

Title: Association between change in employment participation and quality of life in middle-aged colorectal cancer survivors compared with general population controls

Short title: Employment and quality of life in colorectal cancer survivors

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**ABSTRACT**

**Objective:** To examine the association between change in employment participation over a 12-month period and quality of life among individuals with colorectal cancer compared to general population controls.

**Methods:** This was a prospective, registry-based study that enrolled middle-aged (45-64 years) residents of Queensland, Australia, who were in the paid workforce, and newly-diagnosed with colorectal cancer. Participants completed structured telephone interviews at six and 12 months after diagnosis assessing quality of life and employment status ('retired/ceased work', 'increased work', 'decreased work' and 'maintained work'). Survivors were matched on demographic and occupation characteristics in a 1:2 ratio with individuals from the general population who had participated in both Wave 10 (2010) and 11 (2011) of the Household, Income and Labour Dynamics in Australia (HILDA) Survey.

**Results:** Almost half (66/148, 45%) of colorectal cancer survivors ceased or decreased work during the study period, compared to 27% in the control group (79/295,  $p=0.001$ ). Physical and mental wellbeing did not fluctuate over time in the general population. However, there were significant improvements in physical wellbeing, functional wellbeing and overall quality of life over the study period for participants with colorectal cancer. At 12 months post-diagnosis participants with colorectal cancer who maintained or increased work had significantly better functional wellbeing and overall quality of life compared to those who decreased work or retired.

**Conclusions:** A diagnosis of colorectal cancer often impairs the ability of a person to maintain work. The impairments are predominantly physical and functional. Interventions to assist with occupational rehabilitation should be trialed.

## BACKGROUND

Colorectal cancer is the third most commonly diagnosed cancer in males and the second in females globally with approximately 1,361,000 cases diagnosed each year, and an overall 5-year survival rate of 65% [1]. In Australia, colorectal cancer is the second most common cancer with ~15,000 cases diagnosed nationally each year [2] and ~3,000 in the state of Queensland [3]. Colorectal cancer and its treatments are associated with adverse side-effects and comorbidities that significantly affect physical and psychological functioning, quality of life and ability to maintain work [4, 5].

A significant number (~50%) of cancer survivors are diagnosed with cancer in working ages when career and occupation are likely to be disrupted [6, 7]. It is estimated approximately 73% of cancer survivors return to employment within 18 months of diagnosis although this differs between 64-82% depending on type of cancer and the specific disease and treatment-related sequelae [7]. Returning to employment may often be seen as a symbol of recovery and a critical aspect of re-establishing normality [8]. Reasons for not returning to employment include low annual income, comorbidity burden (e.g., arm swelling), receipt of chemotherapy, and cognitive dysfunction [9, 10]. A recent systematic review of 30 studies suggested that, even among cancer survivors returning to employment, ongoing physical and/or psychosocial problems such as fatigue, difficulty lifting, treatment-induced menopause symptoms, cognitive limitations, depression and anxiety may persist and cause work-related difficulties [8].

Dedicated cancer occupational rehabilitation services do not exist in Queensland and the issue of return to work is receiving growing attention in Australia. There are a range of issues relating to how employers accommodate and exercise flexibility and compassion for employees affected by cancer, and for communication to improve by all parties [4]. To date, employment participation and employment issues after a diagnosis of colorectal cancer are not well quantified or understood [11]. Given the high prevalence of colorectal cancer and a growing number of colorectal

cancer survivors, examining the specific impact of cancer on employment and quality of life for this population is timely and important so that employment can be maintained, remain a source of livelihood, purpose and positive social interaction.

The purpose of this study was to examine the association of changes in employment over a 12-month period on quality of life among individuals with colorectal cancer compared to a gender and age-matched general population comparison group.

## **METHODS**

### **Sample and procedures**

Study details have been previously described in detail [5, 11]. In brief, this study was a prospective, registry-based study of middle-aged (45-64 years) residents of Queensland, Australia, who were in the paid workforce, and newly-diagnosed with colorectal cancer. Middle-aged people were chosen because they will be at a similar life-stage and colorectal cancer is rare in persons aged <45 years. Participants were identified through the Queensland Cancer Registry, which incorporates all notifiable cases, from January 2010 to September 2011. Doctors' consent for researchers to contact potential participants was obtained for 705 out of 1098 potential participants identified. A total of 239 participants were recruited to the study (response rate 34%) [5]. Non-participation was due to: no response (n=301), declined to participate (n=148); unable to contact (n=14) or too sick (n=3).

Participants completed structured telephone interviews at six and 12 months after diagnosis about their employment, and postal surveys at these same time-points about more sensitive questions related to their current quality of life. At the six-month assessment, participants recalled employment changes from the time they were diagnosed with cancer (baseline), while at 12-month assessment they recalled employment information over the previous six months.

Of the 239 participants, 190 completed the quality of life survey at 6 months after diagnosis and a total of 150 participants (79%) completed the 12 month telephone interview and both postal

questionnaires, and were therefore eligible to contribute data to this analysis. These 150 participants were matched in a 1:2 ratio (case-control matching using 'radmatch' in Stata) to comparison individuals from the general population using the following list of matching variables: 5-year age group, gender, marital status, education, household income, occupation group and comorbidities. Comparison individuals had participated in both Wave 10 (2010; baseline) and 11 (2011; 12 month follow-up) of the Household, Income and Labour Dynamics in Australia (HILDA) Survey [12]. Therefore, participants in both the cancer and comparison groups provided data during the same time period of 2010-2011. The HILDA survey data were collected through face-to-face interviews and have wave-on-wave response rates of >90% [12].

Ethics approval for the study was obtained from the Human Ethics Research Committees of QIMR Berghofer Medical Research Institute (P1128), Griffith University (MED/19/09/HREC) and the Queensland Health Research Ethics and Governance Unit (RD003482).

### **Quality of life measures**

Generic quality of life was evaluated in both groups (i.e., colorectal cancer survivors and general population controls) using the Medical Outcomes Survey Short Form (SF-12v1/UK)[13]. The SF-12 is a shorter version of the 36-item Short Form Health Survey and its' 12 items yield a physical composite score (PCS) and mental composite score (MCS)[13]. Response categories vary by question and include dichotomous yes/no responses to 5 or 6 level Likert scale responses. Composite scores range from 0 to 100 and higher scores indicate better quality of life [13].

Within the colorectal cancer group only, disease-specific quality of life was assessed by the Functional Assessment of Cancer Therapy – Colorectal (FACT-Colorectal) measure [14, 15]. The FACT-Colorectal is a 36-item questionnaire assessing physical well-being (7 items); social/family well-being (7 items); emotional well-being (6 items); functional well-being (7 items); and colorectal cancer-specific symptoms (CCS) (7 items). Colorectal cancer survivors were asked to rate how they felt (e.g., I have swelling or cramps in my stomach area, I can digest my food well) over the past

seven days, on a scale of 0 ('not at all') to 4 ('very much'). Each subscale was scored and then summed to provide an overall quality of life score. We consider a minimally important difference of five points on the FACT-Colorectal [16] and for subscales used the greater than one third standard deviation rule [17]. Higher scores indicate better quality of life.

### **Employment participation measure**

Changes in employment participation, from baseline to 12 months, were categorised as four mutually exclusive categories: 'retired/ceased work' (changed to 0 hours work), 'increased work' (by  $\geq 4$  hours per week), 'decreased work' (by  $\geq 4$  hours per week) and 'maintained work' (work hours changed by  $< 4$  hours per week). A four-hour margin in work transition categories was chosen to focus on meaningful changes in hours worked. Cancer survivors had the following employment experiences: ceased work (n=37, 25%), decreased work (n=29, 20%), increased work (n=2, 1%) and maintained work hours (n=80, 54%). To increase statistical power, these four categories were collapsed into two categories: 'maintained/increased' and 'decreased/ceased'.

### **Covariates**

Identical items were used to assess socio-demographic and employment status information in both the colorectal cancer and general population groups. These items included questions from validated tools from Australian government surveys (e.g. Australian Bureau of Statistics (ABS) Labour Force Survey, ABS 1999 Survey of Living Standards), and included: age, gender, country of birth, marital status, remoteness of residential area, education, income, occupation, employer type, employer size and work schedule. Additionally, the colorectal cancer group completed measures of height and weight (for body mass index), comorbidities, sleep duration, and cancer treatment(s) received. Pathology reports indicating American Joint Committee of Cancer (AJCC)

stage of disease were only available through the Queensland Cancer Registry for 62 out of 150 participants and thus stage of disease was excluded from this analysis.

### **Statistical Analyses**

Data management and statistical analysis was completed using Stata 14.1 (Stata Corp, College Station, Texas). Differences in quality of life over time and/or between study groups were assessed using chi-squared, Wilcoxon rank-sum and t-tests, and baseline adjusted ANCOVA models. Linear models were used to investigate relationships between change in work participation and quality of life. For the FACT-C analyses, models were adjusted for covariates associated with the outcome measures at the  $p < 0.05$  level during bivariable analysis. Endogeneity was assessed with a simultaneous equation model (cdsimeq in Stata). The influence of missing data was assessed by comparing the baseline socio-demographic and employment characteristics of those colorectal cancer survivors excluded compared with those included. No adjustment was made for multiple comparisons;  $p < 0.05$  was considered as statistically significant.

### **RESULTS**

A total of 150 colorectal cancer survivors were eligible for this analysis, and 300 general population controls were matched to form an overall sample size of  $n=450$ . The 40 ineligible colorectal cancer survivors excluded from further analysis had similar characteristics at baseline to those eligible for this analysis with the exception of a higher proportion ( $p < 0.044$ ) of attrition in men (Table 1).

Compared with 6 month scores, cancer survivors reported significantly higher physical wellbeing (both in the generic  $p=0.008$  and cancer-specific measures  $p < 0.001$ ), functional wellbeing ( $p=0.005$ ) and overall cancer-related quality of life ( $p=0.019$ ) at the 12 month follow-up (Table 2). For generic quality of life, physical composite score in the colorectal cancer group



changed from 41.7 to 46.8 and was significantly different compared to the negligible change in the general population comparison group over the study period ( $p=0.008$ ). However, physical wellbeing scores were lower for cancer survivors at 6 months 41.7 (SD 12.0) than for the general population comparison group 49.6 (SD 8.87). Mental health remained unchanged during the study period in both groups.

Outcome data was missing for two participants with cancer and five general population comparators. Almost half, 45% (66/148), of colorectal cancer survivors decreased or ceased work participation during the study period, which was significantly greater than 27% (79/295) in the comparison group ( $p=0.001$ ). Physical wellbeing as measured by SF12 PCS was significantly worse for cancer survivors (44.8) who had decreased/ceased employment compared with the general population comparison group (52.0)  $p=0.005$ , while no differences were found in the mental composite score (Table 3). Those who maintained/increased employment had similar physical and mental wellbeing in the cancer and general population groups.

Unadjusted results indicated participants with colorectal cancer who decreased or ceased work participation had significantly lower physical wellbeing (both in the generic and cancer-specific measures), functional wellbeing, and overall quality of life when compared to those survivors who maintained or increased work participation, both 6 months and at 12 months of follow-up (Table 4). The differences in functional wellbeing and overall quality of life at 12 months post-diagnosis remained significant after adjustment for baseline values and confounding factors. Furthermore, functional wellbeing improved significantly more over time in colorectal cancer survivors who maintained or increased work compared to those who decreased or ceased work participation. No endogeneity was found between employment participation change and the various quality of life change variables.

## CONCLUSIONS

While we observed similarities in mental components of quality of life between the two cohorts, physical wellbeing was much poorer among people with colorectal cancer and participation in work was significantly compromised compared with their general population counterparts. Moreover, we found that cancer survivors who decreased or ceased work after their diagnosis had significantly lower quality of life and functional wellbeing compared to survivors who maintained or increased employment participation. These findings are informative for occupational rehabilitation and suggest that support programs that aid daily function may assist colorectal cancer survivors in returning to and/or maintaining work at pre-morbid levels. In particular, support with occupational components, such as adjusting to work tasks, coping mechanism such as illness acceptance and ability to enjoy life and help with sleeping (i.e. the items measured under functional wellbeing) should be considered priorities of a tailored intervention trial focused on return to work in this population.

While our work decrease/retirement rates significantly differed between the colorectal cancer survivor and general population comparison groups, the 45% rate among of colorectal cancer survivors was similar to those from recent studies that have examined multiple tumor groups. For example, amongst prostate, endometrial, non-Hodgkin's and Hodgkin's lymphoma survivors, Mols et al. found 51% of survivors were either working fewer hours, or retired [18] and among a sample of early-stage breast cancer survivors, Johnsson et al. reported 41% had not returned to work [19]. Several studies have reported on predictors of returning to employment after a cancer diagnosis, however few studies have prospectively examined differences and changes in quality of life in survivors returning to employment and those not returning to employment. Similarly to us, a significantly greater decrease in the physical component scores of the SF-12 was observed in men with prostate cancer with declined employment status at three months post-surgery compared to those who maintained or improved their employment status [20]. Consistent with this, Lundh et al.

[21] found breast cancer survivors on sick leave/disability pension and retirement pension reported higher levels of symptoms compared to employed women, whereas employed women reported consistent improvements in role and social functioning, and reduced pain.

In our cancer population, physical and functional wellbeing and quality of life were already poorer at six months post-diagnosis in the group who decreased/ceased work compared to those who maintained/increased work group. Our previous analysis at 6 months post-diagnosis showed that stage was not associated with work cessation after adjustment for work-related and socio-demographics [5]. Instead, factors associated with work cessation were older age, lower body mass index and, for work reduction, were lower education, employers with >20 employees, chemotherapy and longer hospital stay [5]. Despite the similarities in employment patterns and deteriorating physical scores between studies of cancer patients, it is likely that the type of physical burden attributed to this is somewhat unique to the type of cancer. Our previous research indicates that for patients with colorectal cancer the main reasons for stopping work were bowel problems and having a stoma, loss of strength, and medication adverse effects [22]. For some cancer survivors it is the loss of work ability above the loss of health that is what made their life situation really hard [4]. With only one feasibility study specific for an intervention to return individuals affected by colorectal cancer to work [23], our work supports the need for further clinical trials in this group.

Strengths of the study include the prospective design, the inclusion of a general population comparison group, the focus on one tumor group rather than a heterogeneous sample, and the use of valid and reliable (and both generic and disease-specific) quality of life scales. Limitations include the low response rate and relatively small sample size with implications for reduced generalizability however, a comparison of the participants and non-participants reported previously [5] showed no statistically significant differences for place of residence and clinical characteristics of the tumor, but a higher proportion of participants were male (n = 159, 67%) versus non-participants (n = 500,

58%) ( $p = 0.02$ ). Additionally this work was limited by lack of adjustment for stage of disease and differences in matching by gender, although some studies indicate quality of life does not vary by gender [24] and therefore we believe the successful balancing of other demographic and employment variables was adequate and that the over representation of male participants may not affect these results. More advanced stage of disease can significantly worsen quality of life of cancer survivors [25] however our previous analysis showed it was not associated with stopping work [5] and thus may not be a confounder of these analyses.

In conclusion, colorectal cancer survivors who decreased employment participation or retired had significantly lower quality of life compared to survivors who maintained or increased employment participation. It has been suggested that return to employment and employment issues are not a trivial component of quality of life, but should rather be recognized as a major contributing factor [26]. New insights from this study suggest that specific to people with colorectal cancer, the functional aspects of wellbeing including having the ability to adjust to work tasks, use of coping mechanism such as illness acceptance and positive framing, and having healthy sleep behaviors may have the most clinical impact when it comes maintaining work in this group. Thus interventions to assist with these aspects of daily functioning should be trialed to help facilitate maintenance of work and quality of life in this cancer population.

## **CONFLICT OF INTEREST**

The authors declare that they have no conflict of interest.

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**Table 1.** Participant characteristics at baseline

	Colorectal cancer survivors with complete data n=150	Colorectal cancer survivors with incomplete data n=40	General population controls n=300
Age (years) <sup>a</sup>	56.3(5.2)	56.1(5.1)	54.4(5.0)
Gender (male)	94(63%)	32(80%)	216(72%)
Country of birth (Australia)	117(82%)	24(75%)	232(77%)
Marital status (married or partnered)	120(84%)	24(75%)	260(87%)
Area (major cities)	77(51%)	20(50%)	176(59%)
Education (up to high school)	96(67%)	16(52%)	170(57%)
Household income <sup>b</sup> :			
up to \$35,999	11(8%)	0(0%)	19(6%)
\$36,000 to \$77,999	41(32%)	7(27%)	76(25%)
\$78,000 to \$103,999	27(21%)	10(38%)	63(21%)
\$104,000 and above	51(39%)	9(35%)	142(47%)
Occupation group:			
professional/managerial	31(22%)	9(28%)	88(29%)
trades, logistics	65(46%)	14(44%)	129(43%)
clerical, retail, services	46(32%)	9(28%)	83(28%)
Employer type (private/for profit)	112(78%)	19(61%)	207(69%)
Employer size (≥20 employees)	79(56%)	20(62%)	155(52%)
Work schedule (day shift)	109(76%)	20(62%)	227(76%)
Comorbidities <sup>c</sup> :			
none	60(42%)	15(47%)	133(44%)
one	45(31%)	9(28%)	95(32%)
two or more	38(27%)	8(25%)	72(24%)
Body Mass Index <sup>a</sup>	27.0(4.9)	28.4(4.4)	28.0(5.4)
Sleep duration:			
< 7 hours per day	84(57%)	20(54%)	n/a
7 to < 9 hours per day	37(25%)	13(35%)	n/a
≥ 9 hours per day	27(18%)	4(11%)	n/a
Procedure (excision)	91(61%)	26(65%)	n/a
Chemo/radiotherapy (either)	85(56%)	15(47%)	n/a

Note: percentages calculated using number of non-missing values in denominator thus frequencies may not add up to total group size; <sup>a</sup> mean and standard deviation; <sup>b</sup> in 2010 Australian Dollars, average household income 2009/10 \$74,000; <sup>c</sup> Further details of comorbid conditions are presented in Gordon et al. (2014)[5] n/a = not applicable



**Table 2.** Quality of life among colorectal cancer survivors and their matched population controls at 6 and 12 month follow-ups

	Colorectal cancer survivors n=150	General population controls n=300	p-value
SF-12v1 Physical score			
6 months	41.7(12.0)	49.6(8.87)	
12 month follow-up	46.8(11.6)	49.3(9.42)	0.008 <sup>a</sup>
change	5.09(10.9)*	-0.26(7.65)	
SF-12v1 Mental score			
6 months	46.9(11.9)	48.5(10.2)	
12 month follow-up	48.0(11.9)	48.6(9.72)	0.989 <sup>a</sup>
change	0.92(12.2)	0.17(9.53)	
FACT-C Physical wellbeing			
6 months	21.6(5.54)	n/a	
12 month follow-up	24.0(4.51)	n/a	n/a
change	2.43(4.38)*	n/a	
FACT-C Social wellbeing			
6 months	22.0(4.58)	n/a	
12 month follow-up	22.0(4.71)	n/a	n/a
change	-0.00(4.06)	n/a	
FACT-C Emotional wellbeing			
6 months	19.8(3.50)	n/a	
12 month follow-up	20.0(3.64)	n/a	n/a
change	0.24(2.81)	n/a	
FACT-C Functional wellbeing			
6 months	19.5(5.54)	n/a	
12 month follow-up	21.2(5.70)	n/a	n/a
change	1.70(4.90)*	n/a	
FACT-C Colorectal cancer symptoms			
6 months	20.6(4.43)	n/a	
12 month follow-up	21.5(4.10)	n/a	n/a
change	0.83(4.23)	n/a	
FACT-C Overall quality of life			
6 months	104(16.9)	n/a	
12 month follow-up	109(16.1)	n/a	n/a
change	5.29(13.5)*	n/a	

Note: mean and standard deviation shown, unless otherwise indicated; SF-12v1 = short form health survey, version 1; FACT-C = Functional Assessment of Cancer Therapy-Colorectal; n/a = not applicable; <sup>a</sup>testing difference between groups using baseline adjusted ANCOVA; \*statistically significant difference using the Wilcoxon rank-sum test

**Table 3.** Quality of life by employment participation change and study group

SF-12v1 domain	Employment participation change over 12 months					
	Maintained <sup>a</sup> or Increased <sup>b</sup>			Decreased <sup>b</sup> or Ceased		
	Cancer survivors n=81	General population controls n=189	<i>P</i> <sup>c</sup>	Cancer survivors n=66	General population controls n=79	<i>P</i> <sup>c</sup>
Physical score <sup>d</sup>	53.3(47.9-55.8)	52.1(45.6-55.0)	0.892	44.8(31.2-54.0)	52.0(45.0-55.8)	0.005
Mental score <sup>d</sup>	53.0(45.4-56.1)	51.3(44.8-54.5)	0.796	50.6(38.9-56.0)	51.8(46.5-56.0)	0.407

*SF-12v1 = short form health survey, version 1; <sup>a</sup> changed by <4 hours per week; <sup>b</sup> changed by ≥4 hours per week; <sup>c</sup> p-value of group effect of t-tests; <sup>d</sup> median (25<sup>th</sup> and 75<sup>th</sup> percentiles)*

**Table 4.** Associations between employment participation and quality of life among colorectal cancer survivors

	<i>Unadjusted models</i>			<i>Adjusted models<sup>a</sup></i>		
	Maintained <sup>b</sup> or increased <sup>c</sup> employment	Decreased <sup>c</sup> or ceased employment	<i>p</i> -value <sup>d</sup>	Maintained <sup>b</sup> or increased <sup>c</sup> employment <i>Mean</i> (95% <i>CI</i> )	Decreased <sup>c</sup> or ceased employment <i>Mean</i> (95% <i>CI</i> )	<i>p</i> -value <sup>e</sup>
SF-12v1 Physical score						
6 months	45.6(11.1)	37.1(11.4)	<0.001			
12 month follow-up change	50.2(9.43) 4.72(9.58)	42.6(12.8) 5.28(12.2)	<0.001 0.756	49.1(48.1-50.2)	46.5(44.9-48.2)	0.068
SF-12v1 Mental score						
6 months	47.9(11.4)	45.8(12.5)	0.290			
12 month follow-up change	49.0(11.5) 1.05(11.3)	46.6(12.4) 0.75(13.5)	0.226 0.885	47.0(45.7-48.3)	47.2(46.2-48.2)	0.892
FACT-C Physical wellbeing						
6 months	23.3(4.43)	19.4(6.09)	<0.001			
12 month follow-up change	25.0(3.97) 1.81(4.06)	22.8(4.88) 3.12(4.58)	0.004 0.077	24.0(23.4-24.5)	23.7(23.2-24.3)	0.853
FACT-C Social wellbeing						
6 months	21.8(4.62)	22.3(4.27)	0.552			
12 month follow-up change	21.9(4.52) 0.13(4.26)	22.1(4.97) -0.20(3.86)	0.820 0.636	21.8(21.3-22.3)	21.8(21.1-22.4)	0.943
FACT-C Emotional wellbeing						
6 months	20.2(3.00)	19.3(4.02)	0.096			
12 month follow-up change	20.8(2.74) 0.53(2.27)	19.1(4.33) -0.04(3.38)	0.007 0.234	20.4(20.0-20.8)	19.7(19.3-20.2)	0.211
FACT-C Functional wellbeing						
6 months	20.8(5.35)	17.9(5.48)	0.002			
12 month follow-up change	23.2(4.72) 2.48(4.80)	18.7(5.86) 0.63(4.87)	<0.001 0.024	22.7(22.2-23.2)	19.3(18.7-20.0)	<0.001
FACT-C Colorectal cancer symptoms						
6 months	21.4(4.13)	19.8(4.60)	0.022			
12 month follow-up change	22.0(4.24) 0.63(4.17)	20.9(3.82) 0.99(4.21)	0.090 0.604	21.8(21.4-22.3)	21.3(20.9-21.6)	0.360
FACT-C Overall quality of life						
6 months	109(15.0)	99.2(17.9)	0.001			
12 month follow-up change	113(14.3) 5.66(12.7)	103(16.7) 4.71(14.2)	<0.001 0.715	111(109-113)	107(105-109)	0.046

Note: *SD* = standard deviation; *CI* = confidence interval; <sup>a</sup>ANCOVA models adjusted for baseline levels, age, co-morbidities, body-mass index, sleep duration, surgery and chemo/radiation treatment; <sup>b</sup>changed by <4 hours per week; <sup>c</sup>changed by ≥4 hours per week; <sup>d</sup>*p*-value shows *t*-tests of difference in *QoL* scores between employment participation groups at each time point and each group's difference over time scores; <sup>e</sup>*p*-value of employment participation over time adjusted for covariates