



## Associations of sedentary time and patterns of sedentary time accumulation with health-related quality of life in colorectal cancer survivors

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### ABSTRACT

Sedentary behavior (sitting/lying at low energy expenditure while awake) is emerging as an important risk factor that may compromise the health-related quality of life (HRQoL) of colorectal cancer (CRC) survivors. We examined associations of sedentary time with HRQoL in CRC survivors, 2–10 years post-diagnosis. In a cross-sectional study, stage I–III CRC survivors ( $n = 145$ ) diagnosed (2002–2010) at Maastricht University Medical Center+, the Netherlands, wore the thigh-mounted MOX activity monitor 24 h/day for seven consecutive days. HRQoL outcomes were assessed by validated questionnaires (EORTC QLQ-C30, WHODAS II, Checklist Individual Strength, and Hospital Anxiety and Depression Scale). Confounder-adjusted linear regression models were used to estimate associations with HRQoL outcomes of MOX-derived total and prolonged sedentary time (in prolonged sedentary bouts  $\geq 30$  min), and usual sedentary bout duration, corrected for waking wear time. On average, participants spent 10.2 h/day sedentary (SD, 1.6), and 4.5 h/day in prolonged sedentary time (2.3). Mean usual sedentary bout duration was 27.3 min (SD, 16.8). Greater total and prolonged sedentary time, and longer usual sedentary bout duration were associated with significantly ( $P < 0.05$ ) lower physical functioning, and higher disability and fatigue scores. Greater prolonged sedentary time and longer usual sedentary bout duration also showed significant associations with lower global quality of life and role functioning. Associations with distress and social functioning were non-significant. Sedentary time was cross-sectionally associated with poorer HRQoL outcomes in CRC survivors. Prospective studies are needed to investigate whether sedentary time reduction is a potential target for lifestyle interventions aiming to improve the HRQoL of CRC survivors.

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**Abbreviations:**  $\beta$ , unstandardized regression coefficient; BMI, body mass index; CI, confidence interval; CIS, Checklist Individual Strength; CRC, colorectal cancer; EnCoRe study, Energy for life after ColoRectal cancer study; EORTC QLQ-C30, European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; HADS, Hospital Anxiety and Depression Scale; HRQoL, health-related quality of life; ICF, International Classification of Functioning, Disability and Health; MET, metabolic equivalent; MVPA, moderate-to-vigorous physical activity; SD, standard deviation; WHO, World Health Organization; WHODAS II, 12-item World Health Organization Disability Assessment Schedule II.

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## 1. Introduction

Worldwide, there are over 3.5 million colorectal cancer (CRC) survivors (Bray et al., 2013). Due to CRC and/or its treatment, these individuals can experience persisting declines in multiple health-related quality of life (HRQoL) domains, such as physical, social, and emotional functioning (Jansen et al., 2010; Caravati-Jouvencaux et al., 2011). As the number of CRC survivors is increasing (Parry et al., 2011), a major research priority is to identify modifiable targets for interventions aimed at improving HRQoL of survivors with persisting health problems (Demark-Wahnefried et al., 2006).

Previous cross-sectional and prospective studies in CRC survivors have shown that moderate-to-vigorous intensity physical activity (MVPA) is beneficially related to HRQoL (Johnson et al., 2009; Buffart et al., 2012; Mosher et al., 2009; Peddle et al., 2008; Grimmert et al., 2011; Lynch et al., 2008; Vallance et al., 2014; van Roekel et al., 2015). However, many CRC survivors likely struggle to exercise at these intensities, which is related to their number of comorbidities and age (Brown & Schmitz, 2014). Instead, CRC survivors spend most ( $\approx 60\%$ ) (Vallance et al., 2014) waking time sedentary (sitting/lying while awake with a low energy expenditure (Sedentary Behaviour Research Network, 2012)). A growing body of evidence (albeit, mostly cross-sectional) from general adult populations suggests that more time spent sedentary is unfavorably related to several health outcomes (Dunstan et al., 2012), including HRQoL outcomes such as overall HRQoL, physical and mental functioning, and vitality in the general population (Dempsey et al., 2014; Rosenkranz et al., 2013), and physical and social functioning in elderly individuals (Meneguci et al., 2015). Importantly, the manner in which sedentary time is accrued may also be relevant, particularly for cardio-metabolic outcomes (Healy et al., 2008; Healy et al., 2011), and also body composition and muscle quality specifically in older adults (Chastin et al., 2012). As sedentary behavior may be associated with CRC-related problems strongly affecting HRQoL, such as bowel problems and distress regarding CRC recurrence, associations of sedentary behavior with HRQoL in this population may be more pronounced than in the general population. Research into associations of sedentary time and patterns of sedentary time accumulation with HRQoL of CRC survivors is therefore timely (Lynch et al., 2013).

Prospective studies in CRC survivors have found that more time spent in leisure-time sitting (Campbell et al., 2013) and television viewing (Arem et al., 2015) (a specific sedentary behavior) were associated with increased all-cause mortality, and that television viewing was also associated with weight gain (Wijndaele et al., 2009), a higher incidence of cardiovascular disease (Hawkes et al., 2011), and reduced HRQoL (Lynch et al., 2011a). However, these studies used self-report measures of sedentary behavior, with associated biases (Boyle et al., 2015), and did not examine sedentary time accumulation patterns.

Activity monitors, including accelerometers, provide date-time stamped information about activity enabling objective assessment of sedentary time, and patterns of sedentary time accrual (accumulation of sedentary time in long uninterrupted bouts versus shorter bouts interspersed with other activities). In contrast to previous prospective studies, a recent cross-sectional study of 178 colon cancer survivors did not observe significant associations of hip-worn accelerometer-derived total and prolonged sedentary time (in uninterrupted bouts of  $\geq 30$  min) with HRQoL (Vallance et al., 2014). However, measurement error in such accelerometers may lead to failure to detect associations as their indirect classification of time as sedentary from low movement alone has low accuracy, particularly for distinguishing low energy activities with different postures, such as standing (not sedentary) from sitting (sedentary) (Berendsen et al., 2014).

Thigh-mounted monitors that measure leg position and thereby posture, have been shown to accurately distinguish sitting and lying from upright postures (including standing) (Berendsen et al., 2014; Annegarn et al., 2011), and are thereby better suited to studying associations of sedentary time and sedentary time accumulation patterns

with HRQoL. This study aimed to examine associations of sedentary time and patterns of sedentary time accumulation, measured using an accurate thigh-mounted activity monitor (Berendsen et al., 2014; Annegarn et al., 2011), with HRQoL in CRC survivors.

## 2. Materials and methods

### 2.1. Study design and participants

Data from the cross-sectional part of the Energy for life after ColoRectal cancer (EnCoRe) study was used. The EnCoRe study consists of a cross-sectional and ongoing prospective part (van Roekel et al., 2014). The cross-sectional part was conducted in CRC survivors, recruited 2–10 years post-diagnosis. Eligible individuals, i.e. persons diagnosed with and treated for stage I–III CRC between 2002 and 2010 at Maastricht University Medical Center+, the Netherlands, were preselected via the Netherlands Cancer Registry (managed by Comprehensive Cancer Centre the Netherlands). Participants were recruited between May 2012 and December 2013. Reasons for exclusion are shown in Fig. 1. The EnCoRe study has been approved by the Medical Ethics Committee of the Academic Hospital Maastricht and Maastricht University, the Netherlands. Written informed consent was obtained from all participants.

### 2.2. Data collection

When designing the EnCoRe study, a conceptual model was developed for studying lifestyle and HRQoL in CRC survivors (van Roekel et al., 2014), based on WHO's International Classification of Functioning, Disability and Health (ICF) (World Health Organization, 2001). Compared to the traditional biomedical concept of health and disability as separate entities with a strong emphasis on physical health, the ICF adopts a broader bio-psychosocial definition of human functioning, as a multidimensional and universal concept which includes health and disability within a single spectrum (Kostanjsek, 2011). Thus, the ICF does not only incorporate physical health components (body perspective), but also an individual's ability to perform his/her daily activities and societal role (individual and societal perspective). Further, it enables identification of environmental and personal factors and the presence of health conditions that can influence functioning. The previously developed model (van Roekel et al., 2014) was adapted for the current research question to identify relevant variables to be measured and included in data analyses (Supplementary Fig. 1).

#### 2.2.1. Sedentary and physical activity time

The validated tri-axial MOX activity monitor (MMOXX1, upgraded version of the CAM monitor) was used for objective measurement of sedentary and physical activity time (Maastricht Instruments B.V., NL). The MOX has a high reproducibility, and excellent validity for estimating time spent in activities and postures in both controlled laboratory (100% accuracy and kappa of 0.99; compared with direct observation (Berendsen et al., 2014) and 100% accuracy compared to a standardized protocol (Annegarn et al., 2011)) and in free-living conditions (intraclass correlation coefficient of 0.98 compared with diary records (Berendsen et al., 2014) and 100% accuracy in comparison with video recording (Annegarn et al., 2011)). The monitor was waterproofed in a finger cot (VWR International B.V., NL) and attached via plaster (BSN medical, NL) to the anterior thigh 10 cm above the knee. Participants were instructed to wear the monitor 24 h/day on seven consecutive days, and to record sleep and any non-wear periods.

A customized Matlab program (Version R2012a, The MathWorks, Inc., USA) was used to classify each 1-second epoch as sedentary (sitting/lying with an energy expenditure  $\leq 1.5$  METs (Sedentary Behaviour Research Network, 2012)), standing (standing with an energy expenditure  $\leq 1.5$  METs), or physical activity (all activities with an energy expenditure  $> 1.5$  METs, including light and moderate-to-vigorous intensity activities). This was done using previously validated thresholds for parameters of

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