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The association between life satisfaction, vitality, self-rated health, and risk of cancer

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Abstract

Purpose Only few prospective studies have been conducted on the contribution of quality of life-related factors to the risk of cancer. The aim of this study was to investigate the prospective associations of three quality of life-related factors with the risk of cancer; life satisfaction, vitality, and self-rated health.

Methods In 2009–2011, 7189 participants in the Copenhagen Aging and Midlife Biobank were asked to rate their life satisfaction, their vitality, and their health. The study population was followed until the end of 2015 for registration of cancer in the Danish National Patient Register.

Results During the follow-up period, cancer was diagnosed in 312 individuals. Life satisfaction was not associated with the risk of cancer. Vitality was significantly associated with the risk of cancer, but the association became non-significant after adjustment for age, sex, socioeconomic position, and lifestyle factors. However, when additionally adjusting for life satisfaction, individuals who rated their vitality as low had a hazard ratio of 1.46 (95% confidence interval [CI] 1.04–2.07) for the development of cancer. Individuals who rated their health as poor had a hazard ratio of 1.70 (95% CI 1.27–2.26) for the development of cancer, compared with individuals with good, very good, or excellent self-rated health. The association remained significant after adjustment for basic confounders, life satisfaction, and vitality.

Conclusion A better grasp of the significance of quality of life-related factors for the risk of cancer may be of great importance to population-based cancer prevention that aims to target early risk factors for development of cancer across widespread cancer sites.

Keywords Cancer · Quality of life · Prospective study · Life satisfaction, vitality · Self-rated health

Introduction

Despite extensive knowledge of the intricate relations among psychological, biological, and behavioral characteristics of individuals, the overall evidence for a causal link between psychological factors and the risk of cancer is quite weak, as illustrated across several thorough systematic reviews of this hypothesis including prospective and retrospective studies [1–7]. Only one review of prospective studies has suggested a causal link between psychological distress and the risk of cancer [8], but this review has been substantially criticized for poor methodological quality of the included studies [9].

So far, most of the reviewed prospective studies have focused on psychological factors such as negative life events, depression, fatigue, feelings of helplessness, perceived stress, distress, stress-prone personality, unfavorable coping styles, and depressive mood [1, 2, 8, 10–12]. However,

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in recent years, a few studies have emerged on the prospective association of the risk of cancer with self-rated health (SRH) and quality of life (QOL) [13, 14]. Such quality of life-related factors may be of great importance to population-based cancer prevention, which aims to target early, inclusive, and easily identifiable risk factors for development of cancer, in general, or for specific sites [15].

In one of these studies, a population of 4451 Danish men and women aged 31–33 years were followed for up to 14 years finding that a high QOL was inversely associated with the risk of cancer, irrespective of a number of potential confounding factors such as age, sex, income, lifestyle factors, and a number of health problems. SRH and social relations were not found to be significantly associated with the risk of cancer [13]. In another study, the association between SRH and the risk of cancer was investigated in a population of 12,843 Danish female nurses aged 44 + with a maximum of 12 years' follow-up adjusting for marital status, lifestyle factors, body mass index, and estrogen replacement therapy [14]. The study did not find an increase in the risk of cancer among women with poor SRH, neither regarding overall cancer incidence nor regarding specific cancers such as breast, colorectal, and lung cancers.

This latter finding is in line with two previous prospective studies of SRH and cancer risk comprising smaller study populations and fewer cancer cases [16, 17]. One was a recent American study of 4700 middle-aged men and women (51–61 years) with a maximum of 14 years of follow-up. This study found that SRH was a significant predictor of onset of any chronic condition excluding cancer [16]. The other study was an older study of 783 elderly Dutch men (65–85 years) with a maximum of 5 years' follow-up. This study found that SRH did not independently predict the incidence of cancer or other chronic diseases [17]. Although one large Norwegian study of 25,532 participants found an increased risk of lung cancer among individuals with poor SRH [18], the general impression from prospective studies does not seem to suggest that SRH plays an independent role in overall cancer causation. Regarding the role of QOL as a potential predictor of the risk of cancer, the issue is much less studied. So far, the only available study has found a positive association between QOL (measured by a single-item scale) and the subsequent risk of overall cancer [13]. We have found no other studies on the relation between QOL and the risk of cancer using available multi-item scales of QOL such as the WHO-5 Well-Being Index [19] or The Short Form Health Survey (SF-36) which is a widely used generic measure of HRQOL (Health-Related QOL) [20–22].

The Short Form Health Survey (SF-36) comprises eight subscales that can be divided in a physical and a mental HRQOL component. The SF-36 vitality scale is considered a mental component and has been suggested as the best of the eight SF-36 subscales at discriminating between levels of health [21, 23]. It consists of four items evaluating the vitality domain of HRQOL by questions on energy level and fatigue. The SF-36 vitality scale has previously been associated with several medical conditions, including cardiovascular disease and mortality risk [23, 24] suggesting that somatic aspects of health may also be captured by the SF-36 vitality scale. We have found no previous studies on the relation between vitality and risk of cancer.

Vigor is a closely related concept to vitality referring to individuals' feelings that they possess physical strength, emotional energy, and cognitive liveliness [25]. While vigor has been shown to predict the risk of various health outcomes such as coronary heart disease and inflammatory processes [26, 27], we have found no prospective studies on vigor and the risk of cancer. So far, the number of studies is still too few for an adequate review on the association between various QOL-related factors and the risk of cancer. Thus, the aim of the current study was to prospectively investigate the associations of life satisfaction, vitality, and self-rated health with the risk of cancer in a healthy population of Danish middle-aged men and women.

Methods

Participants

The baseline data were derived from the Copenhagen Aging and Midlife Biobank (CAMB), which was established in 2009–2011 as a follow-up study of three existing cohorts: The Metropolit Cohort [28], the Danish Longitudinal Study on Work, Unemployment and Health [29], and the Copenhagen Perinatal Cohort [30]. A total of 17,937 eligible cohort members living in the eastern parts of Denmark were invited to participate in CAMB. Of these, 7189 individuals (40%) with an age range of 48–62 years completed the postal questionnaire and were included in the present study. A more detailed description of the CAMB can be found in Lund et al. [31].

Exposure measures

Three different predictors of cancer were investigated in the present study: The first measure was the *Satisfaction With Life Scale* (*SWLS*) [32]. It consists of five general statements about the respondents' life satisfaction, e.g., "I am satisfied with my life," with response categories on a 7-point scale ranging from 1 = strongly disagree to 7 = strongly agree, resulting in a total sum-score ranging from 5 to 35. Based on the tertiles of the SWLS scores, a categorical variable with three categories was constructed and used in the main analyses. The following three categories were used: 5–24: Average or below, 25–29: High,

30–35: Very high. The SWLS has shown satisfactory psychometric properties regarding reliability and validity [32, 33].

The second measure was the v*itality scale* of the MOS 36-Item Short Form Health Survey (SF-36) [20]. Vitality is based on four items referring to feelings of energy and fatigue within the last month, e.g., "How much of the time during the past 4 weeks did you have a lot of energy?" with response categories on a 6-point scale ranging from 1 = all the time to 6 = none of the time, resulting in a total sum-score ranging from 4 to 24. Corresponding to previous studies, raw scores from the SF-36 vitality scale were transformed to scores ranging from 0 to 100 with 100 indicating the highest level of vitality [22, 24, 34, 35]. Based on the tertiles of the SF-36 vitality scale scores, a categorical variable with three categories was constructed and used in the main analyses. The following three categories were used: 0–55: Low, 56–75: Medium, 76–100: High. The Danish translation of the SF-36 vitality scale has shown satisfactory psychometric properties with regard to both reliability and validity [21, 36].

The third measure was *self-rated health* (SRH), which was measured with a single question: "In general, would you say your health is? (Excellent; Very good; Good; Fair; Poor)" [36]. In the present study, the following two categories were used: Fair or poor, and Good, Very good, Excellent. The value of SRH as a predictor of mortality and other health outcomes has been documented in numerous studies where SRH has been shown to retain an independent effect even after controlling for a wide variety of health-related measures of medical, physical, cognitive, emotional, and social status [15, 37].

Follow-up

Cancer diagnoses were obtained from the Danish National Patient Register [38], which contains information on all admissions to Danish hospitals since 1977 and diagnoses were classified according to the International Classification of Diseases (ICD) using the 8th revision until 1994 and the 10th revision from 1994 until the final registration in 2015. Except for non-melanoma skin cancers, all cancer forms were included in this study; an overview of the sites of cancers seen in the study in addition to the number of individuals in each site is available in Table 1. We excluded 588 individuals from the study who had been registered with a diagnosis of cancer at baseline resulting in a total study population of $n = 6601$. A total of 312 individuals developed cancer in the follow-up period and the mean age at cancer diagnosis was 55.7 years (SD: 3.9).

Statistical analyses

A range of possible confounding factors were considered in the present study; an overview of these is shown in Table 2 in which characteristics of the study population are illustrated according to vitality divided into three categories of approximately equal size. Risk estimates were calculated using Cox proportional hazard regression models with delayed entry and age as the underlying time axis to ensure maximal adjustment for confounding by age. The study sample was followed from the day on which the questionnaire information was completed in 2009–2011 to the date of first registration of cancer ($n = 312$), death ($n = 93$), emigration ($n = 52$), or the end of follow-up (31-12-2015), whichever occurred first. Information on death and emigration was obtained from the Danish Civil Registration System [39]. Five different statistical models for each of the three exposure measures

Table 1 Sites of cancers seen in the study

Cancer site	ICD-10 code	No. of cases
Lip, oral cavity, and pharynx	C00–C14	16
Digestive organs	C15–C26	69
Respiratory and intrathoracic organs	C30–C39	28
Skin	C43–C44	26
Mesothelium and soft tissue	C46–C49	3
Breast	C50	36
Female genital organs	C51–C58	8
Male genital organs	C60–C63	63
Urinary tract	C64–C68	12
Eye, brain, and other parts of central nervous system	C69–C72	6
Thyroid and other endocrine glands	C73–C75	0
Malignant neoplasms of ill-defined, secondary, and unspecified sites	C76–C80	13
Malignant neoplasms, stated or presumed to be primary, of lymphoid, hematopoietic, and related tissue	C81–C96	32

were analyzed (Tables 3, 4, 5). All Cox regression models were conducted using multiple imputation. Thus, missing data in each model were imputed with estimated values by drawing from a multivariate normal distribution of the missing data given the observed data in a particular statistical model. This process was repeated until 40 complete datasets were created. Second, the Cox regression models were run within each of the imputed datasets and the obtained parameter estimates from all the analyzed datasets were combined for inference. To examine bias from potential inclusion of individuals with cancer that were undetected at the time of exposure, we repeated the analyses with a time lag of 1 year,

Table 2 Characteristics of the study population according to self-reported vitality

Characteristic	Vitality			*p* value[a]
	Low	Medium	High	
N (%)	1947 (30.3)	2430 (37.8)	2059 (32.0)	
Men (%)	69.2	71.1	74.2	< 0.001
Mean age (years)	54.4	54.6	54.6	0.13
Low SEP (%)	23.0	7.8	4.7	< 0.001
Obesity (%)	22.9	15.8	11.6	< 0.001
Current smoker (%)	36.8	23.3	18.9	< 0.001
Alcohol intake > 14/21 drinks per week (%)	21.0	17.5	18.6	0.06
Zero hours of physical activity per week (%)	2.4	1.3	0.9	< 0.001
No partner (%)	19.7	15.0	9.8	< 0.001
No good friend (%)	41.0	34.9	25.8	< 0.001
Poor self-rated health (%)	33.1	3.6	0.8	< 0.001

[a]*p* value for γ tests (binary) and ANOVA test (continuous variable), respectively

Table 3 Hazard ratios for cancer according to life satisfaction

Life satisfaction	Age-adjusted HR (95% CI)	Basis-adjusted HR[a] (95% CI)	Adjusted HR for social relations[b] (95% CI)	Adjusted HR for vitality[c] (95% CI)	Adjusted HR for self-rated health[d] (95% CI)
Very high	1	1	1	1	1
High	1.06 (0.81–1.38)	1.03 (0.79–1.35)	1.04 (0.79–1.35)	0.95 (0.72–1.26)	0.98 (0.74–1.30)
Average or below	1.04 (0.78–1.39)	0.91 (0.67–1.24)	0.92 (0.68–1.27)	0.77 (0.55–1.09)	0.76 (0.54–1.07)

Missing data were handled by means of multiple imputation

[a]Adjustment for sex, socioeconomic position and lifestyle (BMI, smoking, alcohol intake, physical exercise)

[b]As in a, plus social relations: partner status and social relations

[c]As in a, plus SF-36 vitality scale

[d]As in a, plus self-rated health

Table 4 Hazard ratios for cancer according to vitality

Vitality	Age-adjusted HR (95% CI)	Basis-adjusted HR[a] (95% CI)	Adjusted HR for social relations[b] (95% CI)	Adjusted HR for life satisfaction[c] (95% CI)	Adjusted HR for self-rated health[d] (95% CI)
High	1	1	1	1	1
Medium	1.22 (0.92–1.63)	1.19 (0.90–1.58)	1.21 (0.91–1.60)	1.25 (0.93–1.69)	1.17 (0.87–1.58)
Low	1.46 (1.09–1.94)	1.31 (0.96–1.77)	1.33 (0.98–1.81)	1.46 (1.04–2.07)	1.13 (0.78–1.65)

Missing data were handled by means of multiple imputation

[a]Adjustment for sex, socioeconomic position, and lifestyle (BMI, smoking, alcohol intake, physical exercise)

[b]As in a, plus social relations: partner status and social relations

[c]As in a, plus satisfaction with life

[d]As in a, plus self-rated health

Table 5 Hazard ratios for cancer according to self-rated health

Self-rated health	Age-adjusted HR (95% CI)	Basis-adjusted HR[a] (95% CI)	Adjusted HR for social relations[b] (95% CI)	Adjusted HR for life satisfaction[c] (95% CI)	Adjusted HR for vitality[d] (95% CI)
Excellent, very good, good	1	1	1	1	1
Fair or poor	1.70 (1.27–2.26)	1.52 (1.11–2.10)	1.54 (1.12–2.13)	1.66 (1.18–2.32)	1.49 (1.04–2.13)

Missing data were handled by means of multiple imputation

[a]Adjustment for sex, socioeconomic position, and lifestyle (BMI, smoking, alcohol intake, physical exercise)

[b]As in a, plus social relations: partner status and social relations

[c]As in a, plus satisfaction with life

[d]As in a, plus SF-36 vitality scale

Table 6 Correlation matrix showing Spearman correlation coefficients among all exposure variables

	Life satisfaction	Vitality	Self-rated health
Life satisfaction	1		
Vitality	0.48[a]	1	
Self-rated health	0.45[a]	0.58[a]	1

[a] <0.0001

thus eliminating 1 year of follow-up after baseline from the analyses (data not shown). We tested the assumptions of the proportional hazards model, but detected no violations. Spearman correlations between each of the three exposure measures are shown in Table 6. All statistical analyses were conducted by means of the statistical software package SAS 9.4.

Results

Of the 6601 individuals included in the study, 1880 were women and 4721 were men. Descriptive results for vitality showed that individuals who reported their vitality as low were more likely to be women, have a low SEP, be obese, smoke, have a low level of physical activity, have no partner, have no good friend, and have a poor self-rated health (Table 2).

Life satisfaction was not significantly associated with the risk of cancer in any of the statistical models (Table 3). Vitality was inversely associated with the risk of cancer in the age-adjusted model (Table 4): When compared with individuals with high vitality, those with low vitality had a hazard ratio of 1.46 (95% confidence interval (CI) 1.09–1.94) for developing cancer, but the association became non-significant after adjustment for basic confounders. Nevertheless, further adjustment for life satisfaction made the association statistically significant again (the coefficients for life satisfaction were: "Very high": 1, "High": 0.94 (0.71–1.24), "Average or below": 0.76 (0.54–1.08) (data not shown)).

SRH was also inversely associated with the risk of cancer in the age-adjusted model (Table 5): When compared with individuals who rated their health as good, very good, or excellent, those who rated their health as fair or poor had a hazard ratio of 1.70 (95% CI 1.27–2.26) for cancer. The association remained significant after adjustment for basic confounders, life satisfaction, and vitality (the coefficients for life satisfaction were: "Very high": 1, "High": 0.98 (0.74–1.29), "Average or below": 0.76 (0.54–1.07) (data not shown)).

Inserting a time lag of 1 year to examine reverse causation did not change the interpretation of the investigated associations considerably. Thus, only the previously statistically significant associations between SRH and the risk of cancer in the age-adjusted model and in the model adjusted for life satisfaction became insignificant (data not shown). The correlation matrix (Table 6) showed that the three exposure measures—life satisfaction, vitality, and SRH—were moderately correlated with correlation coefficients between 0.45 and 0.58.

Discussion

Vitality and SRH of 6601 individuals followed for up to 6 years were inversely associated with the risk of cancer. These associations were significant in age-adjusted models and in models adjusted for basic confounders and life satisfaction. Life satisfaction was not associated with the risk of cancer in any of the statistical models.

The findings of the study suggest that there is an inverse association between vitality and the risk of cancer in the sense that decreasing vitality is associated with increases in the risk of cancer. However, the association is only significant when comparing individuals who rated their vitality as low and high, respectively. Thus, the study adds nuance to the sparse literature on the role of quality of life (QOL) as a

potential predictor of the risk of cancer. While the only other available study has found a positive association between QOL and the risk of cancer measured by a single-item QOL-scale [13], this study suggests that it is only one of the multi-item QOL-scales investigated—the vitality scale and not the Satisfaction With Life Scale (SWLS)—that may indicate a potential risk of cancer. While the SWLS is a purely psychological scale (satisfaction with life as a whole), the vitality scale also integrates somatic components (feelings of energy and fatigue).

Regarding self-rated health (SRH), the findings of our study suggest that there is an inverse association between SRH and the risk of cancer in the sense that individuals who rated their health as poor had a significantly higher risk of cancer than individuals who rated their health as good, very good, or excellent.

It is noteworthy that our results regarding the inverse association between SRH and the risk of cancer differ from the results of previous prospective studies, which have found no evidence indicating that SRH plays an independent role in overall cancer causation [13, 14, 16–18]. Compared with some of these studies [13, 16, 17], the present study comprises a larger study population and thus more statistical power. A Norwegian cohort study included 25,532 participants and 10 years of follow-up, but no data were reported on marital status, which is associated with QOL and is an important predictor of the development of cancer [18]. A Danish cohort study included 12,843 nurses aged 44 + and 12 years of follow-up, but data were only available for women [14].

In our study, the associations of vitality and SRH with the risk of cancer both became stronger when adjusting for life satisfaction. This finding could suggest that it is the variance in SRH and vitality, which is independent of life satisfaction that is associated with risk of cancer. If it is hypothesized that life satisfaction captures the psychological component of SRH and vitality this may suggest that it is the somatic components of SRH and vitality that is associated with risk of cancer.

The inverse association between vitality and SRH and the risk of cancer might be explained by several plausible mechanisms [37]. Direct physiological pathways could be involved and biological susceptibility could influence both personality (and therefore a tendency to experience vitality and SRH as positive or negative) and the risk of cancer. Vitality and SRH may be adequate as sensitive, early, inclusive, and easily identifiable predictors of cancer, because they reflect a broad range of experiences and factors [15, 40]. However, this also makes it more difficult to exclude the possibility of residual confounding.

The main advantage of the present study is the prospective design in combination with three different self-reported psychological exposure measures at baseline and access to nationwide population-based registers of cancer morbidity. The prospective design minimized recall bias, and the 6-year follow-up made it possible to investigate psychological risk factors for cancer in midlife over a relatively narrow time span without using repeated measurements. Finally, we had access to data on a range of possible confounding factors, which made it possible to adjust for these factors in the analyses. One limitation is the relatively low participation rate in CAMB (40%) and the relatively low number of cancer cases, which was the reason the study did not have sufficient power for analyses of cancers at specific sites. Thus, it would have been preferable to conduct separate analyses for each cancer site to investigate potential differences for each of the exposure measures.

Although all residents in Denmark have equal access to hospitals and all treatment is free of charge, we cannot exclude the possibility that participants with early symptoms of undiagnosed cancer at baseline had lower vitality or SRH, and that the results reflect reverse causation. Given the complex etiology of cancer and often long latency period, it is imaginable that an early-stage cancer was present but not detected at baseline and developed further over the follow-up period [41, 42]. In Denmark, there are effective national cancer-screening programs for cervical cancer, breast cancer, and colorectal cancer [43–45]. The cervical cancer-screening program has been implemented since the 1960s. It is targeted at women (23–64 years) and runs every third year (every fifth year for women 50–64 years). The screening program for breast cancer is from 2009. It is targeted at women (50–69 years) and runs every second year. The program for colorectal cancer is from 2014 (it was not implemented at the time of this study's baseline). It is targeted at men and women (50–74 years) and runs every second year. Although our study was implemented in a prospective way, we cannot be certain that the results go in one direction only, from exposure to risk of cancer. However, inserting a time lag of 1 year did not change the interpretation of the results considerably. This may indicate that reverse causation was not a considerable problem in this study.

In this study, five different statistical models were analyzed to account for different confounding factors. However, as in all observational studies, there may have been unrecognized confounding factors such as poor diet, less health motivation and optimism [46, 47], or less attention to recommendations for prevention and screening [15, 48], that were not included in the analyses as the appropriate data were not available.

In conclusion, we found that vitality and SRH were inversely associated with the risk of cancer when adjusted for life satisfaction in a healthy population of middle-aged men and women in Denmark. So far, relatively few prospective studies have investigated the associations of SRH and various multi-item conceptualizations of QOL with

the risk of cancer. A better grasp of the significance of such factors for the risk of cancer may be of great importance to population-based cancer prevention, which aims to target early risk factors for the development of cancer across the domain of widespread cancer sites.

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Compliance with ethical standards

Conflict of interest The article has not been submitted elsewhere or published previously and the authors have no relationships that might lead to conflicts of interest. All authors have read the final version of the manuscript; they meet the requirements for authorship and believe that the manuscript represents honest work.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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