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A prospective association between quality of life and risk for cancer

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ABSTRACT

Aim: The contributions of social and especially of psychological factors to cancer development have been questioned. The goal of this study was to investigate, in a longitudinal setting, the prospective associations between self-reported measures of social relations, subjective health (physical and mental) and quality of life and the risk for cancer.

Methods: In 1993, 4493 people in the Copenhagen Perinatal Cohort were asked to rate their social relations, their physical and mental health and their quality of life. The study population was followed until the end of 2006 for registration of cancer in the Danish Hospital Discharge Register.

Results: During the follow-up period, cancer was diagnosed in 102 people. When compared with people with very good quality of life, those who rated their quality of life as poor had a hazard ratio of 1.90 (95% confidence interval [CI], 1.1–3.4) for cancer, and those who rated their quality of life as good had a hazard ratio of 1.31 (95% CI, 0.8–2.2), after adjustment for age, sex, income, lifestyle factors and number of health problems. Self-rated physical and mental health were significantly associated with the risk for cancer, but the estimates became non-significant after adjustment for confounding factors. Social relations were not associated with the risk for cancer.

Conclusion: Broad assessment of general well-being, self-rated as global quality of life, appears to be a better predictor of cancer risk than more specific information on social relations and health.

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1. Introduction

The question of whether social and psychological factors contribute to cancer has attracted attention for centuries.¹ Although genetic, environmental, lifestyle and socioeco-

nomic factors have been identified as potentially increasing the risk for cancer,² the contributions of social and especially of psychological factors have been questioned.

Reviews indicate that there is weak evidence for a relation between social support or personality factors and breast

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cancer³ and inconsistent evidence for the role of psychological factors in cancer.^{4,5} A recent review only of prospective studies suggested, however, that psychological distress, including depression, anxiety and poor quality of life, leads to a considerable increase in both the incidence of and mortality from cancer.⁶ Substantial criticism has been made of this review,⁷ because of the poor quality of the studies that were included as well as a number of methodological and statistical issues.

Methodological criticisms have also been made of previous studies of the influence of social and psychological factors on cancer. First, most of the studies were cross-sectional, retrospective or quasi-prospective and therefore cannot show causation, i.e. whether the factors contributed to the development of cancer or were the results of cancer. Secondly, the type of comparison group used has been criticised, especially in the quasi-prospective studies, in which the controls were known to be at risk, such as women who had undergone biopsy: the appropriateness of using women with benign breast disease as controls in a study of breast cancer is questionable, as benign breast disease may be a risk factor for breast malignancies. Thirdly, the follow-up period in most of the prospective studies was between 2 and 5 years,³ while the time between initiation and detection has been estimated to be up to 18 years for breast cancer and up to 22.5 years for lung cancer.⁸ Consequently, the observed relations between social and psychological factors and cancer might reflect associations with continued tumour growth rather than with initial tumour development. Other serious methodological issues are insufficient sample size, insufficient statistical power and insufficient adjustment for potentially confounding factors.

In this large prospective study of 4493 people without cancer, we addressed most of these methodological issues and evaluated social relations, self-rated physical health, self-rated mental health and quality of life as risk factors for cancer, focusing especially on quality of life, which has rarely been investigated as a potential risk factor for cancer. Baseline data were obtained by questionnaire when the members of the study cohort were 31–33 years old, and their risk for admission to a hospital with cancer was followed for up to 14 years.

2. Materials and methods

2.1. Participants

The baseline data were derived from a population study conducted in 1993, in which 7222 people were sent a questionnaire for self-evaluation of quality of life⁹ and health, social and life-style factors. That study was a follow-up of the Copenhagen Perinatal Cohort, which originally comprised 8400 children born between 1959 and 1961 at the National University Hospital in Copenhagen and who survived their first year.¹⁰ The questionnaire was returned by 4493 people (response rate, 62.2%), who were tracked in several national registers. All the respondents were aged 31–33 years.

2.2. Follow-up

We obtained cancer diagnoses from the Danish Hospital Discharge Register,¹¹ which contains information on all admissions to Danish hospitals since 1976. Diagnoses were classified according to the International Classification of Diseases (ICD), in the 8th revision until 1994 and the 10th revision from 1994 onwards. The cancer diagnoses in this study were those covered by ICD-8 codes 140–239 and ICD-10 codes C00–C97, with the exclusion of non-melanoma skin cancers (Table 1). We excluded 37 people from the statistical analysis who had been registered with a diagnosis of cancer at baseline. The study sample was followed from the day on which the questionnaire was filled in 1993 to the date of first registration of cancer ($n = 102$), death ($n = 91$), emigration ($n = 64$) or the end of follow-up (31 December 2006), whichever occurred first. Date of death was obtained from the Danish Causes of Death Register.¹²

2.3. Statistical analyses

We calculated risk estimates using Cox proportional hazard regression models, with delayed entry. To ensure maximal adjustment for confounding by age, we used age as the time axis. We adjusted the risk estimates for the potential

Table 1 – Sites of cancers seen in the study.

Cancer site	ICD-10 code	No. of cases
Lip, oral cavity and pharynx	C00–C14	2
Digestive organs	C15–C26	9
Respiratory and intrathoracic organs	C30–C39	7
Skin	C43–C44	12
Mesothelium and soft tissue	C46–C49	1
Breast	C50	24
Female genital organs	C51–C58	21
Male genital organs	C60–C63	8
Urinary tract	C64–C68	4
Eye, brain and other parts of central nervous system	C69–C72	4
Thyroid and other endocrine glands	C73–C75	1
Malignant neoplasms of ill-defined, secondary and unspecified sites	C76–C80	1
Malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic and related tissue	C81–C96	8

Table 2 – Characteristics of the study population according to self-reported quality of life.

Characteristic	Quality of life		
	Very good	Good	Neither good nor bad, bad, very bad
N (%)	1177 (26.6)	2250 (50.8)	1003 (22.6)
Men (%)	43.3	46.8	47.6
Mean age (years)	32.3	32.3	32.4
Income < 100,000 DKr (13,400 euros) per year (%)	10.1	10.0	20.4
Current smoker (%)	49.7	50.7	60.8
Alcohol intake >21 drinks per week (%)	3.3	4.2	9.8
Zero hours of physical activity per week (%)	19.8	19.9	26.2
Number of health problems (average) ^a	1.0	1.1	1.4
No partner (%)	8.7	17.3	34.1
No good friend (%)	18.8	29.6	45.7

^a Reduced hearing, reduced vision, back problems, diabetes, nervous or psychiatric diseases, epilepsy, paralysis anywhere in the body, high blood pressure, cardiac embolism, cerebral haemorrhage or embolism, chronic bronchitis, asthma, allergy, hay fever, eczema, psoriasis, lupus, ulcer, gallstone, kidney stone, HIV infection, AIDS, cancer, hereditary illness, amputation of arm or leg, venereal disease, anorexia nervosa or bulimia, menstruation problems, abdominal disease, conic section, and removal of uterus.

confounding factors sex, yearly income, smoking, alcohol intake, physical activity and number of health problems at the time of investigation (Table 2). The potential confounding factors were used together in joint analyses referred to as ‘basis adjustment’ (Tables 3–5).

To examine bias from inclusion of cases of cancer that were undetected at the time exposure was measured, we repeated the analyses with a time lag of 3 years, thus eliminating 3 years 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 correlation coefficients were calculated for all predictor variables (Table 6). All statistical analyses were conducted by means of the statistical software package SAS 9.1.

3. Results

Of the 4451 people eligible for the study, 2369 were women and 2082 were men. Stratification of descriptive results according to quality of life showed that those who reported poor quality of life were more likely to be men, to have a lower income, to be smokers, to have a high alcohol intake, to have a low level of physical activity, to have more health problems, to be single, and to be without a good friend than people reporting very good quality of life (Table 2).

Social relations, measured as not having a friend to talk to about everything or not having a partner, were not significantly associated with risk for cancer (Table 3). Self-rated physical health was inversely associated with risk for cancer (Table 4), the age-adjusted hazard ratio for cancer associated with bad or very bad physical health being 2.7 (95% confidence interval [CI], 1.3–5.3) when compared with having very good physical health; however, adjustment for confounding factors made the association non-significant. Elimination of the effect of existing health problems at baseline, by excluding this variable from the ‘basis adjustment’, did not have a noteworthy effect on the estimates (data not shown). Self-rated mental health was also significantly associated with the risk for cancer, but the estimate also became non-significant after adjustment for confounding factors (Table 4).

Quality of life was inversely associated with the risk for cancer (Table 5). The age-adjusted hazard ratio of people who rated their quality of life as neither good nor bad nor very bad was 2.1 (95% CI, 1.2–3.7) when compared with people who rated their quality of life as very good; and the age-adjusted hazard ratio of people who rated their quality of life as only good was 1.35 (95% CI, 0.8–2.3). There was therefore a dose-response relation between decreasing quality of life and increasing risk for cancer, although people in the middle category of quality of life had a non-significantly higher risk.

Table 3 – Hazard ratios for cancer according to social relations.

Social relation	No. of cases	Age-adjusted HR (95% CI)	Basis-adjusted ^a HR (95% CI)	Adjusted HR for self-rated health ^b (95% CI)	Adjusted HR for quality of life ^c (95% CI)
Friend you can talk to about everything					
Yes	3060 (65)	1	1	1	1
Not sure or no	1332 (33)	1.17 (0.77–1.77)	1.25 (0.81–1.94)	1.13 (0.71–1.78)	1.14 (0.73–1.78)
Partner					
Yes	3601 (82)	1	1	1	1
Not sure or no	839 (20)	1.05 (0.65–1.71)	0.98 (0.58–1.66)	0.97 (0.57–1.68)	0.88 (0.52–1.50)

^a Adjustment for sex, income, lifestyle (smoking, alcohol intake, physical exercise) and number of health problems.

^b As in a, plus self-rated physical and mental health.

^c As in a, plus self-rated quality of life.

Table 4 – Hazard ratio for cancer according to self-evaluated health.

Self-evaluated health	No. of cases	Age-adjusted HR (95% CI)	Basis-adjusted HR ^a (95% CI)	Adjusted HR for health ^b (95% CI)	Adjusted HR for quality of life ^c (95% CI)	Adjusted HR for social relations ^d (95% CI)
Physical						
Very good	1536 (25)	1	1	1	1	1
Good	1954 (52)	1.65 (1.02–2.65)	1.61 (1.00–2.62)	1.25 (0.73–2.15)	1.50 (0.92–2.45)	1.58 (0.97–2.59)
Neither good nor bad	682 (14)	1.28 (0.67–2.47)	1.25 (0.64–2.46)	1.04 (0.50–2.15)	1.04 (0.52–2.09)	1.27 (0.64–2.50)
Bad or very bad	252 (11)	2.72 (1.34–5.53)	1.68 (0.70–4.07)	1.42 (0.56–3.58)	1.36 (0.55–3.37)	1.67 (0.68–4.08)
Mental						
Very good	1623 (25)	1	1	1	1	1
Good	1652 (44)	1.74 (1.07–2.84)	1.60 (0.98–2.63)	1.47 (0.85–2.53)	1.42 (0.84–2.41)	1.67 (1.00–2.80)
Neither good nor bad, bad, very bad	1032 (28)	1.79 (1.04–3.06)	1.61 (0.92–2.81)	1.50 (0.81–2.78)	1.10 (0.56–2.17)	1.70 (0.94–3.07)

^a Adjustment for sex, income; lifestyle (smoking, alcohol intake, physical exercise) and number of health problems.^b As in a, plus self-rated mental and physical health.^c As in a, plus self-rated quality of life.^d As in a, plus social relations; partner status and social relations.

Except for self-rated health, none of the potential confounding factors changed the risk significantly, and all the estimates remained significant after adjustment.

Inserting a time lag of 3 years to minimise reverse causation did not notably change the estimates for any of the predicting factors (in fact, all the estimates increased) (data not shown). The inter-correlation matrix (Table 6) shows that several predictors were interrelated. High correlations were observed among self-rated physical health, self-rated mental health and quality of life, the correlation between mental health and quality of life being particularly high, with a coefficient of 0.56. The correlations with social relations were generally low.

4. Discussion

The quality of life of 4451 people followed up for cancer for up to 14 years, was inversely associated with risk for cancer, irrespective of a number of potential confounding factors. Good self-reported physical and mental health were also inversely associated with risk, although risks became non-significant after adjustment for confounding factors. Social relations were not significantly associated with risk for cancer.

Associations between cancer and psychological factors have been observed in quasi-prospective studies, which showed that type A behaviour¹³ and major life events¹⁴ were associated with increased risks, while a retrospective study concluded that a repressive coping style was associated with cancer.¹⁵ In prospective studies, however, no associations have been found between psychological factors and risk for cancer. One study showed no association between psychological distress (assessed from self-rated happiness, depressive symptoms, anxiety symptoms and sleep disturbances) and risk for cancer among people with no cancer history.¹⁶ Other prospective studies showed no association with symptoms of fatigue¹⁷ and depression,^{17,18} and a large study of women gave no evidence of an association between the incidence of breast cancer and personality traits such as anxiety, depression, optimism and the expression of emotions.¹⁹ In Danish prospective studies, the effects of the personality traits of neuroticism,^{20,21} extraversion,^{20,21} physis vulnerability²¹ and depression²² on cancer incidence were investigated, with no significant associations. Except for one study,⁵ which has been heavily criticised,⁷ reviews of studies on psychological factors and risk for cancer have concluded that there is no convincing evidence of an association.^{3,4,22} Generally, therefore, prospective studies have not demonstrated significant associations between psychological factors and risk for cancer. None of the previous studies, however, investigated self-rated quality of life as a predictor.

Few prospective studies have addressed associations between social relations and risk for cancer. A Danish study showed that people who lived alone had a higher incidence of cancer than people living with a partner,²² and another found no such association for men but showed that women with weak social relationships had a higher risk for dying from cancer.²³ Other prospective studies showed no association between measures of social networks and cancer risk,^{24–26}

Table 5 – Hazard ratios for cancer according to quality of life.

Quality of life	No. of cases	Age-adjusted HR (95% CI)	Basis-adjusted HR ^a (95% CI)	Adjusted HR for self-rated health ^b (95% CI)	Adjusted HR for social relations ^c (95% CI)
Very good	1177 (19)	1	1	1	1
Good	2250 (49)	1.35 (0.80–2.29)	1.31 (0.77–2.23)	1.18 (0.66–2.12)	1.21 (0.70–2.07)
Neither good nor bad, bad, very bad	1003 (34)	2.12 (1.21–3.72)	1.90 (1.06–3.40)	1.98 (0.98–4.03)	1.86 (1.01–3.40)

^a Adjustment for sex, income; lifestyle (smoking, alcohol intake, physical exercise) and number of health problems.

^b As in a, plus self-rated physical and mental health.

^c As in a, plus social relations: partner status and social relations.

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

	Friend	Partner	Self-rated physical health	Self-rated mental health	Quality of life
Friend	1				
Partner	0.03	1			
Self-rated physical health	0.11 ^a	0.08 ^a	1		
Self-rated mental health	0.20 ^a	0.18 ^a	0.49 ^a	1	
Quality of life	0.21 ^a	0.22 ^a	0.34 ^a	0.56 ^a	1

^a <0.0001.

while some found associations only for specific populations.^{27,28} The general picture of social networks and risk for cancer is therefore unclear, perhaps because different measures of social relations were used.

The main advantages of the study reported here include the prospective design and the combination of self-reported social and psychological factors and access to nationwide population-based registers of cancer morbidity from 1976. The prospective register-based design minimised selection and recall bias, and the 14-year follow-up made it possible to investigate risk factors for cancer over a relatively long time. One limitation of our study is that the exposure variables were measured only once, in 1993. Further limitations are the relatively low participation rate (62%) and the small number of cancer cases; this reflects the fact that the most important risk factor for cancer is age, and none of the participants had reached the age of 50 by the end of follow-up. As there were relatively few cases, the study did not have sufficient power for analyses of cancers at specific sites. As 'cancer' comprises many different diseases (Table 1), separate analyses should be conducted for each, with predictors that have been shown to play a role in the aetiology of cancer at each site. We should be able to do this in the future, as follow-up studies will be conducted on the ageing study population.

In Denmark, all residents have equal access to hospitals, and all treatment is free of charge. We cannot exclude the possibility, however, that participants with early symptoms of undiagnosed cancer at baseline had poorer self-rated physical and mental health or quality of life, and this would explain the inverse associations found. Nevertheless, the association with all predicting factors persisted (and even became stronger) when we used a time lag of 3 years to control for potential reverse causation. As in all observational studies, there may have been unrecognised confounding. Un-

healthy habits such as smoking, heavy alcohol intake and lack of physical activity were commonest among people reporting poor quality of life; although adjustment for these confounding factors did not change the estimates notably (data not shown), other, unobserved confounding factors may have played a role. Factors that would diminish quality of life and increase the risk for cancer are poor diet, poor sleep and less health motivation. These factors were not included in the analyses as the appropriate data were not available.

The inverse association between quality of life and cancer might be explained by several plausible mechanisms. Direct physiological pathways could be involved, or common biological susceptibility could influence both personality (and thereby a tendency to experience quality of life as positive or negative) and the risk for cancer. Furthermore, psychosocial factors such as quality of life might be associated with an unhealthy lifestyle, and an unhealthy lifestyle might have a negative influence on quality of life.

A measure of the global quality of life appears to be a better predictor of cancer than more specific evaluations of social relations, physical health and mental health, perhaps because global evaluations reflect a broad range of experiences and factors. The fact that global evaluations are affected by a diverse range of life circumstances, however, also makes it more difficult to exclude the possibility of residual confounding.

The correlation matrix (Table 6) shows that quality of life, physical health and mental health are interrelated, the correlation between self-rated mental health and quality of life being as high as 0.56. The associations with cancer might reflect either overlapping variance between self-rated health and quality of life or different mechanisms. In the Cox regression analyses, the significant association between mental health and cancer disappeared after adjustment for quality of life, while the significant association between quality of life

and cancer persisted, irrespective of adjustment for self-rated physical and mental health. This suggests that quality of life is a more robust predictor of cancer than self-rated physical and mental health.

5. Conclusion

In this relatively strongly designed study, the risk for cancer of people who rated their quality of life as poor was almost double that of people with the most positive rating. We cannot exclude the possibility that residual confounding explains this association, and it should be further investigated. Social relations were not associated with the risk for cancer, and the associations between self-rated physical and mental health and cancer became non-significant after adjustment for confounding factors. Consequently, our results suggest that people's overall evaluation of their quality of life is a stronger predictor of cancer risk than more specific measures of social relations and health. Studies of high methodological quality should, however, be conducted to evaluate this conclusion and to derive evidence of an association between quality of life and cancer risk in other study populations.

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Conflict of interest statement

None declared.

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