

# The value of vitamins after a colorectal cancer diagnosis

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The results of this thesis shed light on the role of supplement use and blood biomarkers of vitamin D and B-vitamins in relation to fatigue and quality of life of colorectal cancer survivors. As stated in this thesis, findings contribute to the body of scientific evidence necessary for the development of clear-cut recommendations and personalized advice regarding the use of supplements and the vitamin status of colorectal cancer survivors. This paragraph will take a broader perspective and elaborate on the value of the findings for areas outside the scientific field, such as clinical practice and society in general.

#### *Growing population of colorectal cancer survivors*

The number of people diagnosed with colorectal cancer continues to rise. Colorectal cancer is the third most commonly diagnosed cancer worldwide, after lung- and breast cancer, and accounted for 10% of the total number of new cancer cases in 2018.<sup>1</sup> In the Netherlands in 2019, 13,000 new cases of colorectal cancer were identified and the 5-year prevalence was 55,000.<sup>2</sup> The growing population of colorectal cancer survivors results in an increasing demand for health care services. In addition, the increase in the population of colorectal cancer survivors has economic consequences due to the increased number of individuals who are (temporarily) removed from the workforce and other social roles such as volunteer work, resulting in a loss of societal- and work-related productivity.<sup>3,4</sup>

Following successful anti-cancer treatment, follow-up care of colorectal cancer survivors comprises the surveillance for recurrences and metastases, and also involves guidance in the management of lasting health problems after cancer, such as fatigue, that may contribute to a decreased quality of life.<sup>5</sup> This guidance, however, currently differs in content and intensity between care providers and may be improved in terms of structure and consonance between health care providers involved in follow-up care of colorectal cancer survivors.<sup>6</sup> The development of effective lifestyle recommendations for colorectal cancer survivors may aid in the prevention and/or reduction of health problems in this population, thereby reducing the demand for continued follow-up care. Moreover, self-management strategies, e.g. lifestyle changes that can be made by colorectal survivors themselves, empower colorectal cancer survivors to take control over their own health, resulting in shared involvement of the patients, their social environment, and the health care providers. Consequently, the pressure on the health care provider may be alleviated. In addition, the sooner colorectal cancer survivors fully recover from the consequences of cancer and its treatment, the sooner they will feel fit enough to return to their jobs, resume personal tasks, and participate in society.

#### *Main findings of this thesis*

Considering the observational nature of the research, the results of this thesis cannot be translated directly into implementable recommendations or strategies for improving quality of life of colorectal cancer survivors. This thesis

showed that supplements were used by 40% of colorectal cancer survivors from diagnosis to 2 years post-treatment. Associations were observed between the use of supplements and increased fatigue, which implies that colorectal cancer survivors may initiate the use of supplements as a consequence of fatigue. It was also observed that higher circulating 25OHD<sub>3</sub> concentrations were longitudinally associated with better quality of life and reduced fatigue from 6 weeks to 2 years post-treatment. In addition, two biomarkers of vitamin B6 status were cross-sectionally associated with better quality of life outcomes at 6 months post-diagnosis. Participants who stopped using B-vitamin supplements after diagnosis reported higher fatigue compared to nonusers of supplements. The evaluation of a food frequency questionnaire to measure dietary intake in this population was moderate to good for most nutrients and food groups in comparison to a 7-day dietary record. Findings contribute to the body of evidence that is needed as a scientific foundation for guidelines and advice for this population. Further, as also observed in previous studies, this thesis showed that fatigue is a common problem among colorectal cancer survivors up to 2 years after treatment. This thesis may therefore direct attention towards the problem of fatigue and contribute to the recognition and acknowledgement of this problem among patients, their social environment, and health care providers. It also gives some important directions for further research regarding the use of supplements and vitamin status, as described in chapter 6. For instance, additional prospective studies are needed to further unravel the potential role of vitamin B6 in relation to the quality of life of colorectal cancer survivors.

### *Supplement use*

This thesis discloses several points of interest that are relevant to current colorectal survivorship follow-up practice. An important observation was the frequent use of supplements by colorectal cancer survivors over time, in particular by survivors experiencing fatigue. These findings could be an impetus for colorectal cancer survivorship care providers to discuss the use of supplements with survivors and/or to refer survivors to specialized health professionals for additional guidance on the subject. Health care professionals involved in the follow-up trajectory of colorectal cancer survivorship are generally surgeons, general practitioners, and nurse practitioners. Referral to dietitians and other specialized professionals may be necessary more often to tailor advice on supplement use and better meet the needs of survivors. Colorectal cancer survivors themselves, being the principal subject of this research, would likely benefit from increased information provision, such as evidence-based knowledge about the use of supplements and its needlessness when consuming a sufficiently varied diet, as well as the potential harmful consequences of high doses. Furthermore, the common use of supplements, despite the recommendation to not use supplements (only in case of deficiencies), reveals low guideline adherence and demonstrates that there may be room for improvement in guideline communication and implementation.

### *Vitamin D*

This thesis could additionally serve as a scientific foundation for potential actions that may need to be taken by health care professionals regarding the frequently low vitamin D status of colorectal cancer survivors. Individuals with vitamin D deficiencies would benefit from knowledge regarding the improvement of vitamin D levels, such as spending time outdoors in order to expose the skin to sunlight. Consequently, potential health problems that result from vitamin D deficiencies, possibly including fatigue and low quality of life, could be prevented or alleviated. Checks of vitamin D status may be necessary more often to evaluate whether vitamin deficiencies are at hand and whether a deficiency is a potentially underlying cause for complaints. The Dutch vitamin D supplementation recommendation, although implemented for the prevention of osteoporosis, might be brought under the attention of older colorectal cancer survivors more. Given the association between low 25OHD<sub>3</sub> concentrations and increased colorectal cancer risk, there may be need for increased attention for vitamin D deficiencies among colorectal cancer survivors, especially among them experiencing fatigue or decreased quality of life. The advice to spend more time outdoors could effectively be integrated with the recommendation to reduce sedentary time by, for instance, encouraging survivors to go for a walk outside. Hence, two important lifestyle messages can be communicated at once, which can favor the motivation of survivors. However, it must be noted that the message on vitamin D and sun exposure can be complex when considering the increased risk of skin cancer, such as melanoma, also related to sunlight exposure.

### *Communication of information*

In chapter 6, the practical implications of this thesis were discussed. Important implications were the need for increased attention and alertness among health care professionals about the use of supplements by colorectal cancer survivors, the need for increased recognition and dialogue about the symptom of fatigue, and awareness on the prevalence and possible consequences of vitamin deficiencies in this population. There are a number of channels for the communication of new insights regarding oncological survivorship care, both concerning the communication of research outcomes to care providers and communication from care providers to the patient. Oncoline is an important platform for guidelines in oncological care, including follow-up care in the Netherlands. Besides clinical practice, Dutch platforms to communicate lifestyle recommendations to cancer survivors are the website [voedingenkankerinfo.nl](http://voedingenkankerinfo.nl) and the online tool the Kanker Nazorg Wijzer.<sup>7,8</sup> The integration of these tools into standard follow-up care may aid in providing a more structured, univocal, and personalized approach towards improving the quality of life of colorectal cancer survivors.

### *Dissemination of results*

This PhD project was funded by Kankeronderzoekfonds Limburg (KOFL).

During the trajectory, the results of this thesis have been presented at several meetings organized by KOFL, including meetings of “Business Vrienden Kankeronderzoekfonds Limburg”, aimed at raising funds for cancer research. The results of chapter 2 have been published on the website and in the newsletter of the Wereld Kanker Onderzoek Fonds (WKOF).<sup>9</sup> The results of chapter 3 have been published on the website and in the newsletter of the World Cancer Research Fund (WCRF) international.<sup>10</sup> These organisations reach both scientists and professionals involved in colorectal cancer survivorship care. Lastly, results were disseminated within the FOCUS consortium, were published in scientific articles, and presented at several conferences and meetings that attract both scientists and professionals working in clinical practice.

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