REVIEW PAPER

Psychosocial Risk Factors for Colorectal Cancer: A Systematic Review

Zainal NZ¹, Mohamed S²

¹Department of Psychological Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur 50603, Malaysia
²Department of Psychological & Behavioural Medicine, Faculty of Medicine, UiTM, Batu Caves 68100, Selangor, Malaysia

Abstract

Aims: To review the psychosocial risk factors for colorectal cancer (CRC), report the types and explore their association with CRC. Methods: We followed PRISMA guidelines to conduct the systematic review. We searched electronic databases (PubMed, CINAHL, PsychINFO and EMBASE) and hand searched up to 15th April 2015 for studies on psychosocial or stress or depression or anxiety or personality or support or coping as risk factor for CRC. We extracted information about the place of the study, study design, measurement tools, participant’s characteristics, psychosocial risk factor and its association with CRC. We limited the studies in English language only. The findings were synthesized and analysed. We presented them in tables and text. Results: We identified eight research papers which met the criteria. The studies reported four different types of psychosocial factor i.e. personality, stress, anxiety and depression. Four studies explored on personality, two on stress, one on anxiety and one on depression. There were four case-control studies and three longitudinal prospective studies. Two of the studies showed a significant association between personality and risk of CRC and two studies reported otherwise. Aggressive-hostility personality and negative emotions were significantly associated with risk of CRC. One study reported high level of job stress, higher anxiety levels and high level of depressive symptoms in females was also associated with increased risk of CRC. However, one study showed a lower risk of CRC in highly stressed females and no clear relationship between stress and risk of CRC in men. Conclusion: There is still inconclusive evidence to show that psychosocial factors are risk for colorectal cancer.

Keywords: Colorectal Cancer, Systematic Review, Personality, Stress, Anxiety, Depression
Introduction

Colorectal cancer (CRC) is one of the three most common types of cancer. The incidence of colorectal cancer in United States is 49.44 per 100,000 population\(^1\), 16.79 per 100,000 population in China\(^2\) and 18.4 per 100,000 population in Peninsular Malaysia\(^3\). Studies have shown that family history of colon cancer\(^4\), increased BMI\(^5\), red meat intake, cigarette smoking\(^6\), alcohol consumption\(^7,8\), low physical activity\(^9\) and low fruit consumption\(^10\) were associated with increased risk of CRC. Recent development in the study of gene polymorphism has shown its association with risk of CRC\(^11,12\).

There is an increasing interest to study psychosocial factors in the aetiology or risk for cancer\(^13,14\). Studies on looking at the relationship between psychosocial issues such as distress, depression, anxiety, coping, support and personality, and breast cancer yielded controversial reports\(^15,16\). On the other hand, longitudinal prospective studies have shown a more significant association between psychosocial issues and breast cancer development than the findings from cross-sectional or retrospective studies\(^16\).

Patients with colorectal cancer may experience high psychological distress due to the effect of cancer itself, its treatment and social sequelae\(^17\). Similarly, depression and anxiety have been described in post-surgery of colorectal cancer\(^18\). It is important to determine the prevalence of psychological issues in patients diagnosed with colorectal cancer. Similarly, it is equally important to explore whether psychological issues experienced by a person may increase the risk to develop colorectal cancer. However, to date, there is no published systematic review looking at the psychosocial factors as risk for colorectal cancer. Hence, this paper aims to review systematically studies that investigated whether distress, depression, anxiety, coping, support and personalities are a risk factor for colorectal cancer.

Methods

The review methods were guided by PRISMA (Preferred reporting items for systematic reviews and meta-analyses) statement\(^19\).

Search Strategy

All relevant studies were identified by searching the electronic databases (PubMed, CINAHL, PsychINFO and EMBASE) with the last search being up to 15th April 2015. The search terms used were (Psychosocial OR Distress OR Depression OR Anxiety OR Coping OR Support OR Personality) AND (Risk factor OR Aetiology) AND (Colon OR Colorectal OR rectum) AND (Cancer OR Tumour OR Neoplasm). Studies published in the non-English language were excluded. A further hand search was done according to the reference lists of the relevant articles to identify appropriate studies.

Data collection and analysis

We reviewed each title and abstract to retrieve the full-text of relevant articles. The inclusion criteria to consider the studies were as follows: (i) adult patients (aged \(\geq\) 18); (ii) all or predominantly colon or colorectal cancer (iii) adequate data on risk factors and (iv) all observational studies (cross-sectional, prospective, retrospective and case-control). All methods of screening or diagnosing psychosocial factors (distress, depression, anxiety, coping, support and personality) were allowed. Clinical trials and experimental studies, reviews, commentaries and case reports were excluded.
Data from all the eligible studies were entered them into a pre-designed data extraction form. The country of the study done, study design, measurement tools for psychosocial factors, description of the participants’ characteristics and the psychosocial risk factors studied were extracted. The results were synthesized in a narrative review.

**Results**

A total of 237 articles were identified from PubMed, CINAHL, PsychINFO and EMBASE databases and the hand searched reference lists. Further screening for relevant articles based on titles and abstract yielded 12 articles. After reviewing and applying the inclusion criteria, 4 articles were excluded. Therefore, 8 studies that were published between 1991 and 2008 were eligible for a systematic review. The flowchart is shown in Figure 1.

**Figure 1.** Flow chart of study diagram
Description of included studies

Methods of studies

The study design and characteristics of the studies included in this systematic review are listed in Table 1. Three of the studies were conducted in the United States, and the others were conducted in Japan (n= 2), Australia, United Kingdom and Denmark. The majority of the studies were case-control studies (n= 4), whereas the others were prospective (n= 3) and cross-sectional studies.

Subjects

There was a total of 138,577 subjects included from the eight studies (Table 1). This gives a median sample size of 744 with a range of 61 to 81612. The age of the subjects ranged from 30 to 65 years. There were two studies focussed on one gender only. The other studies included both genders and most showed male preponderance while one study studied the differences between male and female in terms of risk to develop colorectal cancer.

Table 1. Study design and characteristics of the included studies

<table>
<thead>
<tr>
<th>Authors</th>
<th>Place of study</th>
<th>Study design</th>
<th>No of subjects</th>
<th>Mean age, years</th>
<th>Gender (% male)</th>
<th>Site of cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kune et al, 1991</td>
<td>Melbourne, Australia</td>
<td>Case-control</td>
<td>Case: 637 Control: 714</td>
<td>65 for both</td>
<td>Case: 54%</td>
<td>Colorectal</td>
</tr>
<tr>
<td>Kavan et al, 1995</td>
<td>USA</td>
<td>Case-control</td>
<td>Case: 61 Control: 61</td>
<td></td>
<td>100% male</td>
<td>Colon</td>
</tr>
<tr>
<td>Courtney et al, 1996</td>
<td>USA</td>
<td>Case-control</td>
<td>Case &amp; control: 744</td>
<td>61.4 vs 6.2</td>
<td>56%</td>
<td>Colon</td>
</tr>
<tr>
<td>Nakaya et al, 2003</td>
<td>Japan</td>
<td>Prospective cohort (7 years)</td>
<td>30,277</td>
<td>-</td>
<td>-</td>
<td>Colorectal</td>
</tr>
<tr>
<td>Robb et al, 2004</td>
<td>United Kingdom</td>
<td>Cross-sectional</td>
<td>11,254</td>
<td>55-64 years</td>
<td>46%</td>
<td>Colorectal</td>
</tr>
<tr>
<td>Kroenke et al, 2005</td>
<td>USA</td>
<td>Prospective cohort (8 years)</td>
<td>81,612</td>
<td>30-55 at baseline</td>
<td>All females</td>
<td>Colorectal</td>
</tr>
<tr>
<td>Nielsen et al, 2007</td>
<td>Denmark</td>
<td>Prospective cohort (20 years)</td>
<td>11,914</td>
<td>Male: 56 Female: 57</td>
<td>67% and 23%</td>
<td>Colon Rectal</td>
</tr>
<tr>
<td>Nagano et al, 2008</td>
<td>Japan</td>
<td>Case-control</td>
<td>Case: 497 Control: 809</td>
<td>60 vs. 59</td>
<td>Case: 58%</td>
<td>Colon Rectal</td>
</tr>
</tbody>
</table>


Table 2. Psychosocial risk factors studied in the included studies

<table>
<thead>
<tr>
<th>Authors</th>
<th>Scale used</th>
<th>Risk factors for colorectal cancer studied</th>
<th>Comments/Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kune et al, 1991</td>
<td>22 item psychosocial questionnaire</td>
<td>Personality factors</td>
<td>Negative emotions (denial, anger suppression), conforming to social norms of external appearance of being ‘good’ or ‘nice’, suppression of offensive reactions and conflict avoidance showed statistically significance difference between cases &amp; controls.</td>
</tr>
<tr>
<td>Kavan et al, 1995</td>
<td>Minnesota Multiphasic Personality Inventory</td>
<td>Personality factors</td>
<td>Aggressive hostility was related to subsequent development of colorectal cancer</td>
</tr>
<tr>
<td>Courtney et al, 1996</td>
<td>Job control &amp; demand – Karasek’s model questionnaire Job social support – self report</td>
<td>Stress due to poor job control and job demand</td>
<td>Job stress is associated with risk of colon cancer but not a strong determinant.</td>
</tr>
<tr>
<td>Nakaya et al, 2003</td>
<td>Eysenck Personality Questionnaire</td>
<td>Personality (extraversion, neuroticism, psychoticism, lie)</td>
<td>No significant association between risk of colorectal cancer and personality</td>
</tr>
<tr>
<td>Robb et al, 2004</td>
<td>Perceived risk questionnaire State Trait Anxiety Inventory</td>
<td>Psychosocial factors</td>
<td>Family history of colorectal cancer, poorer subjective health, more symptoms and higher anxiety levels were associated with increased perceived risk of colorectal cancer.</td>
</tr>
<tr>
<td>Kroenke et al, 2005</td>
<td>Mental Health Index (subscale of SF-36)</td>
<td>Depressive symptoms</td>
<td>High levels of depressive symptoms in women were associated with elevated risk of colorectal cancer.</td>
</tr>
<tr>
<td>Nielsen et al, 2007</td>
<td>2 item measure scale on perceived stress</td>
<td>Perceived stress</td>
<td>Stress is associated with lower risk for colon cancer in female. No clear relationship between stress and risk of colorectal cancer in men</td>
</tr>
<tr>
<td>Nagano et al, 2008</td>
<td>Stress Inventory</td>
<td>Personality</td>
<td>Personalities related to emotional suppression and loss-hopelessness were not risk factors. Ambivalent connection and egocentricity were protective factors</td>
</tr>
</tbody>
</table>


Psychosocial risk factors for colorectal cancer

The psychosocial factors studied were personality, stress, anxiety and depression. All of the 8 studies included used different diagnostic tools although several of the studies were measuring similar outcomes (Table 2). In assessing for personality risk factors, four studies used different diagnostic tools. Kune et al, (1991)\textsuperscript{20} used a psychosocial questionnaire while Kavan et al, (1995)\textsuperscript{21}, Nakaya et al, (2003)\textsuperscript{23} and Nagano et al, (2008)\textsuperscript{27} used Minnesota Multiphasic Personality Inventory (MMPI), Eysenck Personality Questionnaire (EPQ) and Stress Inventory respectively. Similarly, Courtney et al, (1996)\textsuperscript{22} and Nielsen et al, (2007)\textsuperscript{26} used different questionnaires to assess for stress and its relationship to colorectal cancer development. In assessing for other psychological risk factors, State-Trait Anxiety Inventory was used to measure anxiety levels in the subjects\textsuperscript{24} while Kroenke et al, (2005)\textsuperscript{25}, used Mental Health Index (a subscale of SF-36) to assess for depressive symptoms in their subjects.

Of the four studies that looked at the relationship between personality factors and subsequent development of colorectal cancer, two of them found positive associations. In a retrospective case-control study conducted in 1991, Kune and colleagues\textsuperscript{20} found that negative emotions such as denial, anger and suppression, the pressure of conforming to social norms of external appearance of being ‘good’ or ‘nice’, suppression of offensive reactions and conflict avoidance showed a higher risk of developing CRC as compared to the control group. In a study involving 61 male veterans\textsuperscript{21}, it was reported that those with aggressive-hostility personality as measured by the MMPI was also had a higher risk of developing colorectal cancer. In contrast, Nakaya et al, (2003)\textsuperscript{23} found no significant association between personality and risk of specific cancers that included colorectal cancer. Interestingly, Nagano et al, in 2008\textsuperscript{27} found that using the Stress Inventory, those with hysterical personalities especially those who scored high on the ambivalence and egocentricity sub-scores were protected from developing colorectal cancer. They did not find a relationship between negative emotions such as emotional suppression and loss-hopelessness as a risk factor for colorectal cancer.

Two studies included were studying the association between stress and subsequent development of colorectal cancer. In the retrospective case-control study\textsuperscript{22}, there was a weak association between job stress and the risk of developing colon cancer. In another study Nielsen et al, (2007)\textsuperscript{26} found that perceived stress is associated with lower risk of colon cancer in female whereas, in their male subjects, the relationship is unclear.

In a large cross-sectional study conducted in the UK, Robb et al, (2004)\textsuperscript{24} found that higher levels of anxiety were associated with increased perceived risk of colorectal cancer in both male and female. Meanwhile, Kroenke et al, (2005)\textsuperscript{25} reported that high levels of depressive symptoms were also associated with higher risk of developing colorectal cancer for women.

Discussion

Despite the high prevalence of colorectal cancer, there were not many studies looking at the psychosocial risk factors for colorectal cancer as compared to the breast cancer studies\textsuperscript{15,16,26-31}. Although there were eight studies included, the studies were published between 1991 and 2008. There was no new study published within the last seven years. In this review, we reported studies with
different design i.e. four case-control, three longitudinal prospective and one cross-sectional study.

In the included studies, four psychosocial factors were identified i.e. personality, stress, anxiety and depression. Half of the studies in this review were looking at the influences of personality as the risk factor for colorectal cancer. However, only two studies\textsuperscript{20, 21} supported the association of personality with increased risk of CRC. The Hostility-Disease Model was proposed that hostile persons have more frequent episodes of anger that may affect their immune and hormonal response to stress\textsuperscript{21}. Hence, that may expose the person to the risk of ill health such as cancer. On the other hand, anger suppression found earlier by Kune et al, (1991)\textsuperscript{20} was also associated with risk of CRC. The other two studies\textsuperscript{23, 27} failed to find a relationship between personality and risk of CRC. This no association is similar to breast cancer studies, where none of the personality factors were associated with increased risk of breast cancer\textsuperscript{12-34}. In addition, a large prospective, population-based study found Type D, extraversion and neuroticism personalities were not associated with the development of cancers at all sites\textsuperscript{35}.

High level of stress, anxiety and depression found in this review were associated with increased risk of CRC. Similar findings are seen in studies of other types of cancers\textsuperscript{36-39} which were conducted in a large prospective longitudinal follow-ups. Therefore, the long period of exposure to major life stress may have increased the risk to develop cancer where breast cancer showed the strongest association. Kroenke et al, (2005)\textsuperscript{25} conducted their study in all females subjects that showed high levels of depressive symptoms had increased the risk of CRC. The fact that the study was done on females only, the depressive symptoms may have been confounded by the gender. The positive association between depression and risk of cancer may be better explained by the role of immune activation and inflammation in the pathophysiology of both depression and tumour growth\textsuperscript{13}. On the other hand, a large European cohort study reported job stress is less likely to be an important risk factor for colorectal, breast, lung, or prostate cancers\textsuperscript{40}. Similarly, some studies did not support the notion that depression increased the risk of cancer\textsuperscript{15, 41}. However, these discrepancies in the findings can be due to many factors such as variation in study design, the effects of confounding factors, duration of exposure and measurement tool that may have influenced the results.

Similar to the epidemiology studies of psychosocial issues in breast cancer\textsuperscript{16}, there are also differences in the findings of the different study of colorectal cancer. The study by Kune et al\textsuperscript{20} reported a positive association between personality and risk of CRC. However, the study was conducted retrospectively which may be subject to recall bias. Many authors agreed that prospective study design is suitable to investigate the risk of psychosocial factors on the development of cancer. However, in this review, three prospective studies\textsuperscript{23, 25, 26} failed to show a conclusive significant association between psychosocial factors and CRC, except for depression. Nakaya et al\textsuperscript{23} reported no association between personality subscales (extraversion, neuroticism, psychoticism and lie) and risk of cancer. The author felt that their study methods had the advantages of prospective design and had controlled the confounding factors.

Perhaps the biopsychosocial model of disease causation can be taken into consideration when one explore the risk
factors for cancer. There is a suggestion that molecular studies should be able to demonstrate the effects of stress on the cells that would involve intracellular pathways affected by cortisol. The suppressive effect of cortisol on the DNA repair and apoptosis genes may be connected to the tumour development.

In conclusion, there is still limited number of studies on psychosocial factors for the development of colorectal cancer, and the findings are still inconclusive. Further research in molecular studies relating stress, anxiety and depression in colorectal cancer perhaps would give a better understanding.

Acknowledgement

We would like to thank our Head of Departments for encouraging us to conduct this review.

References


10. Sanjoaquin MA, Appleby PN, Thorogood M, Mann JI, Key TJ. Nutrition, lifestyle and colorectal cancer incidence: a prospective investigation of 10998 vegetarians and non-vegetarians in the United


**Corresponding Author**
Professor Dr Nor Zuraida Zainal
Department of Psychological Medicine,
Faculty of Medicine, University of Malaya,
Lembah Pantai, 50603 Kuala Lumpur, Malaysia
Tel: +60-79493052
Fax: +60-3-79556477

**Email:** zuraida@ummc.edu.my