

# Predictors of health-related quality of life of colorectal cancer survivors: a systematic literature review

B.W.A. van der Linden

Maastricht University

bwa.vanderlinden@student.maastrichtuniversity.nl

## Abstract

*Background.* The population of colorectal cancer survivors is growing. A colorectal cancer diagnosis and its treatment can bring along adverse long- and short term effects that influence the health-related quality of life (HRQOL) of survivors. In order to prevent these adverse effects and deteriorating HRQOL, the right care needs to be offered to the right individual at the right time. For early identification of survivors at risk for deteriorating HRQOL, it is important to know which factors are predictive of HRQOL. Therefore, the aim of this study was to identify possible predictors of HRQOL of colorectal cancer survivors.

*Methods.* A systematic literature review was conducted using the search engines MEDLINE/PubMed, EMBASE, and Google Scholar to find available literature on the relation between lifestyle, clinical, and socio-demographic variables and HRQOL in colorectal cancer survivors. Additional articles were found by citation tracking.

*Results.* In total, 29 studies met the inclusion criteria. The most relevant lifestyle predictors of lower HRQOL that were identified were low levels of physical activity and higher BMI. Higher stage, presence of a stoma, having comorbidities, having fecal incontinence, and having rectal cancer were the most relevant clinical predictors of lower HRQOL. The most relevant socio-demographic predictors of lower HRQOL were low income, no private health insurance, negative cancer threat appraisal, low levels of social support, and pessimism.

*Discussion and conclusion.* Evidence suggests that the predictors, found in the studies included in this systematic review, could help in identifying colorectal cancer survivors at increased risk of deteriorating HRQOL. For some predictors the evidence appeared inconclusive or contradictory, and therefore, more research is needed with special focus on these associations. Especially lifestyle predictors are an important area for future research,

since these factors are mostly related to modifiable behavior and changing them thus could help in improving HRQOL. The predictors identified in this systematic review can be used for developing, validating, and testing prediction models for HRQOL of colorectal cancer survivors.

## Keywords

Health-related quality of life, Colorectal cancer survivors, Predictors, Systematic review

## Introduction

Cancer is a leading cause of death worldwide, accounting for 8.2 million deaths in 2012, of which 8.5% was attributable to colorectal cancer<sup>1</sup>. Colorectal cancer is defined as a cancer of the colon and/or rectum. Worldwide it is the third most common cancer in men, after lung- and prostate cancer, and the second in women, after breast cancer<sup>1</sup>. According to a recent report from the Dutch Cancer Registry, over 13 000 new cases of colorectal cancer are diagnosed each year in the Netherlands<sup>2</sup>. About 80% of all colorectal cancer patients is aged sixty years or older<sup>2</sup>. Due to the ageing of the population, improved methods for earlier detection of cancer, and the scientific advances in anti-cancer treatments, that have led to increased survival rates, more and more people are surviving cancer nowadays<sup>3,4,5</sup>. In this study, cancer survivors are defined as: every person from time of diagnosis until the end of his or her life<sup>6</sup>. Since the chances of surviving cancer have improved and the incidence of colorectal cancer is rising, the population of cancer survivors is getting larger. Data from the Dutch Cancer Registry shows an increase in twenty-year prevalence rates of colorectal cancer from 72 137 people in 2009 to 82 339 in 2012<sup>7</sup>.

Being diagnosed with and treated for cancer can bring along many adverse effects that may affect a survivor's health-related quality of life. Health-related quality of life (HRQOL) can be defined as the effect of a disease and its therapy upon a patient. It is a multidimensional concept that includes at minimum the social, psychological, and physical aspects of health<sup>8</sup>. The different aspects of HRQOL are parts of the well-being of every person and influence a person's health status<sup>9</sup>. HRQOL can be predicted by a number of variables. In this study, the predictors that are included are divided into the following categories; lifestyle factors, clinical, and socio-demographic factors. Colorectal cancer survivors may suffer from adverse reactions to their treatment, and the disease on itself might have an impact on their physical and psychological functioning soon after diagnosis as well as in the long term<sup>10</sup>. These effects can additionally lead to deteriorating HRQOL. In order to offer the right care to the right individual at the right time, it is important to be aware of and to identify risk factors that influence the HRQOL of colorectal cancer survivors.

The aim of this study, based on a systematic review of previous studies, was to identify predictors that at an early stage can help to identify colorectal cancer survivors who are at increased risk of deteriorating HRQOL because of certain personal risk profiles. By identifying those high-risk individuals and offering them the right care, it is possible to prevent future deteriorated HRQOL and to improve their well-being. In this way, the impact of additional, extensive care and the high needs on our health care system can be lessened. The specific objective of this study was to investigate: What are relevant lifestyle, clinical, and socio-demographic predictors of HRQOL of colorectal cancer survivors?

## Material and methods

A systematic literature review was conducted to give an overview of the current evidence based on published research on predictors of the HRQOL of colorectal cancer survivors. The databases MEDLINE/PubMed, Embase, and Google Scholar have been searched. The following search strategy was defined for PubMed: 'colorectal neoplasms' was combined with 'survivor\*'. These two terms were combined with 'quality of life', 'depression', 'pain', 'anxiety', or 'fatigue', and 'health-related quality of life', or 'well-being'. Finally, 'predict\*', 'determinant\*', or 'risk factors' were added. Apart from changing the term 'colorectal neoplasms' to 'colorectal cancer', the same search strategy was used in Embase. In Google Scholar, exactly the same search strategy was used as in PubMed. The systematic search resulted in 305 articles in total by the three search engines. After removal of duplicates, 269 articles remained that potentially met the eligibility criteria for this review. These articles were systematically assessed to arrive at the final selection of articles eligible for full-text screening. For that purpose, three subsequent screening steps were undertaken by two independent reviewers (BvdL and MB). First the titles were screened, second the abstracts were read, and finally the full-texts articles were read. After each step the reviewers reached agreement on which articles to include in the next step during a consensus meeting. Citation tracking of the included studies was used to identify additional relevant articles. In total, 29 studies met the inclusion criteria and were included in this review. In figure 1, a flow diagram of the literature search is shown.



## PRISMA 2009 Flow Diagram

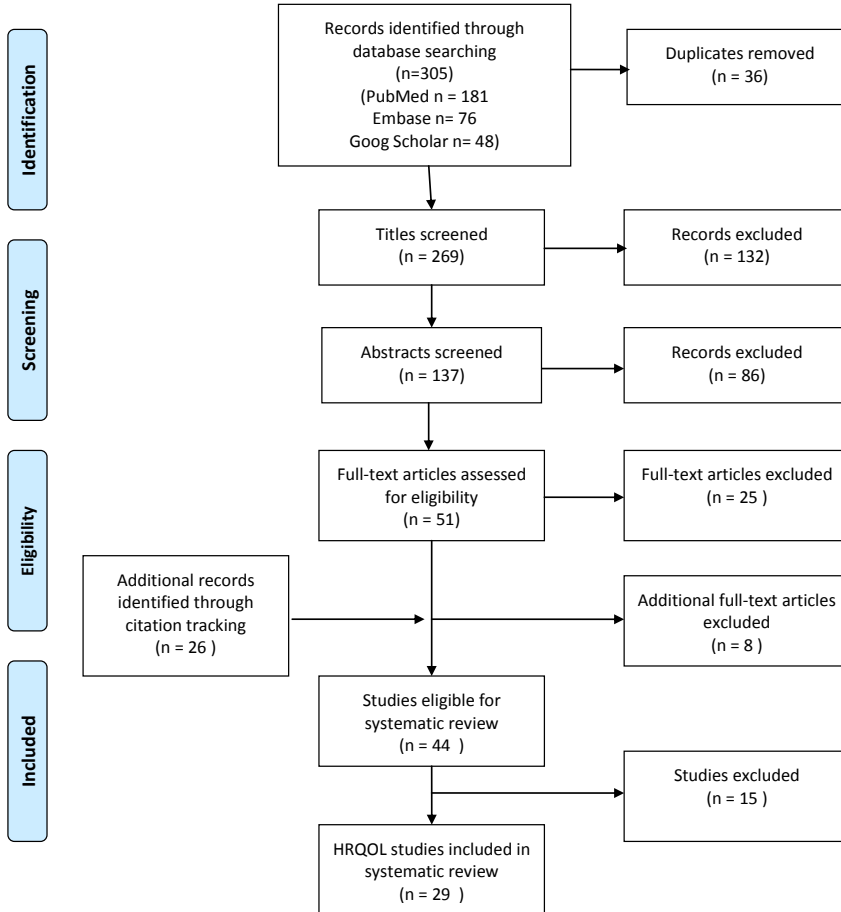


Figure 1: Literature search flow diagram

## Results

Several factors have been identified that are predictive of the HRQOL of colorectal cancer survivors. An overview of the 29 studies included in this systematic review, timing of measurements, sample characteristics, and main results is presented in table 1.

**Table 1:** Overview of the included studies and relevant outcomes

Author	Timing of measurements	Sample characteristics	Main results
Arndt et al. <sup>11</sup> (2004)	Cross-sectional; 1 year after diagnosis.	Newly diagnosed, invasive colorectal cancer survivors. N=309: 174 male, 135 female. Mean age: 65.1.	Stoma patients score lower on most functional scales (physical, role, emotional, social, global QOL).
Baldwin et al. <sup>12</sup> (2009)	Cross-sectional; >5 years after diagnosis.	Colorectal cancer survivors with ostomies. N=286: 168 male, 118 female. Mean age: 72.4.	Women report more sleep disruption and fatigue than men.
Campos-Lobato et al. <sup>13</sup> (2011)	Longitudinal prospective; 30 days before surgery, 6, 12, and 36 months after surgery.	Low rectal cancer survivors. N=153: APR=68 (mean age: 63), LAR=85 (mean age: 55).	APR long-term overall QOL similar to LAR.
Chambers et al. <sup>14</sup> (2012)	Longitudinal prospective; 5 months and 5 years post-diagnosis.	Colorectal cancer survivors. N=763. Most participants in the age category of 60-80 years.	Higher baseline values of HRQOL and global QOL associated with higher values >5 years. Being female, smoking, rectal cancer, stoma, and fatigue associated with lower well-being. Surgery + adjuvant therapy (vs surgery only), social support, optimism, and more positive cancer threat appraisal associated with higher well-being.
Courneya et al. <sup>15</sup> (1999)	Longitudinal retrospective; baseline (pre-diagnosis) and 4 months postsurgical.	Colorectal cancer survivors, postsurgical. N=53: 32 male, 21 female. Mean age: 60.7.	Mild increase in exercise from pre-diagnosis to post-surgery associated with better QOL.
Dunn et al. <sup>9</sup> (2013)	Longitudinal prospective; 5, 12, 24, 36, 48, and 60 months post-diagnosis.	Colorectal cancer survivors. N=1844. Between 20 and 80 years at diagnosis.	Poor social support, low cognitive appraisal, low optimism, and younger age associated with low QOL.
Esnaola et al. <sup>16</sup> (2002)	Longitudinal prospective; various time points (>3 months) after recurrence.	Locally recurrent rectal cancer survivors. N=45: 15 nonsurgical palliation (median age: 63), 30 resection (median age: 61).	Pain has a negative impact on post-treatment QOL. Being female, pain at presentation, total pelvic exenteration, and bony resection are associated with worse pain after treatment.
How et al. <sup>17</sup> (2012)	Longitudinal; preoperatively and 1 year after surgery.	Low rectal cancer survivors. N=62. LAR: 32 (median age: 59.9), APR: 30 (median age: 67).	Patients undergoing APR have better QOL than LAR.

Kilic et al. <sup>18</sup> (2012)	Cross-sectional; >1 year after completion of treatment.	Rectal cancer survivors. N=230: 126 male, 104 female. APR: 65 persons, LAR: 144. Median age: 55 years.	Patients who underwent APR score lower QOL. Severe radiation-induced complications have a negative impact on functioning.
Krouse et al. <sup>19</sup> (2009)	Cross-sectional; >5 years after diagnosis.	Colorectal cancer survivors. N=491. 246 with permanent ostomies (mean age: 72.4), 245 with anastomosis (mean age: 71.1).	Males and females with ostomies report worse HRQOL compared to those without ostomies.
Liu et al. <sup>20</sup> (2010)	Cross-sectional; >5 years after diagnosis.	Colorectal cancer survivors. N=679. 284 with ostomies, 395 with anastomosis. Most participants in the age category 79-96 years.	Fistula associated with lower HRQOL in both groups. Skin and late complications associated with lower HRQOL among rectal cancer, ostomy cases. Among rectal cancer survivors with anastomosis: urinary retention is associated with low HRQOL.
Lundy et al. <sup>21</sup> (2009)	Cross-sectional; >5 years after diagnosis.	Colorectal cancer survivors. N=679: 284 with ostomies (mean age: 72.4), 396 without (mean age: 71.1).	Higher income, higher age, and absence of an ostomy are positive predictors of psychological well-being.
Lynch et al. <sup>22</sup> (2007)	Longitudinal; pre- and post-diagnosis (<5 years).	Colorectal cancer survivors. N=1966. Most participants in the age category 60-80.	Higher levels of physical activity positively associated with QOL.
Ramsey et al. <sup>23</sup> (2000)	Cross-sectional; >1 year after diagnosis.	Colon or rectal cancer survivors, first recorded malignancy. N=161. Mean age: 70.4.	Higher stage has a negative impact on physical well-being and QOL. > 3 years from diagnosis is associated with higher functional and social well-being. Low income is associated with worse pain, ambulation, social and emotional well-being.
Ramsey et al. <sup>24</sup> (2002)	Cross-sectional; >5 years after diagnosis.	Colon or rectal cancer survivors, first recorded malignancy. N=227. Mean age: 74.	Higher levels of comorbidities (chronic diarrhea) and low income associated with lower QOL.
Rauch et al. <sup>25</sup> (2004)	Cross-sectional; >2 years after diagnosis.	Rectal cancer survivors, complete remission. N=121. Median age: 64.	Pain associated with reduced scores of all QOL domains.
Rinaldis et al. <sup>26</sup> (2010)	Longitudinal; 5 and 12 months post-diagnosis.	Colorectal cancer patients. N=1757: 1053 male, 704 female. Median age: 67.	5 month benefit finding positively associated with 5 and 12 month QOL.
Ristvedt et al. <sup>27</sup> (2009)	Longitudinal prospective; soon after treatment and 2-5 years after first measure.	Rectal cancer survivors. N=80. Mean age: 67.5.	High trait anxiety and severe fecal incontinence has a negative influence on HRQOL. Males poorer social well-being.

Salsman et al. <sup>28</sup> (2011)	Cross-sectional; post-diagnosis.	Colorectal cancer survivors. N=826: 426 male, 400 female. Mean age: 65.1.	Meaning/peace component of spiritual well-being positively associated with HRQOL.
Schag et al. <sup>29</sup> (1994)	Cross-sectional; <2 years, 2-5 years, or >5 years after diagnosis.	Colon cancer survivors, free of disease. N=117. Mean age: 64.6.	Higher KPS, treatment in private hospital, male, and not working predict QOL positively. Longer time since diagnosis associated with better QOL.
Soerjomataram et al. <sup>30</sup> (2012)	Cross-sectional; post-diagnosis.	Colorectal cancer survivors. N=1291. Most participants in the age category 65-79.	Stage 4 at diagnosis, middle and low SES, being female, and one or more comorbidities associated with poor perceived health and functional disability.
Steginga et al. <sup>31</sup> (2009)	Longitudinal; 6 and 24 months post-diagnosis.	First, primary colorectal cancer survivors. N=1822: 1094 male, 728 female. Mean age: 65.	Socio-demographic, medical, and psychosocial variables associated with domain specific QOL. Positive cancer threat appraisal positively associated with all five QOL domains.
Stephenson et al. <sup>32</sup> (2009)	Cross-sectional; post-diagnosis.	Colorectal cancer survivors, primary diagnosis. N=67: 35 male, 32 female. Mean age: 60.4.	Higher BMI associated with lower QOL, higher age, more social support, more attachment (emotional closeness), more social integration, more reliable alliance, and more guidance (advice or information) positively correlated with QOL.
Thong et al. <sup>33</sup> (2011)	Cross-sectional; post-diagnosis.	Colon cancer survivors. N=848: 606 without chemotherapy (321 male, 285 female), 242 chemotherapy (121 male, 121 female). Mean age: 69.4.	Age, being married, sex, comorbidities, tumor stage, and metastasis associated with subscales of SF-36 and EORTC QLQ-CR38.
Trentham-Dietz et al. <sup>34</sup> (2003)	Longitudinal; baseline (~1 year post-diagnosis) and 7-11 years post-diagnosis.	Women with invasive cancer of the colon or rectum. N=307. Mean age: 72.	Older age, more comorbidities, and higher BMI associated with lower PCS score. More comorbidities associated with lower MCS.
Tsunoda et al. <sup>35</sup> (2005)	Cross-sectional; after operation.	Colorectal cancer survivors. N=128: 74 male, 54 female. Mean age: 69.	Depression and anxiety are associated with lower QOL.
Wilson et al. <sup>36</sup> (2006)	Cross-sectional; six weeks after hospital discharge from surgery.	Colon and rectal cancer survivors who underwent surgery. N=201. Mean age: 68.2.	Poor performance status, stoma, diarrhea, constipation, <65 years associated with lower QOL.
Wong et al. <sup>37</sup> (2013)	Cross-sectional; post diagnosis.	Colorectal cancer survivors. N=515. Mean age: 63.3.	More advanced stage associated with worse HRQOL.

Abbreviations: APR = abdominoperineal resection; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer, Quality of Life Questionnaire - Core 30; EORTC QLQ-CR38 = European Organization for Research and Treatment on Cancer, Quality of Life Questionnaire - Colorectal 38; EQ-5D = EuroQOL 5 dimensions; FACT-G = Functional Assessment of Cancer Therapy-General; FACT-C = Functional Assessment of Cancer Therapy-Colorectal; KPS = Karnofsky Performance Status; LAR = low anterior resection; mCOH-QOL = City of Hope Quality of Life; MCS = Mental Component Summary Scale; PCS = Physical Component Summary scale; SF-36 = Short Form (36) Health Survey; SF-36v2 = Short Form (36) Health Survey version 2.

The predictors that have been found in the studies were the influence of smoking, physical activity, and BMI on HRQOL. Many different clinical predictors were identified in the included studies. The predictor variables that have been found were; stage of disease, having a stoma, type of treatment, presence of comorbidities, complications, and other symptoms. A number of different socio-demographic predictors were identified in the studies. Gender, age, and income were predictors that were observed in several studies.

## Discussion/Conclusion

In total, 29 studies that assessed predictors of HRQOL in colorectal cancer survivors were included in the systematic review. Figure 2 presents an overview of the relevant and less relevant predictors of deteriorated HRQOL that were identified per category (lifestyle, clinical, and socio-demographic). Based on design characteristics, sample size, and number of studies that have found specific variables predictive of deteriorated HRQOL, the relevance of each predictors was assessed.

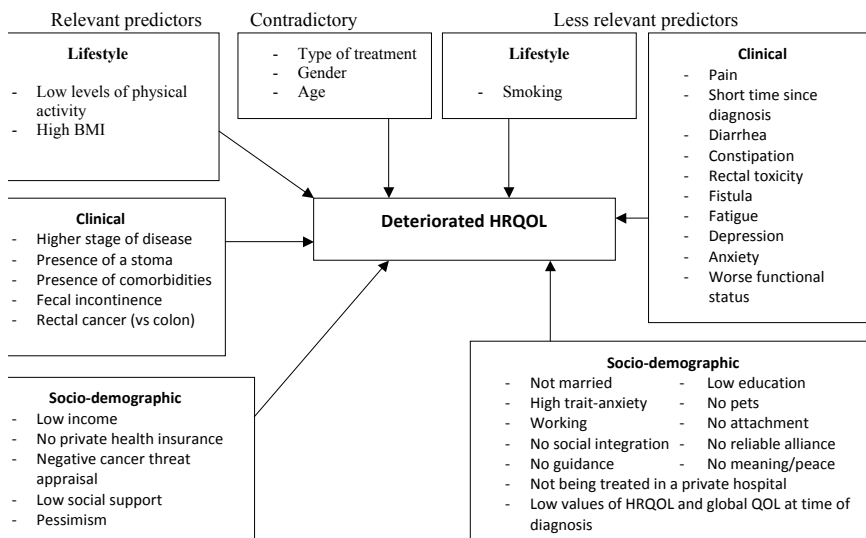


Figure 2: Predictors of deteriorated HRQOL



The most relevant lifestyle predictors of deteriorated HRQOL found appeared to be little to no physical activity and high BMI. The most relevant clinical predictors of deteriorated HRQOL were found to be; higher stage of disease, presence of a stoma, presence of comorbidities, fecal incontinence, and rectal cancer. Finally, the most relevant socio-demographic predictors of deteriorated HRQOL seemed to be; low income, no private health insurance, negative cancer threat appraisal, low social support and pessimism. The evidence found on the predictor's mode of treatment, age, and gender was contradictory, which would indicate that more research into the predictive value of these factors is warranted. It is important that more studies, preferably longitudinal studies, will look into the association between lifestyle factors and HRQOL. From the point of tertiary prevention, this category is especially important since lifestyle factors are mostly related to modifiable behavior and changing them thus could help in improving HRQOL.

This current systematic literature review has several strengths. Through proper and transparent methods, the risk of bias and/or errors is low. The search strategy was developed in such a way that all-important aspects of the research questions were covered. Selection of relevant articles was done by two independent reviewers, who held several consensus meetings during which it was agreed upon which articles should be included in the review. A limitation of this review is that no standardized list of methodological quality criteria was used to assess the quality of the selected studies.

Taken together, the primary aim of this review was to find relevant predictors of HRQOL of colorectal cancer survivors. The results presented in this study regarding identified HRQOL predictors have clinical implications. The findings of this review can help to identify individual survivors at increased risk of a future decrease in HRQOL by developing a prediction model based on the identified predictors in this study. When high-risk survivors are identified, they can be offered the right care at the right time, which should preferably include a lifestyle intervention, to prevent deterioration of HRQOL in the future and improve their well-being.

## Role of the student

B.W.A. van der Linden was an undergraduate student working under the supervision of M.J.L. Bours when the research in this report was performed. The topic was proposed by the supervisor. The data extraction, the processing of the results as well formulation of the conclusions and the writing were done by the student.

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