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Lifestyle factors associated concurrently and prospectively with co-morbid cardiovascular disease in a population-based cohort of colorectal cancer survivors

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ABSTRACT

Aims: To assess self-reported lifetime prevalence of cardiovascular disease (CVD) among colorectal cancer survivors, and examine the cross-sectional and prospective associations of lifestyle factors with co-morbid CVD.

Methods: Colorectal cancer survivors were recruited ($n = 1966$). Data were collected at approximately 5, 12, 24 and 36 months post-diagnosis. Cross-sectional findings included six CVD categories (hypercholesterolaemia, hypertension, diabetes, heart failure, kidney disease, and ischaemic heart disease (IHD)) at 5 months post-diagnosis. Longitudinal outcomes included the probability of developing (*de novo*) co-morbid CVD by 36 months post-diagnosis. Lifestyle factors included body mass index, physical activity, television (TV) viewing, alcohol consumption, and smoking.

Results: Co-morbid CVD prevalence at 5 months post-diagnosis was 59%, and 16% of participants with no known CVD at baseline reported *de novo* CVD by 36 months. Obesity at baseline predicted *de novo* hypertension (odds ratio [OR] = 2.20, 95% confidence intervals [CI] = 1.09, 4.45) and *de novo* diabetes (OR = 6.55, 95% CI = 2.19, 19.53). Participants watching >4 h of TV/d at baseline (compared with <2 h/d) were more likely to develop ischaemic heart disease by 36 months (OR = 5.51, 95% CI = 1.86, 16.34).

Conclusion: Overweight colorectal cancer survivors were more likely to suffer from co-morbid CVD. Interventions focusing on weight management and other modifiable lifestyle factors may reduce functional decline and improve survival.

1. Introduction

Colorectal cancer is a commonly diagnosed cancer in Europe and incidence increases rapidly with age.[1] The risk of chronic conditions occurring concomitantly with colorectal cancer (such as cardiovascular disease; CVD) also increases with age.[2] Colorectal cancer survivors have an elevated risk of co-morbid disease which can be attributed to genetic predisposition as well as shared lifestyle risk factors.[3] Lifestyle risk factors common to colorectal cancer and other chronic diseases, and with CVD in particular, include overweight/obesity, physical inactivity, poor diet and smoking. Given the strong evidence that most chronic diseases are preventable through lifestyle modification[4], lifestyle improvement following a

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cancer diagnosis may mitigate existing co-morbid chronic disease progression and reduce the risk of developing such diseases.

Co-morbid chronic conditions have a significant impact on the management of, and prognosis for, cancer survivors.[5] Patients presenting with co-morbid conditions are usually excluded from clinical trials, and co-morbidity affects the presentation and recognition of cancer symptoms[5–7], as well as post-operative morbidity. Further, co-morbid chronic conditions (especially CVD) can have a negative effect on colorectal cancer survival.[8]

A number of studies have documented the prevalence of co-morbid chronic conditions in colorectal cancer survivors.[9] A recent population-based study found that 30% of colorectal cancer survivors had co-morbid conditions[8], whilst another study reported that 35% of colorectal cancer survivors under 70 years, and 61% of those over 70 years of age, suffered from other chronic conditions which were higher than that observed in the general population.[10] The most commonly observed co-morbid condition was CVD, followed by previously diagnosed cancers, hypertension, COPD and diabetes.[10] In developed countries, CVD is a major cause of morbidity, mortality and economic burden. As trends in population ageing continue, the incidence of CVD and related health care costs are expected to continue to rise.[11,12] As such, it is essential to manage, or preferably prevent, CVD in those at high risk.

Whilst earlier studies have reported co-morbidity at the time of colorectal cancer diagnosis, they have not investigated co-morbidity development following cancer diagnosis. Further, there has been no previous report examining the association between modifiable lifestyle risk factors and co-morbid chronic illness among colorectal cancer survivors. Understanding how these lifestyle risk factors may be associated with the development of co-morbid disease could inform the development of behavioural interventions to reorient the trajectory of functional decline and ultimately improve survival for colorectal cancer survivors.

This study aims to: (i) assess the self-reported lifetime prevalence of CVD, one of the most commonly reported and costly co-morbid conditions among recently diagnosed colorectal cancer survivors; and (ii) examine the cross-sectional and prospective associations of modifiable lifestyle factors (body mass index, physical activity, television (TV) viewing, alcohol consumption and smoking) with co-morbid CVD.

2. Materials and methods

2.1. Study sample

Data were collected as part of the Colorectal Cancer and Quality of Life Study, which has been described in detail elsewhere.[13] In brief, all persons resident in Queensland, Australia, with a histologically confirmed diagnosis of a first, primary CRC, notified to the Queensland Cancer Registry between 1 January 2003 and 31 December 2004, were eligible for the study. Eligibility criteria also included: speaking English; having no hearing, speech or cognitive disabilities that would prevent completing a telephone interview; and being aged between 20 and 80 years at the time of diagnosis. A flow diagram describing recruitment to, and participation in, the study is presented in Fig. 1. Baseline interviews were completed by 1966 eligible participants, giving an overall response rate of 57.4%, and 80% of participants completed the baseline interview within approximately 5 months of their diagnosis (mean = 4.5 months, SD = 1.5 months).

Colorectal cancer survivors who provided written, informed consent were telephoned by a trained interviewer, at approximately 5, 12, 24 and 36 months post-diagnosis. The University of Queensland's Behavioural and Social Science Ethical Review Committee approved the study's procedures.

2.2. Measures

2.2.1. Dependent variables

Cross-sectional outcomes comprised six CVD categories recommended by a senior cardiologist at the Royal Brisbane and Women's Hospital, Queensland derived using a broad definition of CVD commonly employed by government agencies such as the Australian Institute of Health and Welfare for administrative purposes. Categories included: hypercholesterolaemia; hypertension; diabetes; heart failure; kidney disease; and ischaemic heart disease or IHD (including myocardial infarction; percutaneous coronary intervention; and, coronary artery bypass graft surgery). Participants were asked whether they had been diagnosed with any of these conditions, and the age at which the diagnosis had been made. Participants were also asked to report any other heart conditions or health problems. Responses to these open-ended questions were reviewed by two authors (ALH, BML) and re-categorised into the CVD categories listed above, if appropriate.

Longitudinal outcomes comprised any new diagnoses of CVD reported at follow-up interviews. Participants were asked whether they had been diagnosed with any of the CVD categories described, above, since their last interview. Participants also provided the date when a new diagnosis had been made. New diagnoses were classified as *de novo* cases of the six CVD categories.

2.2.2. Independent variables

2.2.2.1. Body mass index (BMI). Height and weight were reported at 5 months post-diagnosis; weight was also reported at subsequent interviews. BMI was calculated for each time point and, for descriptive purposes, participants were categorised as *underweight* (BMI < 18.5 kg/m^2), *healthy weight* (BMI 18.5–24.9 kg/m^2), *overweight* (BMI 25.0–29.9 kg/m^2), or *obese* (BMI $\geqslant$ 30.0 kg/m^2).[14]

2.2.2.2. Physical activity. The Active Australia Survey, a standard instrument used to monitor physical activity participation in the Australian adult population[15,16] was used to assess physical activity. Participants were asked to report the amount of time they spent, in a usual week over the past month: walking for transport or recreation; in other moderate-intensity physical activity (e.g. gentle swimming, social tennis, golf); and in vigorous-intensity physical activity (e.g. jogging, cycling, aerobics, competitive tennis). Total weekly physical activity was calculated by adding together the time spent in each activity category. Current Australian public-health guidelines advocate achieving the equivalent of

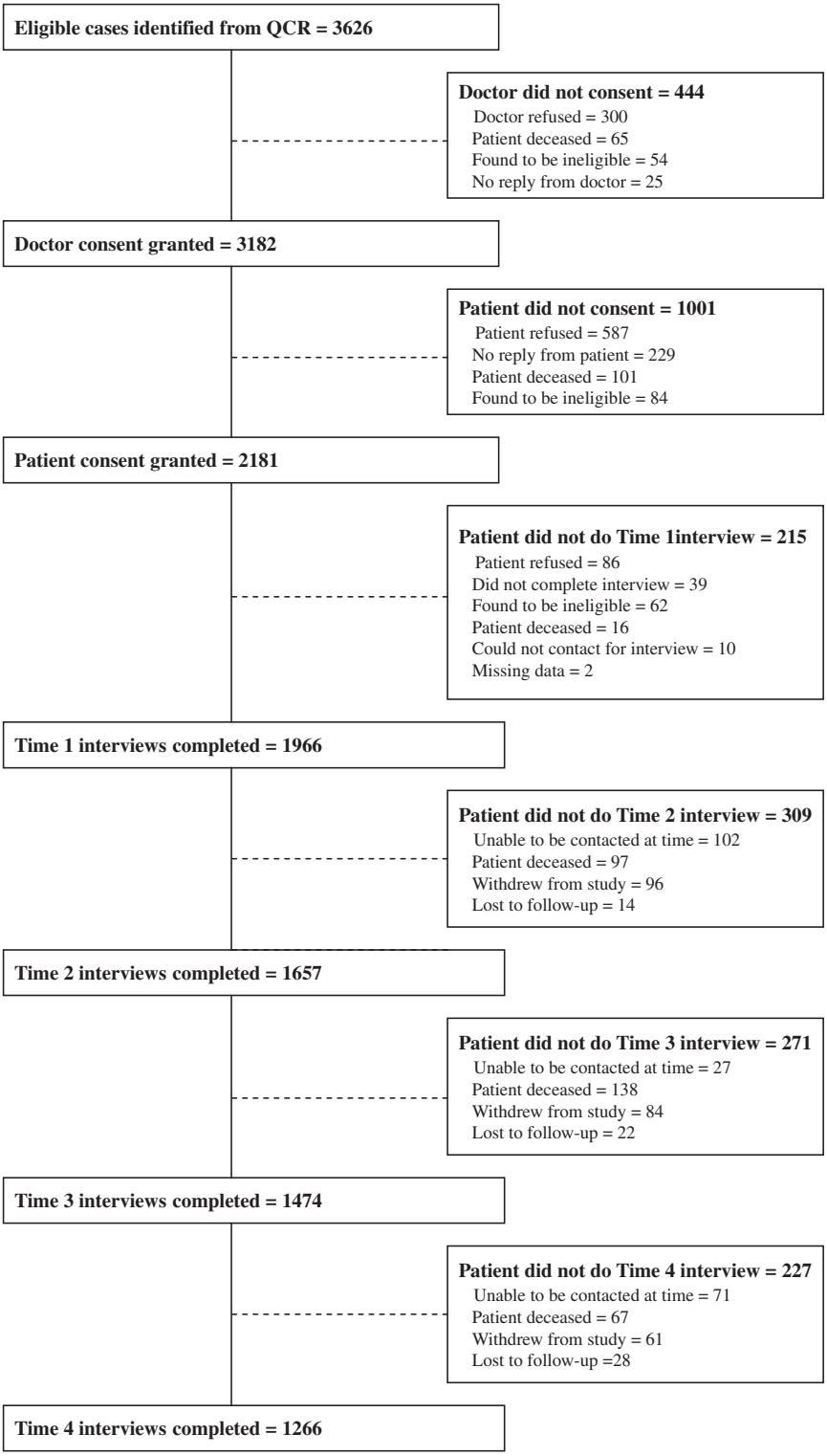

Fig. 1 – Flow diagram of study recruitment and participation.

150 min of moderate-intensity activity per week.[17] Based on these guidelines, participants were categorised as being either *inactive* (0 min/week), *insufficiently active* (1–149 min/week) or *sufficiently active* (150 min or more per week).

2.2.2.3. *TV viewing*. Within epidemiological and health behaviour research, measurement of adults' sedentary behaviour has often focused on TV viewing, one of the most frequently reported leisure-time activities.[18] Participants provided an estimate of the total time spent watching TV, on an average day, over the past month. Self-reported TV viewing has been shown to be a reasonably reliable and valid measure for adults.[19] Participants' estimate of their TV viewing was categorised as follows: *<2 h of TV/d*; *2–4 h of TV/d*; and *>4 h of TV/d*.

Table 1 – Socio-demographic and clinical characteristics and lifestyle factors for colorectal cancer survivors at 5, 12, 24 and 36 months post-diagnosis.

Characteristic	% of Participants				Non-participants $n = 1456$
	5 months $n = 1966$	12 months $n = 1657$	24 months $n = 1474$	36 months $n = 1266$	
Sex					
Male	59.8	59.4	58.7	56.7	57.7
Female	40.2	40.6	41.3	43.3	42.3
Age category					
20–49	8.5	8.6	8.8	8.5	7.6
50–59	19.4	19.6	20.5	20.2	16.4
60–69	33.7	33.4	33.6	34.2	28.0
70+	38.4	38.4	37.1	37.1	48.0
Marital status					
Married or de facto	74.1	74.2	75.0	75.0	–
Widowed	10.8	11.1	11.0	11.0	–
Divorced or separated	10.7	10.4	10.1	10.0	–
Never married	4.4	4.3	3.9	4.0	–
Educational attainment					
Less than 8 years	14.2	14.0	12.6	12.6	–
8–11 years	39.4	39.9	40.4	40.4	–
12 years (high school)	10.0	10.2	10.5	10.6	–
Technical college	23.1	23.0	23.1	23.0	–
University	13.3	12.9	13.4	13.4	–
Cancer site					
Colon	69.9	69.5	69.7	69.4	66.5
Rectum	30.1	30.5	30.3	30.6	33.5
Stage of disease					
Duke's A	24.7	25.5	27.2	33.2	22.9
Duke's B	35.2	36.9	38.8	35.6	34.3
Duke's C	30.3	29.8	29.8	30.4	37.9
Duke's D	10.1	7.8	4.4	0.8	4.9
Body mass index					
Underweight (<18.5 kg/m^2)	2.8	2.5	2.0	1.3	–
Healthy weight (18.5–24.9 kg/m^2)	43.3	35.9	32.0	30.3	–
Overweight (25.0–29.9 kg/m^2)	36.1	40.0	42.3	43.1	–
Obese ($\geqslant 30.0$ kg/m^2)	17.8	21.6	23.7	25.3	–
Physical activity					
Inactive (0 min/week)	41.1	36.5	34.7	34.9	–
Insufficiently active (1–149 min/week)	26.5	26.2	26.2	26.1	–
Sufficiently active ($\geqslant 150$ min/week)	32.4	37.4	39.2	39.0	–
Television viewing					
<2 h/d	43.9	47.1	43.4	41.1	–
2–4 h/d	42.1	41.9	45.6	48.1	–
>4 h/d	14.0	11.0	11.0	10.9	–
Alcohol consumption					
Low risk	75.2	71.8	75.0	79.0	–
Moderate risk	14.2	17.4	16.6	14.0	–
High risk	10.6	10.8	8.4	7.0	–
Smoking status					
Current smoker	39.8	39.5	43.7	42.1	–
Former smoker	52.3	52.3	49.4	51.1	–
Never smoker	7.9	8.2	6.9	6.8	–

2.2.2.4. *Alcohol consumption*. Participants provided an estimate of the average number of standard alcoholic drinks they consumed per week. Participants' estimate of their alcohol consumption was categorised as follows: *low risk* if they consumed <7 drinks per week and were female, or <14 drinks per week and were male; *moderate risk* if they consumed 7–13 drinks per week and were female, or 14–27 drinks per week and were male; and *high risk* if they consumed $\geqslant 14$ drinks per week and were female, or $\geqslant 28$ drinks per week and were male. These categories were created based on the current Australian guidelines for minimising harm from alcohol consumption.[20]

2.2.2.5. *Smoking*. Participants were questioned about their current smoking status and were categorised as: *current smokers*; *former smokers*; or *never smokers*.

2.2.2.6. *Clinical variables*. Date of diagnosis, tumour site, approximate stage of colorectal cancer and form of treatment were collected from pathology reports held within the Queensland Cancer Registry.

2.2.2.7. *Socio-demographic variables*. Marital status and educational attainment were self-reported at interview; age and gender were collected from pathology reports held within the Queensland Cancer Registry.

2.3. Analytic strategy

To examine the representativeness of the sample at each time point, participants were compared with those that were eligible for the study but did not complete the initial telephone interview (non-participants). Comparisons were made across the variables that were available for non-participants. Descriptive statistics were used to describe the attributes of the sample at each time point. Multivariate cross-sectional and longitudinal analyses were limited to hypercholesterolaemia, hypertension, diabetes and IHD, because we observed few cases of reported heart failure and kidney disease. In cross-sectional analyses, logistic regression models were constructed to examine the associations between modifiable lifestyle factors (physical activity; TV viewing; smoking; alcohol consumption; BMI) and lifetime prevalence of CVD outcomes (hypercholesterolaemia; hypertension; diabetes; IHD). Adjusted odds ratios, with 95% confidence intervals (CIs), were computed, and each model was adjusted for sex, age, educational attainment and marital status. Sex-specific models were generated as the health behaviours of men and women are known to differ. Further, site specific (colon versus rectal cancer survivors) models were generated as health behaviours of colon versus rectal cancer survivors are also thought to differ. Site-specific models were not compared for men and women due to small cell sizes.

In longitudinal analyses, logistic regression was used to determine the effect of baseline lifestyle factors (physical activity; TV viewing; smoking; alcohol consumption; BMI) on the probability of developing *de novo* cases of hypercholesterolaemia, hypertension, diabetes or IHD, controlling for socio-demographic factors. There were insufficient cases of *de novo* CVD to allow sex-specific analyses.

Interaction terms (BMI * physical activity and alcohol consumption * smoking) were included in the cross-sectional and longitudinal analyses. Further, logistic regression models were constructed to examine the cross-sectional and longitudinal associations between clinical variables (colorectal cancer site, colorectal cancer stage, and form of treatment) and CVD outcomes.

3. Results

Socio-demographic characteristics and lifestyle factors of study participants, and available data for non-participants, at each time point are shown in Table 1.

Table 2 – Cross-sectional proportions *n* (%) of colorectal cancer survivors with self-reported cardiovascular disease (CVD) categories for all participants, males and females.

CVD categories	Total (n = 1966)	Males (n = 1176)	Females (n = 790)
Hypercholesterolaemia	564 (28.7%)	325 (27.6%)	239 (30.3%)
Hypertension	804 (40.9%)	491 (41.8%)	313 (39.6%)
Diabetes	247 (12.6%)	161 (13.7%)	86 (10.9%)
Heart failure	4 (0.2%)	2 (0.2%)	2 (0.3%)
Kidney disease	1 (0.1%)	–	1 (0.1%)
Ischaemic heart disease (IHD)	225 (11.4%)	155 (13.2%)	70 (8.9%)
Myocardial infarction	151 (7.7%)	116 (9.9%)	35 (4.4%)
Percutaneous coronary intervention	21 (1.1%)	10 (0.9%)	11 (1.4%)
Coronary artery bypass graft surgery	53 (2.7%)	47 (4.0%)	6 (0.8%)

Table 3 – *De novo* cases (n) of self-reported cardiovascular disease (CVD) categories for all participants, males and females.

CVD categories	At risk[a] n	Total (n = 1057)	Males (n = 583)	Females (n = 474)
Hypercholesterolaemia	722	77 (10.7%)	39	38
Hypertension	616	86 (14.0%)	43	43
Diabetes	933	32 (3.4%)	17	15
Heart failure	1055	–	–	–
Kidney disease	1057	2 (0.2%)	2	–
Ischaemic heart disease	954	32 (3.4%)	18	14
Myocardial infarction	987	16 (1.6%)	7	9
Percutaneous coronary intervention	1043	10 (1.0%)	5	5
Coronary artery bypass graft surgery	1039	10 (1.0%)	8	2

[a] The total number of participants in the longitudinal sample that did not have the CVD category as a co-morbidity at baseline.

Table 4 – Cross-sectional associations between cardiovascular disease (CVD) categories and lifestyle factors for all participants, males and females.

		Total		Males		Females	
		OR	95% CI	OR	95% CI	OR	95% CI
Hypercholesterolaemia							
Body mass index (BMI)	18.5–24.9 kg/m^2						
	<18.5 kg/m^2	0.78	0.40, 1.55	0.58	0.16, 2.12	0.91	0.40, 2.07
	25.0–29.9 kg/m^2	1.39	1.10, 1.76	1.33	0.99, 1.79	1.39	0.95, 2.06
	⩾30.0 kg/m^2	1.68	1.26, 2.23	1.33	0.90, 1.95	2.26	1.47, 3.49
Physical activity	0 min/week						
	1–149 min/week	0.83	0.64, 1.07	0.65	0.46, 0.91	1.16	0.78, 1.71
	⩾150 min/week	0.84	0.66, 1.07	0.84	0.62, 1.14	0.86	0.57, 1.30
Television viewing	<2 h/d						
	2–4 h/d	0.92	0.74, 1.14	0.92	0.69, 1.23	0.92	0.64, 1.31
	>4 h/d	0.97	0.71, 1.32	0.86	0.57, 1.29	1.11	0.67, 1.84
Smoking status	Never smoked						
	Former smoker	1.18	0.94, 1.48	1.28	0.94, 1.74	1.14	0.80, 1.61
	Current smoker	1.16	0.75, 1.80	1.33	0.77, 2.32	0.99	0.46, 2.12
Alcohol	Low risk						
	Moderate risk	0.79	0.58, 1.08	0.73	0.51, 1.04	0.98	0.53, 1.83
	High risk	0.96	0.68, 1.35	0.87	0.56, 1.37	1.04	0.61, 1.77
Hypertension							
BMI	18.5–24.9 kg/m^2						
	<18.5 kg/m^2	0.88	0.47, 1.64	0.37	0.10, 1.35	1.22	0.56, 2.63
	25.0–29.9 kg/m^2	1.45	1.17, 1.81	1.58	1.20, 2.08	1.13	0.77, 1.66
	⩾30.0 kg/m^2	2.72	2.07, 3.58	2.48	1.72, 3.56	3.21	2.09, 4.94
Physical activity	0 min/week						
	1–149 min/week	0.82	0.64, 1.04	0.91	0.66, 1.24	0.67	0.45, 0.99
	⩾150 min/week	0.84	0.67, 1.06	0.81	0.61, 1.09	0.92	0.62, 1.36
Television viewing	<2 h/d						
	2–4 h/d	1.05	0.86, 1.30	1.13	0.87, 1.47	0.89	0.63, 1.27
	>4 h/d	1.09	0.81, 1.47	1.01	0.69, 1.47	1.12	0.68, 1.83
Smoking status	Never smoked						
	Former smoker	0.96	0.78, 1.19	1.07	0.81, 1.41	0.87	0.61, 1.22
	Current smoker	0.77	0.51, 1.17	0.82	0.48, 1.39	0.85	0.42, 1.75
Alcohol	Low risk						
	Moderate risk	0.14	1.29, 0	0.90	0.65, 1.24	1.33	0.73, 2.42
	High risk	1.04	0.75, 1.43	1.07	0.70, 1.62	1.01	0.60, 1.70
Diabetes							
BMI	18.5–24.9 kg/m^2						
	<18.5 kg/m^2	0.80	0.28, 2.34	1.01	0.22, 4.74	0.83	0.18, 3.86
	25.0–29.9 kg/m^2	1.93	1.38, 2.70	1.89	1.26, 2.84	1.94	1.05, 3.61
	⩾30.0 kg/m^2	3.19	2.18, 4.66	2.65	1.62, 4.34	4.16	2.24, 7.75
Physical activity	0 min/week						
	1–149 min/week	0.89	0.63, 1.26	1.03	0.67, 1.59	0.69	0.38, 1.25
	⩾150 min/week	0.81	0.57, 1.13	0.89	0.59, 1.34	0.73	0.39, 1.37
Television viewing	<2 h/d						
	2–4 h/d	1.05	0.77, 1.43	1.08	0.74, 1.57	0.99	0.57, 1.70
	>4 h/d	1.26	0.84, 1.90	1.33	0.80, 2.20	1.11	0.55, 2.26
Smoking status	Never smoked						
	Former smoker	1.55	1.12, 2.13	1.81	1.17, 2.81	1.34	0.80, 2.25
	Current smoker	2.28	1.28, 4.07	3.11	1.54, 6.31	1.25	0.39, 4.05
Alcohol	Low risk						
	Moderate risk	0.54	0.34, 0.85	0.56	0.34, 0.93	0.47	0.14, 1.59
	High risk	0.58	0.34, 0.99	0.77	0.42, 1.42	0.30	0.09, 1.01
Ischaemic heart disease							
BMI	18.5–24.9 kg/m^2						
	<18.5 kg/m^2	0.75	0.25, 2.22	1.16	0.24, 5.6	0.47	0.10, 2.22
	25.0–29.9 kg/m^2	1.47	1.04, 2.06	1.71	1.13, 2.57	0.85	0.44, 1.66
	⩾30.0 kg/m^2	1.85	1.22, 2.80	1.91	1.13, 3.22	1.77	0.88, 3.57
Physical activity	0 min/week						
	1–149 min/week	0.81	0.56, 1.18	0.86	0.54, 1.36	0.71	0.38, 1.34
	⩾150 min/week	0.81	0.57, 1.16	1.04	0.68, 1.58	0.35	0.15, 0.80

Table 4 (continued)

		Total		Males		Females	
		OR	95% CI	OR	95% CI	OR	95% CI
Television viewing	<2 h/d						
	2–4 h/d	0.94	0.68, 1.30	0.95	0.64, 1.41	0.76	0.41, 1.40
	>4 h/d	1.33	0.87, 2.04	1.32	0.78, 2.23	1.13	0.52, 2.42
Smoking status	Never smoked						
	Former smoker	1.80	1.27, 2.55	2.23	1.40, 3.57	1.39	0.78, 2.48
	Current smoker	1.51	0.75, 3.04	1.99	0.85, 4.66	1.13	0.30, 4.33
Alcohol	Low risk						
	Moderate risk	0.57	0.36, 0.91	0.47	0.28, 0.80	1.25	0.45, 3.52
	High risk	0.63	0.36, 1.12	0.39	0.17, 0.87	1.50	0.64, 3.50

Comparison of study participants with non-participants found no differences in the sex distribution between the groups at any time point. However, the study sample did under-represent older (age 70–80 years) colorectal cancer survivors, those with rectal cancer, and those with more advanced disease (χ^2 test, $P < 0.05$ for each).

Table 2 includes findings on the proportion of study participants at 5 months with self-reported co-morbid CVD. Overall, 59% suffered from co-morbid CVD, with participants most commonly reporting hypertension (41%), hypercholesterolaemia (29%), diabetes (13%), or IHD (11%).

Table 3 reports *de novo* cases of co-morbid CVD. In total, 16% of participants within the longitudinal cohort were diagnosed with a cardiovascular condition between 5 and 36 months post-diagnosis. As observed at 5 months post-diagnosis, male and female participants were most likely to experience a new diagnosis of hypertension (14%), hypercholesterolaemia (11%), diabetes (3%), or IHD (3%) up to 36 months post-diagnosis.

3.1. *Cross-sectional analyses for all participants, males and females*

The results of the cross-sectional logistic regression analyses for all participants, males and females are shown in Table 4. BMI was the strongest correlate of CVD in this population, being significantly associated with hypercholesterolaemia (total sample and females), hypertension, diabetes and IHD (total sample and males). For physical activity, being insufficiently active was inversely associated with hypercholesterolaemia for males and high blood pressure for females; being sufficiently active was inversely associated with IHD for females. TV viewing was not associated with any of the CVD categories, however there appeared to be a non-significant trend for the total sample and for males with diabetes and IHD. Smoking and alcohol consumption were both associated with diabetes and IHD for the total sample and for males.

Investigation of interaction terms revealed that for: BMI * physical activity there was no significant interaction in the models for hypercholesterolaemia, hypertension, diabetes or IHD. For alcohol consumption * smoking there was no significant interaction in the models for hypercholesterolaemia, hypertension, or IHD. There was a significantly decreased risk for former smokers and moderate alcohol drinkers: OR = 0.23 (0.07, 0.75).

3.2. *Longitudinal analyses for all participants, males and females*

Being obese ($\geqslant 30$ kg/m^2) at baseline significantly predicted *de novo* hypertension (OR = 2.20, 95% CI = 1.09, 4.45) and *de novo* diabetes (OR = 6.55, 95% CI = 2.19, 19.53). Participants who watched more than 4 h of TV/d at baseline (compared with participants who watched less than 2 h/d) were more likely to develop IHD over the 3 years following their colorectal cancer diagnosis (OR = 5.51, 95% CI = 1.86, 16.34). There appeared to be a non-significant trend for smoking with *de novo* hypercholesterolaemia, *de novo* diabetes and *de novo* IHD.

Investigation of interaction terms revealed that for BMI * physical activity there was no significant interaction in the models for *de novo* hypercholesterolaemia, diabetes or IHD. There was a significantly decreased risk of hypertension for overweight participants who were sufficiently active: OR = 0.18 (0.03, 0.95). For alcohol consumption * smoking there was no significant interaction in the models for *de novo* hypercholesterolaemia, hypertension, diabetes or IHD.

3.3. *Cross-sectional analyses for colon and rectum cancer survivors*

The results of the cross-sectional logistic regression analyses for colon versus rectum cancer survivors are shown in Table 5. BMI continued to be the strongest correlate of CVD in this population, being significantly associated with hypercholesterolaemia for both cancer sites, hypertension for both sites, diabetes for both sites and IHD for colon cancer survivors (lost significance for rectal cancer survivors). Current smoking was found to be significantly associated with hypercholesterolaemia for rectal cancer survivors; former and current smoking was associated with diabetes for colon cancer survivors; former smoking was associated with IHD for colon cancer survivors. TV > 4 h/d was associated with IHD for rectal cancer survivors, whereas no association was observed for colon cancer survivors.

3.4. *Longitudinal analyses for colon and rectum cancer survivors*

For site-specific longitudinal analyses, overweight (OR = 2.21, 95% CI: 1.05, 4.66) and obesity (OR = 3.11, 95% CI: 1.24, 7.82) were significantly associated with *de novo* hypertension for

Table 5 – Cross-sectional associations between cardiovascular disease (CVD) categories and lifestyle factors for colon and rectum cancer survivors.

		Colon		Rectum	
		OR	95% CI	OR	95% CI
Hypercholesterolaemia					
BMI	18.5–24.9 kg/m^2				
	<18.5 kg/m^2	0.79	0.28, 2.22	1.57	0.37, 6.72
	25.0–29.9 kg/m^2	1.64	1.20, 2.25	1.18	0.68, 2.03
	⩾30.0 kg/m^2	1.54	1.05, 2.27	2.26	1.14, 4.50
Physical activity	0 min/week				
	1–149 min/week	0.73	0.52, 1.04	0.96	0.53, 1.71
	⩾150 min/week	0.77	0.56, 1.08	1.01	0.56, 1.81
Television viewing	<2 h/d				
	2–4 h/d	0.95	0.71, 1.28	0.74	0.44, 1.26
	>4 h/d	1.04	0.67, 1.62	0.92	0.47, 1.79
Smoking status	Never smoked				
	Former smoker	1.05	0.78, 1.41	1.60	0.89, 2.87
	Current smoker	0.80	0.41, 1.58	4.07	1.69, 9.81
Alcohol	Low risk				
	Moderate risk	0.80	0.52, 1.22	0.75	0.39, 1.43
	High risk	0.80	0.50, 1.28	0.91	0.42, 2.01
Hypertension					
BMI	18.5–24.9 kg/m^2				
	<18.5 kg/m^2	1.38	0.57, 3.34	1.23	0.29, 5.19
	25.0–29.9 kg/m^2	1.71	1.26, 2.31	1.87	1.15, 3.06
	⩾30.0 kg/m^2	2.84	1.96, 4.11	3.60	1.85, 6.98
Physical activity	0 min/week				
	1–149 min/week	0.83	0.59, 1.15	0.86	0.50, 1.47
	⩾150 min/week	0.84	0.61, 1.15	0.84	0.49, 1.43
Television viewing	<2 h/d				
	2–4 h/d	1.02	0.77, 1.36	1.13	0.70, 1.83
	>4 h/d	1.17	0.77, 1.78	0.85	0.45, 1.60
Smoking status	Never smoked				
	Former smoker	0.79	0.60, 1.05	0.98	0.59, 1.62
	Current smoker	0.89	0.49, 1.63	0.91	0.39, 2.13
Alcohol	Low risk				
	Moderate risk	0.95	0.64, 1.41	0.83	0.46, 1.50
	High risk	1.08	0.70, 1.65	0.84	0.40, 1.75
Diabetes					
BMI	18.5–24.9 kg/m^2				
	<18.5 kg/m^2	1.82	0.54, 6.20	No cases	
	25.0–29.9 kg/m^2	2.10	1.30, 3.41	2.09	1.00, 4.37
	⩾30.0 kg/m^2	4.34	2.56, 7.38	2.88	1.14, 7.31
Physical activity	0 min/week				
	1–149 min/week	0.76	0.46, 1.25	0.90	0.42, 1.96
	⩾150 min/week	0.79	0.50, 1.25	1.08	0.49, 2.39
Television viewing	<2 h/d				
	2–4 h/d	1.46	0.96, 2.24	0.76	0.36, 1.57
	>4 h/d	1.56	0.87, 2.18	1.09	0.47, 2.55
Smoking status	Never smoked				
	Former smoker	2.19	1.40, 3.43	1.32	0.60, 2.92
	Current smoker	5.17	2.33, 11.47	1.72	0.48, 6.13
Alcohol	Low risk				
	Moderate risk	0.37	0.19, 0.76	0.77	0.33, 1.79
	High risk	0.66	0.33, 1.28	0.34	0.07, 1.52
Ischaemic heart disease					
BMI	18.5–24.9 kg/m^2				
	<18.5 kg/m^2	0.72	0.15, 3.53	No cases	
	25.0–29.9 kg/m^2	1.52	0.95, 2.41	0.96	0.42, 2.22
	⩾30.0 kg/m^2	1.87	1.06, 3.29	1.76	0.63, 4.90
Physical activity	0 min/week				
	1–149 min/week	0.66	0.39, 1.12	1.02	0.41, 2.52
	⩾150 min/week	0.80	0.50, 1.28	1.31	0.53, 3.25

Table 5 (*continued*)

		Colon		Rectum	
		OR	95% CI	OR	95% CI
Television viewing	<2 h/d				
	2–4 h/d	0.78	0.50, 1.20	1.78	0.74, 4.26
	>4 h/d	1.03	0.56, 1.89	4.50	1.73, 11.74
Smoking status	Never smoked				
	Former smoker	2.02	1.27, 3.22	1.91	0.72, 4.26
	Current smoker	1.82	0.65, 5.06	1.78	0.41, 7.80
Alcohol	Low risk				
	Moderate risk	0.44	0.22, 0.87	0.69	0.26, 1.82
	High risk	0.73	0.35, 1.51	0.32	0.07, 1.56

colon cancer; obesity (OR = 4.35, 95% CI: 1.13, 16.78) with *de novo* diabetes for colon cancer; TV > 4 h/d (OR = 10.63, 95% CI: 2.38, 47.55) and current smoking (OR = 9.50, 95% CI: 1.44, 62.56) with *de novo* IHD. For rectal cancer, being sufficiently active (OR = 3.65, 95% CI: 1.03, 12.89) and a former smoker (OR = 3.55, 95% CI: 1.04, 12.13) were associated with an increased risk of *de novo* hypercholesterolaemia. There were insufficient cases of diabetes and IHD to run the analyses for rectal cancer.

There were no significant cross-sectional or longitudinal associations between clinical variables (colorectal cancer site, colorectal cancer stage, and form of treatment) and CVD outcomes.

4. Discussion

In this population-based cohort of 1966 colorectal cancer survivors, 59% had co-morbid CVD at approximately 5 months post-diagnosis. Sixteen percent of the longitudinal sample ($n = 1057$), with no known CVD at baseline, developed a new cardiovascular condition by 36 months post-diagnosis. BMI was the strongest correlate of co-morbid CVD, with overweight/obese males and females more likely to suffer from hypercholesterolaemia, hypertension, diabetes and IHD. Similarly, those who were obese were more likely to have experienced *de novo* co-morbid hypertension or diabetes. In addition, those who watched more TV were more likely to suffer from co-morbid diabetes or IHD (although this was not statistically-significant) at baseline, and more likely to report *de novo* co-morbid IHD. These findings were similar for colon and rectum cancer survivors alike.

The relatively high incidence of co-morbid CVD in the study sample compared with the incidence in the general population (approximately 18% in Australia)[21] at 5 months post-diagnosis of colorectal cancer was consistent with earlier reports.[10] Our study extends these findings by demonstrating that a significant number of colorectal cancer survivors develop *de novo* co-morbid CVD in the years immediately following a diagnosis. It is well accepted that accurate pre-surgical assessment of co-morbid conditions is important in anticipating post-operative complications and outcomes[22], however *de novo* co-morbidity is also likely to impact on long term health outcomes.

We also investigated the associations between lifestyle risk factors and co-morbid CVD and found that excess body weight was particularly important for colorectal cancer survivors. This finding supports observations from large cohort studies that have shown improved cancer-specific and overall survival among cancer survivors who are physically active and do not gain weight after diagnosis.[23]

TV viewing has been previously associated with weight gain in this sample.[24] Here we observed positive, but not statistically significant, cross-sectional associations of TV viewing with diabetes and IHD, and a statistically significant association between TV viewing and *de novo* IHD. It is possible that our present findings may underestimate these relationships, because we used a broadly estimated and long recall period for TV viewing (on-average daily TV viewing over the past month) than that which has been used in previous Australian studies.[19] Given the generally high prevalence of sedentary behaviour in contemporary society, this is a research area that warrants further attention. Sedentary behaviour is emerging as a distinct behaviour that may contribute to the development of obesity and related chronic diseases via decreasing total activity energy expenditure, and through unique physiological processes such as regulation of lipoprotein lipase.[25,26]

Lifestyle factors are increasingly being recognised as important contributing factors in the management of cancer. The findings of this study highlight that behavioural interventions addressing modifiable lifestyle risk factors (such as physical activity, alcohol intake, smoking, diet, and importantly weight management) may reduce functional decline and potentially improve survival for colorectal cancer survivors.

One of the strengths of our study is the large, population-based cohort of colorectal cancer survivors followed up to 3 years post-diagnosis. However, CVD and lifestyle data were self-reported, and hence subject to recall error and biases such as social desirability. The study was also limited by the small number of cases of many categories of CVD, especially in the longitudinal analyses, which was reflected in the wide confidence intervals for the odds ratios. We observed some interesting associations between co-morbid CVD and physical activity, TV viewing, smoking and alcohol both at baseline and up to 36 months post-diagnosis, but it is difficult to draw any conclusions from these findings due to the small number of *de novo* cases of co-morbid CVD. Finally, due to the habitual nature of lifestyle factors, it is difficult to determine whether *de novo* co-morbid CVD is a result of a change in lifestyle factors post-diagnosis or long term poor lifestyle factors pre-diagnosis of colorectal cancer. As such, randomised controlled trials are necessary to establish whether modification of lifestyle factors

behaviour post-diagnosis of colorectal cancer could contribute to reduced risk of CVD. The authors are currently conducting a population-based trial of a novel telephone-delivered lifestyle intervention for colorectal cancer survivors that may help to answer this question.[27]

5. Conclusion

Co-morbid CVD is common following colorectal cancer diagnosis and may have a negative impact on health outcomes and survival. In the developed world, CVD is a major cause of morbidity, mortality and economic burden[11,12] and it is essential to manage, or preferably prevent, CVD in those at high risk. Overweight or obese colorectal cancer survivors are more likely to suffer from co-morbid CVD, and interventions focusing on weight management and other modifiable lifestyle risk factors (including potentially reducing TV viewing) may help to ameliorate functional decline and potentially improve survival for colorectal cancer survivors.

Conflict of interest statement

None declared.

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