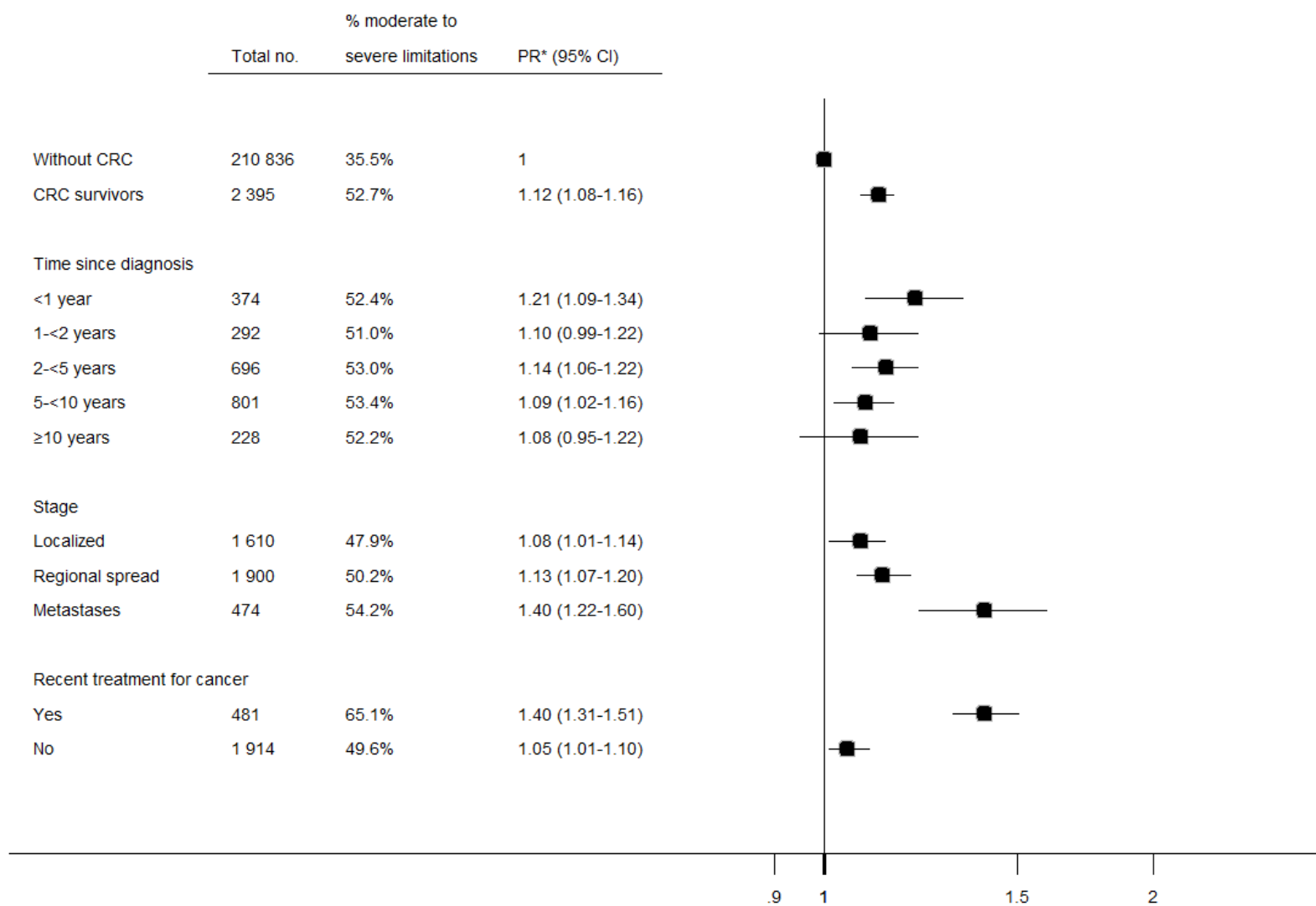


Figure S6 Moderate to severe limitations (MOS-PF¹ ≤ 89) in relation to CRC diagnosis and its clinical characteristics



* Adjusted for age, sex, education, residence, and country of birth

¹Physical functioning scale of Medical Outcome Study

Figure S7 High distress (Kessler 10 score ≥ 22) in relation to CRC diagnosis and its clinical characteristics

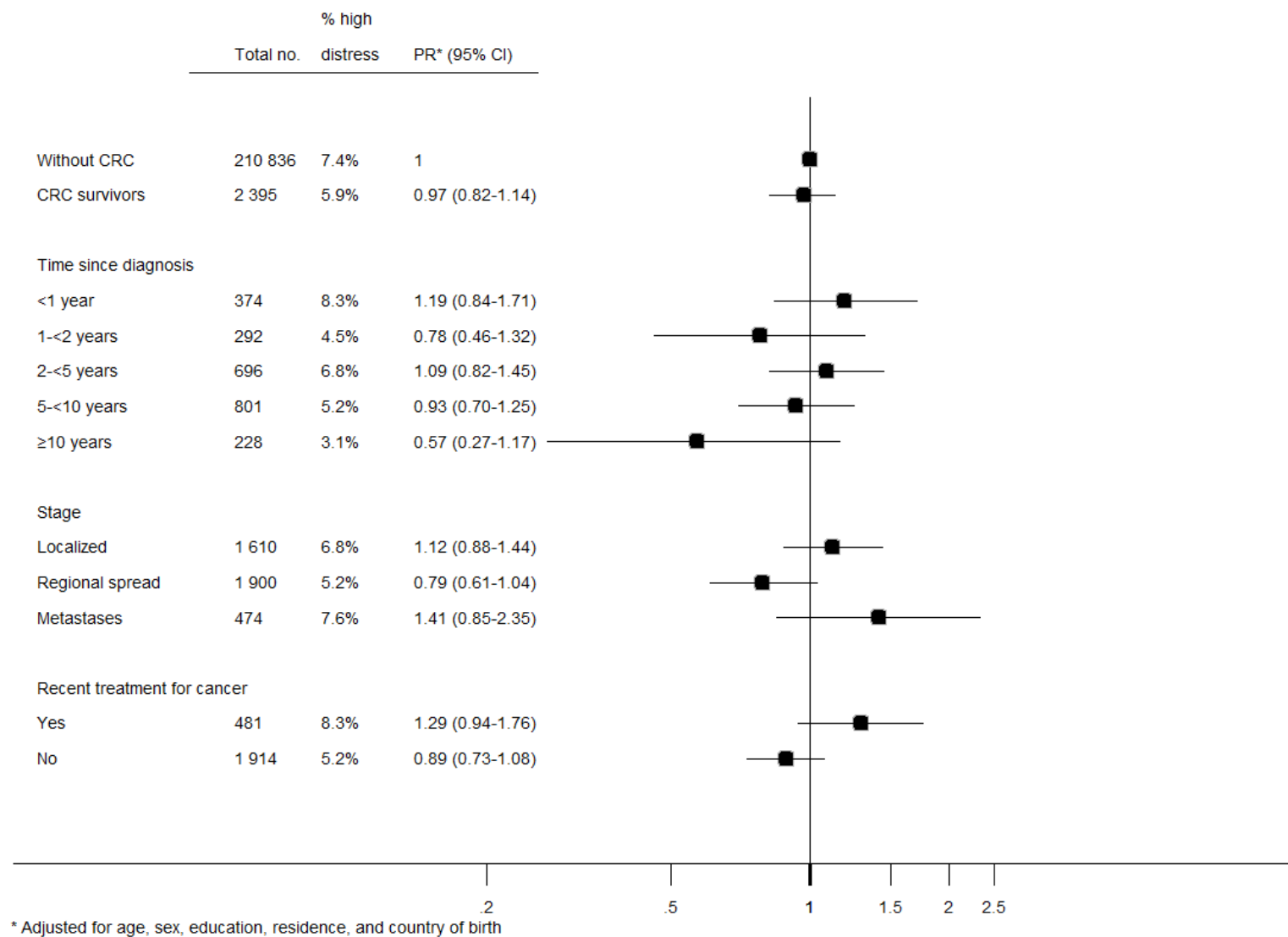
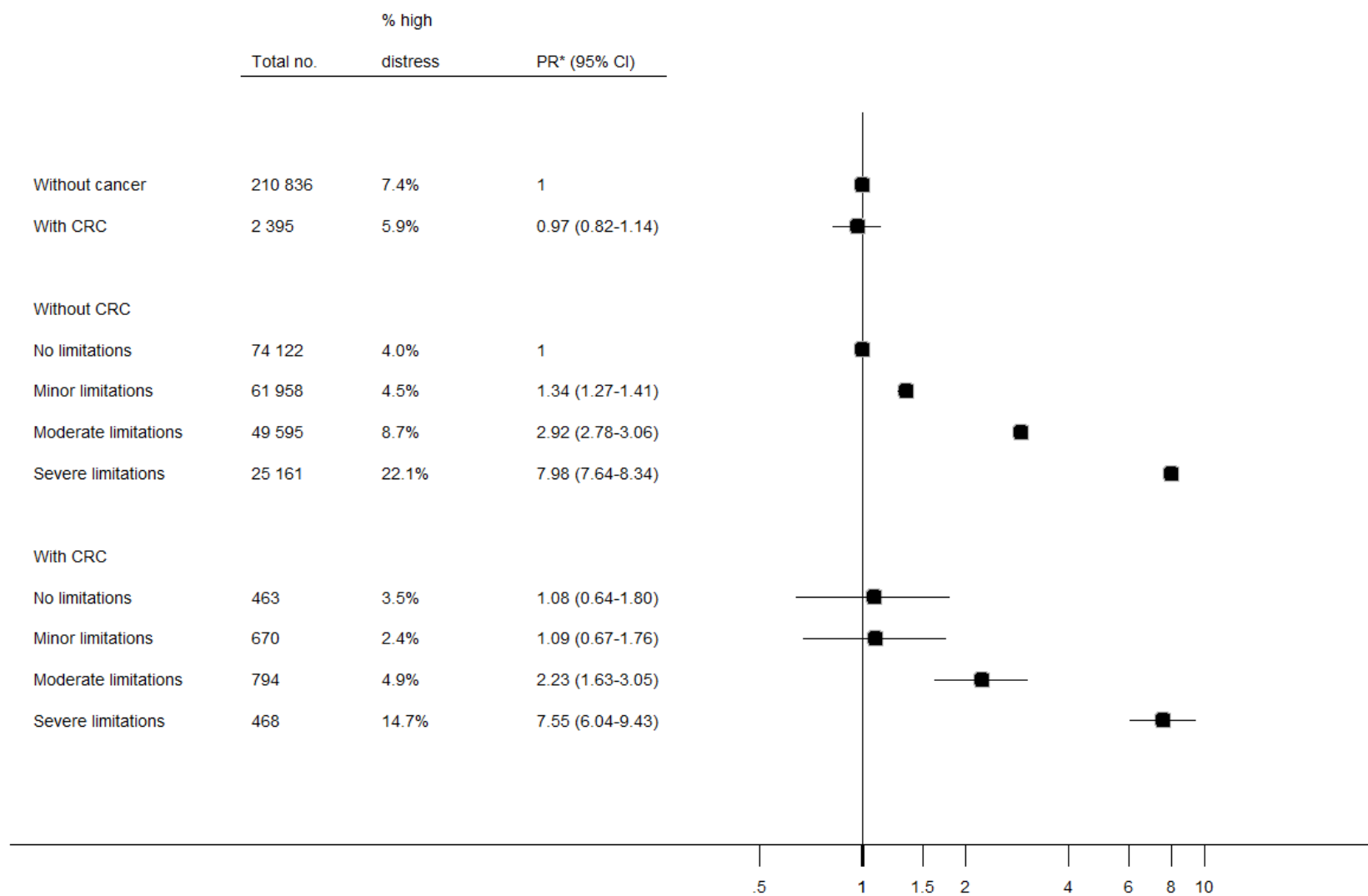


Figure S8 High distress (Kessler 10 score ≥ 22) in relation to CRC diagnosis and physical functional limitations



* Adjusted for age, sex, education, residence, and country of birth