Impact of cancer occurrence on health-related quality of life: A longitudinal pre-post assessment.

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Research

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Abstract

Background: Investigations focusing and implementing on the impact of cancer on health-related quality of life (HRQoL) by the way of a mean comparison between cancer patients and subjects from the general population, are scarce and usually cross-sectional. Longitudinal application of HRQoL instruments to a general, initially healthy population allows for change to be assessed as an event occurs, rather than afterwards. The objective of the present study was to investigate the impact of new cancer on HRQoL.

Methods: The 36-item Short Form (SF-36) and 12-item General Health Questionnaire (GHQ-12) were applied to the French SU.VI.MAX cohort in 1996 and 1998. A controlled longitudinal study was used to determine the impact on HRQoL of newly diagnosed cancer: 84 patients with cancer that occurred between the 2 HRQoL measures were compared with 420 age- and sex-matched cancer-free controls.

Results: Initial HRQoL level was similar in the two groups. A new cancer had a particularly marked effect on the SF-36 Physical functioning, Role-physical and General health dimensions (more than 6.6-point difference in change in HRQoL evolution on a 0–100 scale). The Bodily pain and Vitality dimensions were less severely affected (difference in change varying from 4.4 to 6.3 points), and there was no effect on either the GHQ-12 score or the SF-36 Mental health, Role-emotional and Social functioning dimensions.

Conclusions: The negative impact of cancer on the lives of patients was assessed in terms of HRQoL. The aspects most likely to be affected were those with a physical component, and general health perceptions. These results can thus help quantify the impact of a new cancer on HRQoL evolution and potentially facilitate early intervention by identifying the most affected HRQoL domains.

Background

Technological advances in cancer therapy led to improve objective outcomes such as survival, objective response to treatment, and toxicity. As cancer care management increased its effectiveness, opportunities and need for using patient's health-related quality of life (HRQoL) became more apparent. In other words, physicians now have an opportunity to add life to years, as well as adding years to life.

Although no formal definition of HRQoL has yet been generally accepted, there is broad agreement that it is a subjective, multidimensional construct comprising three major aspects of functioning: physical, psychological and social. However, this is not a complete picture, as a broad range of aspects may be included such as cognitive functioning [1,2].

Despite the difficulties of going from concept to quantification of patient perceptions, the number of instruments available to measure HRQoL psychometrically has increased rapidly. Assessments can now be made in a variety of distinctive ways using both specific and generic measures. Generic scales include items that cover all major aspects of a person's health and are applicable whatever the person's conditions. Specific scales include only those items likely to be affected by the disease concerned or its treatment, and have been developed for particular disease categories, principally cancer (ranging from cancer overall to specific treatments/phases). Most HRQoL instruments were designed for self-administration and are relatively short. There is no gold-standard questionnaire, and the choice is based on psychometric properties, research objectives and study design [1,3-5].

HRQoL is increasingly used as an outcome measure in oncology research studies [6,7], appearing in a variety of forms in numerous different publications. For example, HRQoL measures may provide descriptive information about patients with cancer and allow to explore the relationships between HRQoL and socio-demographic factors (i.e. sex, age, social situation, and education level) [8,9]. Other investigations focus on differences in HRQoL between groups of cancer patients classified by various characteristics such as disease stage [10-13], prognosis [14] and treatment [15-23]. However, most studies look at the influence of treatment on HRQoL, either to determine the impact of a particular intervention or to explore which of several has a better effect. The efficacy of new therapeutic interventions is now evaluated in terms of their impact on both quantity and quality of life, with the aim of extending survival and improving HRQoL. HRQoL scores can also be used to predict survival, as the better they are, the longer the patient is likely to live [24-28]. All

such studies to date have been conducted in populations with established cancer diagnoses.

Investigations comparing HRQoL in cancer patients and subjects from the general population are scarce. They are usually cross-sectional, assessing HRQoL at different times during the course of cancer, and the data collected are generally limited to clinical information (cancer diagnosis, stage, treatment, and prognosis) and demographics (age, sex). HRQoL comparisons with the general (reference) population are invariably less precise and less powerful as many factors with an influence on HRQoL cannot be taken into account, such as family history, personal history (disease), alcohol consumption, tobacco habits, eating habits, life habits, and social situation. Some studies have looked at how HRQoL changes over time, but only in cancer patients with established diagnosis. For example, Ozyilkan et al. [29] and Funk et al. [30] compared one group before and after treatment with a reference population. Other studies have estimated reference population HRQoL scores cross-sectionally [31-33]. None of them considered either how HRQoL varies over the period including the diagnosis of cancer, or how it changes in reference populations. Longitudinal application of HRQoL instruments to a general, initially healthy population would allow for change to be assessed as an event occurs, rather than afterwards. SU.VI.MAX [34,35] longitudinally followed up subjects from a general presumably healthy population, creating an opportunity to track cancer.

The objective of the present study was to investigate the impact of new cancer on HRQoL, using a controlled longitudinal protocol. It is hypothesised that HRQoL was negatively affected by cancer, particularly when the diagnosis is recent.

Methods

SU.VI.MAX study

The data analysed here were drawn from SU.VI.MAX (SUpplementation en VItamines et Minéraux AntioXidants). SU.VI.MAX was a randomised, double-blind, placebo-controlled, primary-prevention trial designed to test the efficacy of daily supplementation with antioxidant vitamins (vitamin C, 120 mg; vitamin E, 30 mg and beta-carotene, 6 mg) and minerals (selenium, 100 µg and zinc, 20 µg) at nutrition-level doses in reducing the mortality, the incidence of cancers (all sites) and ischemic heart diseases in a French general adult population. A total of 13017 eligible subjects (women aged 35 to 60 years and men aged 45 to 60 years) were enrolled in 1994 and were followed for up to 8 years with yearly visits (alternately for laboratory assessment and clinical examination) and morbidity determination using the Minitel Telematic

Network, a small terminal used in France as an adjunct to the telephone.

Data on baseline characteristics of the SU.VI.MAX participants suggested that the selected subjects were close to the national population in terms of geographic density, socioeconomic status, and the distribution of various major risk factors for the diseases under study. The main causes of exclusion were regular use of supplements or refusal of placebo [35]. Subjects included were up to 60 years. The upper cut-off of 60 years was chosen because beyond that age it may be too late to produce an effect with the SU.VI.MAX intervention. The age range was chosen to ensure enough cases of cardiovascular diseases and cancers to achieve adequate statistical power in the SU.VI.MAX study.

HRQoL was a secondary end-point of SU.VI.MAX, with assessment every two years starting in 1996 (questionnaires were sent out by post and returned at the next yearly visit). The complete design of the SU.VI.MAX study is as previously reported [34,35].

HRQoL assessment

Quality of life was assessed using generic questionnaires: the Medical Outcome Study 36-item short form health survey (SF-36) [36] and the 12-item General Health Questionnaire (GHQ-12) [37].

The French-language version of the SF-36 is a validated instrument [38,39] containing 36 items divided into eight dimensions of health using multi-item scales: Physical functioning (10 items), role limitations due to physical functioning (Role-physical) (4 items), Social functioning (2 items), Bodily pain (2 items), Mental health (5 items), role limitations due to emotional functioning (Role-emotional) (3 items), Vitality (4 items) and General Health perceptions (5 items). The eight scales were scored from 0 to 100 (worst to best possible health status). For each dimension, the score represented the mean of item values obtained by the subject when all the items were completed or when the number of missing values was no more than half of the total items. Otherwise, the score was recorded as missing. The frequency of scores for which fewer than half of a scales items were missing ranged from 0.6% (Role-emotional) to 4.7% (Physical functioning).

The French-language version of the GHQ-12 is widely administered to screen for common mental disorders [40-42]. The questionnaire consists of 12 items with four modalities and measures a global psychological dimension. Like the SF-36, the dimension score ranged from 0 to 100. The score was computed as the mean of the item values obtained by the subject when the 12 items were completed or when 6 or more items were present. Otherwise

the score was declared missing; 3.5% of scores missed fewer than half the item values.

These questionnaires were chosen by the SU.VI.MAX investigators for their ability to detect change in HRQoL when a disease occurs, particularly cancer (sensitivity to change), and because they have sufficient validity [43]. Internal consistency ranged from 0.80 to 0.92 according to the SF-36 dimensions [44]. In our sample, we found Cronbach's α coefficients ranging between 0.77 and 0.86. A comparison between the Mental health dimension of SF-36 and the GHQ-12 global score showed the two instruments to have similar psychometric performance (Cronbach's α coefficients were 0.91 and 0. 84 and reliability coefficients were 0.92 and 0.88 for GHQ-12 and SF-36 Mental health dimension respectively), although GHQ-12 is used to detect psychiatric cases, whereas SF-36 estimates mental health in general populations [45]. According to Goldberg et al, psychometric properties of the reduced GHQ versions were comparable to those of the original version. Cronbach's α coefficient was up to 0.8 and the test-retest coefficient was 0.73 for the GHQ-12 [37]. In our sample, Cronbach's α coefficient was 0.87.

SF-36 and GHQ-12 findings at the two first time points, 1996 (T1) and 1998 (T2), were used for the present purposes.

Morbidity assessment

Morbidity was initially addressed in the SU.VI.MAX inclusion questionnaire. Characteristics of interest included: the presence of cancer, body mass index, alcohol consumption, tobacco habits, physical tiredness, cardiovascular disease, diabetes, digestive disorders (stomach or duodenal ulcer, viral hepatitis, intestinal amebiasis, intestinal polyp, hiatal hernia, diaphragmatic hernia or gallstones), miscellaneous comorbid conditions (including asthma, rheumatism, rheumatoid arthritis or renal colic), and number of symptoms (signs of blackout, chest pain, shortness of breath, palpitations, limp, metrorrhagia, leukorrhagia, hemoptysis, hoarseness, dysphagia, gastric pain, intestinal transit problems, rectorrhagia, hematuria, dysuria, pollakiuria, cough-triggered urinary incontinence, cephalgia, rheumatalgia).

During the follow-up period, monitoring of the same comorbidities was by yearly visits (alternately for assessment of laboratory parameters and clinical examination). Details of any abnormality detected were sent to the subject concerned for forwarding to his or her physician. Thereafter, contact was maintained with the participant and the physician in order to monitor medical supervision and verify the conclusions of follow-up visits. In addition, the Minitel allowed participants to provide and receive information via the main SU.VI.MAX computer

server. They were able to complete computerised questionnaires off-line and transmit data during brief telephone connections. Each month, participants had an opportunity to report any health events, medical consultations or hospitalisations that had occurred since the previous assessment. When they occurred, an in-depth investigation was undertaken involving the subject or his or her family (in case of death) and any relevant medical personnel (general practitioner or hospital staff, for example). If the Minitel connection was broken for a long period, or if a participant failed to appear at a SU.VI.MAX follow-up visit, an investigation was launched to determine why and to monitor the subject's subsequent participation. If the family or the SU.VI.MAX investigators reported the death of a patient, the official death certificate was obtained and the cause of death determined. When a suspected event occurred, all relevant records, including the results of diagnostic tests and procedures (imaging, endoscopy, cytology, biopsy, surgery, etc.) were

collected from the subject or the relevant hospital, laboratory, or institution, and scrutinised at the SU.VI.MAX co-ordinating centre. Cancer-related information – i.e. type of cancer (cancer histology), stage, date of diagnosis (as confirmed on the pathology report), treatment at the time of diagnosis, and date of treatment were ascertained by research staff trained to conduct medical reviews and confirmed by mandatory provision of histological evidence.

Subjects
Because 3 recruitment centres were – for logistic reasons – unable to participate in the HRQoL study, only 9223 subjects are considered here; 7468 (81%) filled in T1 HRQoL questionnaire. Those in whom cancers developed between T1 and T2 were defined as cancer cases. If T2 data were missing, the period T1 + 2 years was considered. Those who had a cancer occurrence before T1 were excluded. The constitution of the groups was as illustrated in Figure 1.
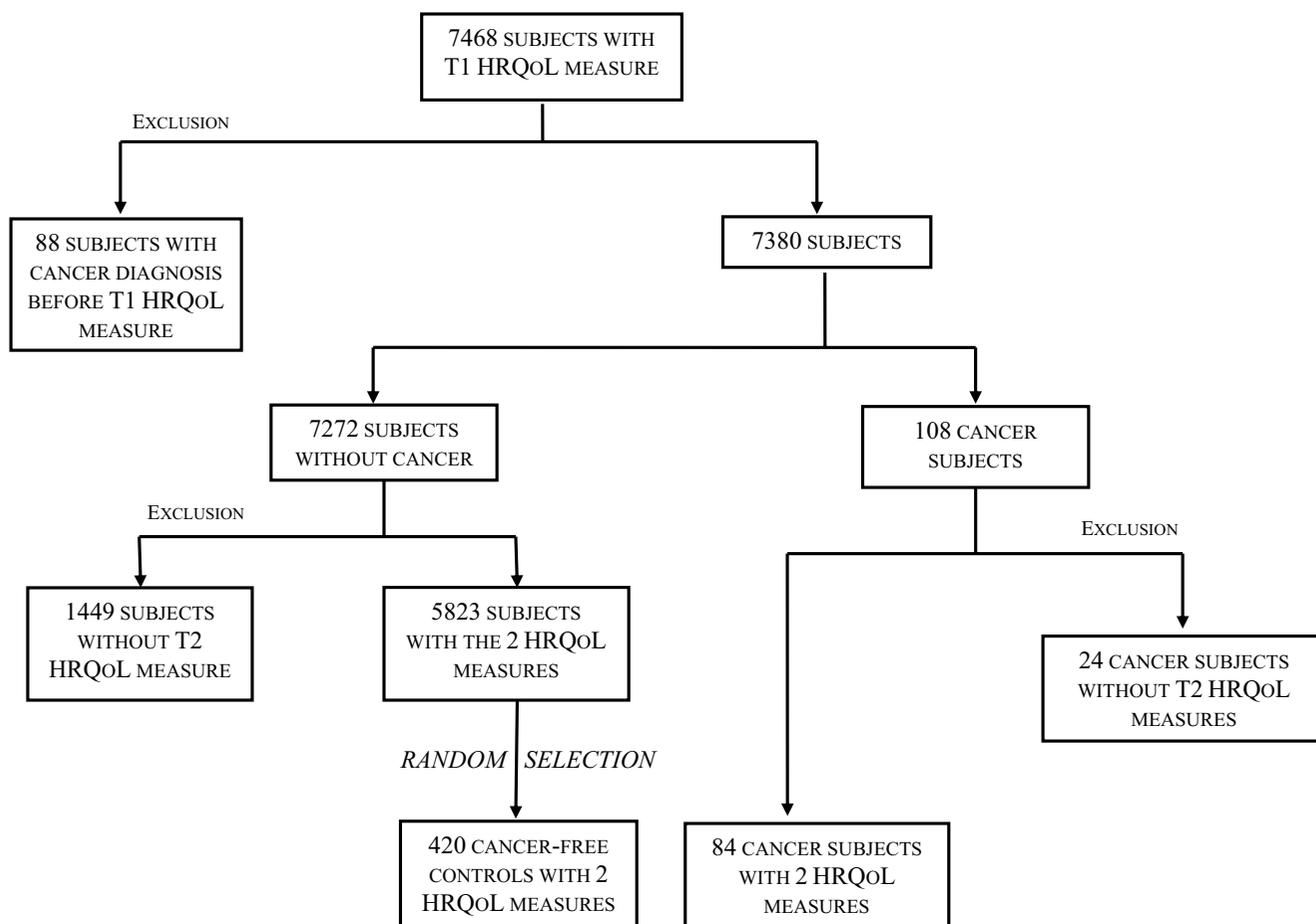

Figure 1
Subjects' inclusion process.

The controlled longitudinal study of the impact of cancer occurrence involved:

• 84 of 108 cancer cases for whom there were both T1 and T2 data; and

• 420 age- and sex-matched controls randomly selected from among a subsample of the 7272 cancer-free subjects: 5823 subjects (80.1%) filled in the T2 HRQoL questionnaire.

With 84 cancer cases, 420 controls were required to detect a difference of 5 points on the SF-36 scale between the two groups using a type I error of 5%, an estimated mean standard deviation of 20, and a power of 80%.

All subjects were selected regardless of how they had been randomised in SU.VI.MAX, the double-blind code of which was not broken.

Statistical analysis of data
Descriptive analysis
All descriptive statistics are presented as means and standard deviations for quantitative variables, and as absolute and relative frequencies for categorical variables. HRQoL scores are presented as means with their 95% confidence intervals.

Controlled longitudinal study of the impact of cancer occurrence
Cancer and cancer-free groups were compared for initial characteristics. Tests based on chi-square and on the t-test were used for categorical and quantitative variables, respectively. Factors that differed between the two groups were selected as adjustment variables in the multivariate analysis.

First, the HRQoL scores for the two groups were compared at T1 (i.e. before cancer occurrence), to confirm that they were similar. Second, the impact on HRQoL over time of cancer occurrence was assessed using a linear mixed model for repeated measures; within variables were the two measures of HRQoL, and between variables were group and adjustment variables.

Two levels of type I error were used:

- 10% to determine a statistically significant difference between those variables to be considered as adjustment variables in the multivariate analysis.

- 5% to determine statistical significance in the final multivariate analysis.

Statistical analysis was performed using SAS ® system [46].

Results
Cancer subjects characteristics
In the cancer group, ages ranged between 36 and 61 years, with a mean of 51 years; 61 subjects (56.5%) were female. Eighty-four (79%) of 108 subjects had both T1 and T2 HRQoL data. The disease characteristics of this subgroup are presented in Table 1.

Most cancers were of the breast (21.4%), cutaneous (30.9%), colo-rectal (13.1%), or prostatic (14.3%). Mean time between date of cancer diagnosis and T2 was 15.2 months (range, 2 days to 2 years). The majority of cases were at stage 0, I or II (95.1%), and treatment was essentially surgical (88.1%). Mean time between surgery and T2 was 15.6 months (range, 13 days to 2 years). With regard to the 24 subjects for whom T2 data were missing, no difference in initial characteristics were observed compared with the remainder, other than that they had more physical tiredness. Types of cancer were: breast (n = 6), cutaneous (n = 3), lung (n = 3), colo-rectal (n = 2), prostate (n = 1), hematologic (n = 4), bladder (n = 2), and other (n = 3). 58.3% had surgery, 33.4% had radiotherapy and 29.2% had chemotherapy. 70.6% were at stage 0, I or II. One reason for missing T2 data was death (11 subjects). 5 died subjects were at stage III or IV. HRQoL scores at T1 were non-significantly lower in the group without T2 data. General health and Mental health dimensions were most affected, with differences in scores of 9.6 (p = 0.01) and 8 (p = 0.05), respectively.

Controlled longitudinal study of the impact of cancer occurrence
Characteristics of the cancer and cancer-free groups are illustrated in Table 2. There was no difference between the 2 groups except that the cancer group was more likely to be educated to high school diploma level (p = 0.09), and felt more physical tiredness (p = 0.07).

After adjustment taking into account theses differences, HRQoL scores at T1 (i.e. before cancer occurrence) were similar in the two groups (Table 3). At T1, the cancer group had non-significantly higher scores in all dimensions other than Role-physical and Role-emotional, which were non-significantly lower. Between T1 and T2, all HRQoL scores decreased in the cancer group, whereas those of the cancer-free group were unchanged. The impact of cancer occurrence was most pronounced in the Physical functioning, Role-physical and General health dimensions. The difference in change (defined as the difference between the cancer and cancer-free groups in how much HRQoL changed) ranged from -6.6 (Physical functioning) to -15.2 (Role-physical). In the Bodily pain and Vitality dimensions, the difference in change was -6.3 and -4.4, respectively. The Role-emotional, Mental health and

Table 1: Cancer group characteristics (n = 84)

	n	proportion	mean	sd [a]
Site				
Breast	18	21.4		
Cutaneous	26	30.9		
Colo-rectal	11	13.1		
Gynaecological	2	2.4		
Hematologic	3	3.6		
Prostate	12	14.3		
Lung	1	1.2		
Thyroid	8	9.5		
Bladder	2	2.4		
Other	1	1.2		
Stage at diagnosis of solid cancer				
0 (in situ)	6	7.4		
I	43	55.6		
II	28	32.1		
III	3	3.7		
Unknown	1	1.2		
Time between diagnosis and T2 QoL assessment (months)			15.2	7.9
Treatment before T2 QoL assessment				
Surgery	74	88.1		
Time between treatment and T2 (months)			15.6	7.7
Radiotherapy	18	21.4		
Time between treatment and T2 (months)			13.9	8.4
Chemotherapy	9	10.7		
Time between treatment and T2 (months)			10.6	6.6
No treatment	7	8.3		

[a] standard deviation

Social functioning dimensions and the GHQ-12 score were not significantly affected by a cancer occurrence.

Comparisons with HRQoL scores in the general French population
When looking for HRQoL scores in a representative sample of the general French population (45–54 years) [44], the scores in the cancer-free group were lower, with absolute differences of 5 points maximum in all dimensions of the SF-36 except Bodily pain and Mental health (difference about 7 points).

HRQoL scores in the cancer-free group were lower compared to scores observed in a sample without chronic disease (except Role-emotional and Social functioning), and better compared to scores observed in a sample with chronic disease. In most of the dimensions, absolute differences were of 5 points maximum [43].

Discussion
The results of the present study show that cancer occurrence had a negative impact on HRQoL. The effect of cancer was strong in all dimensions of the SF-36 (other than Mental health, Role-emotional and Social functioning),

and particularly so in Physical functioning, Role-physical, Bodily pain and General health, for which there was an at least 6.3 point difference in change in HRQoL over time. The GHQ-12 score was not at all affected by cancer occurrence.

The choice of outcome measure may have important effects on the results of studies such as this. HRQoL instruments are used on the assumption that they are valid, reliable and sensitive [43]. The SF-36 has been shown to be valid and reproducible [38,39], and the GHQ-12 has comparable psychometric performance to that of the mental dimension of SF-36, although their objectives are complementary [45]. GHQ-12 has been used as a psychiatric screening instrument and to describe the mental health of a defined population. The SF-36 questionnaire has proven to be useful in monitoring general and specific populations, comparing the burdens of different diseases, differentiating the health benefits of different treatments, and in screening individual patients.

A generic tool was used in the present study both because a general population was involved and in order to allow for a controlled comparison with it. Generic measures

Table 2: Comparison of initial characteristics in the cancer (n = 84) and cancer-free (n = 420) groups

	Cancer				Cancer-free				p value [b]
	n	proportion	mean	sd [a]	n	proportion	mean	sd [a]	
Age (years)			50.9	5.6			50.9	5.5	1.00
Female	48	57.1			240	57.1			1.00
Alone	13	15.9			59	14.4			0.73
Higher diploma									0.09
Without diploma	3	3.6			19	4.5			
Less than High school diploma	21	25.0			154	36.7			
High school diploma and higher	60	71.4			247	58.8			
Body Mass Index (kg/m^2)			23.8	3.6			24.1	3.5	0.43
Alcohol consumption (g/day)			22.5	25.1			20.5	22.9	0.48
Tobacco habits									0.46
Non-smoker	43	51.2			214	51.5			
Former smoker	34	40.5			149	35.8			
Current smoker	7	8.3			53	12.7			
Tobacco consumption (cigarette-year)			7.8	12.5			6.9	11.8	0.54
Physical tiredness	19	22.9			61	14.7			0.07
Morbid conditions									
Cardiovascular disease	1	1.2			8	1.9			1.00
Diabetes	2	2.4			4	1.0			0.26
Digestive disorder [c]	22	26.8			100	24.9			0.78
Miscellaneous comorbid conditions [d]	17	20.5			95	24.1			0.57
Number of symptoms (at enrolment) [e]			3.0	2.2			2.9	2.5	0.74

[a] standard deviation [b] from t-test for quantitative variables and from chi square for categorical variables [c] gastric or duodenal ulcer, viral hepatitis, intestinal amebiosis, intestinal polyp, hiatal hernia or diaphragmatic hernia or gallstones. [d] asthma, rheumatism, rheumatoid arthritis or renal colic. [e] sum of different signs (see text)

cover a broad range of HRQoL dimensions in a single instrument and are applicable in a wide variety of populations, but they are less responsive than specific tools that focus on a particular disease or symptom.

As in most longitudinal investigations, part of the present initial sample was lost to follow-up. It is possible that the factors that led people to refuse to participate or to give up the study between T1 and T2 were related to their state of health.

SUVIMAX inclusion criteria (age up to 60 years) mean that the cancer cases may only represent the population of cancer occurring before 64 years which are a few part of overall cancers. However, it is likely that the impact of cancer on HRQoL doesn't vary much with age.

HRQoL scores in the control group are similar to normative scores described elsewhere [43,44], supporting the validity of our control group. HRQoL among cancer-free controls changed little over the 2 years of follow-up except for a minor improvement (+ 2 points maximum in 2 years) in most dimensions.

Although the cancer group was small and diverse, there were sufficient data concerning characteristics such as

stage of disease and treatment to show that the cancer group was relatively homogeneous in terms of stage (no stage IV and 3 stage III cancers) and treatment (essentially surgical). The mean time between date of surgery and the second HRQoL measurement was 15 months, perhaps leading to a reduce impact of treatment on T2 HRQoL assessment. The sample size did not permit the analysis to be limited to subjects with the same type of cancer, but when stage III was excluded, the results were similar to those presented here, confirming their validity. Moreover, the same results were found when the analyses were repeated excluding cutaneous cancers (which are reputed to be less aggressive), but retaining melanoma. No analysis by cancer site was possible because of lack of power.

Lack of power due to the small sample size may have prevented some of the present results from reaching statistical significance. However, sufficient power was available to detect differences of 5 points from the respective control groups (the matching strategy increased the power). The literature on the SF-36 health survey shows that very small differences on the SF-36 can be interpreted as clinically important. Anyway a difference of 5 points of mean HRQoL scores on a 0–100 scale is considered to be clinically and socially relevant [47].

Table 3: Comparison of HRQoL scores in the cancer (n = 84) and cancer-free (n = 420) groups.

	T1							T2							
	Cancer			Cancer-free			p value [d]	Cancer			Cancer-free			difference in change [e]	p value [f]
	mean [a]	LL [b]	UL [c]	mean [a]	LL [b]	UL [c]		mean [a]	LL [b]	UL [c]	mean [a]	LL [b]	UL [c]		
SF-36															
Physical functioning	90.2	86.5	93.9	87.9	85.4	90.4	0.18	84.5	80.9	88.2	88.8	86.3	91.3	-6.6	<.0001
Role-physical	80.7	73.7	87.7	82.7	78.3	87.1	0.56	65.3	58.3	72.3	82.5	78.1	86.9	-15.2	0.0004
Bodily pain	69.8	64.6	75.1	69.5	66.1	72.9	0.90	62.2	57.0	67.5	68.2	64.8	71.6	-6.3	0.01
Mental health	67.5	63.3	71.6	65.6	62.8	68.4	0.34	65.2	61.0	69.3	66.8	64.0	69.5	-1.1	0.07
Role-emotional	78.5	70.7	86.2	79.9	75.1	84.8	0.70	70.6	62.9	78.3	79.5	74.7	84.4	-7.5	0.11
Social functioning	81.4	76.4	86.4	80.6	77.4	83.8	0.76	77.3	72.3	82.3	81.3	78.1	84.5	-4.8	0.09
Vitality	60.1	55.9	64.2	59.1	56.3	61.8	0.61	57.1	52.9	61.2	60.2	57.4	62.9	-4.4	0.03
General health	71.7	67.4	76.0	68.7	65.8	71.6	0.14	62.6	58.3	66.8	70.7	67.9	73.6	-11.1	<.0001
GHQ-12	69.7	66.7	72.8	68.9	66.9	70.9	0.58	68.8	64.9	71.1	69.5	67.5	71.5	-2.3	0.17

HRQoL = health-related quality of life Scores range from 0 to 100, the higher the score, the better the HRQoL [a] adjusted mean [b] lower limit of the 95% confidence interval [c] upper limit of the 95% confidence interval [d] test of equality of T1 HRQoL score from a linear mixed model adjusted for higher diploma and physical tiredness [e] mean score evolution (cancer) – mean score evolution (cancer-free) [f] test of the interaction between time and group from a linear mixed model adjusted for higher diploma and physical tiredness

All subjects were selected regardless of how they had been randomised in SU.VI.MAX, the double-blind code of which was not broken. SU.VI.MAX was designed to test the efficacy of daily supplementation over a period of 8 years. Our studies used data from 1996 and 1998 (i.e. 4 years at most after the start of daily supplementation). We can reasonably suppose that any protective effect would not yet have been sufficient in this laps of time to influence estimates of the impact of cancer on HRQoL.

The study design adopted here offers the opportunity to track cancer occurrence. Controlled longitudinal analysis enables changes in HRQoL to be monitored over the period of diagnosis. In contrast, most other investigations look at the impact on HRQoL of existing cancer. The present protocol provides an opportunity to compare HRQoL in cancer subjects with that in controls using longitudinal strategies. Compared with the use of normalised data, selection of controls from the same population as the study group leads to a reduction in inter-individual variability. Enrolling controls in the population from which the cancer cases occurred also allowed HRQoL scores to be adjusted for age, sex, and comorbid conditions. In addition, two measures were performed for both the cancer and the control groups, thus more reducing inter-individual variability. Comparison between cancer patients and controls was also more precise and more powerful.

The acute situation facing patients with a new diagnosis of cancer was expected to have a negative effect on HRQoL. However, although all dimensions were indeed negatively affected by the event, recently diagnosed subjects still had a relatively high HRQoL. This may reflect the ability people have to cope with new situations. The dimensions most impaired by the cancer occurrence were Physical functioning, Role-physical and Bodily pain, all of which have a physical aspect. This is not surprising given that the cancer would have been recently diagnosed and treated essentially by surgery. Some indices, particularly the mental and emotional dimensions, were less affected by cancer occurrence. Courtens et al. [13] found that although functioning and physical and psychological well-being were negatively affected by cancer, newly diagnosed patients were satisfied with life in general and had high HRQoL. Cancer patients receive more attention and support from family and friends than do healthy subjects. They may also learn to value life in other, often new, ways. These results underline the importance of the psychological capacity human beings have to adapt and to cope with stressful life events, such as getting cancer. It has been suggested that newly diagnosed (not terminally ill cancer patients) still have a chance of cure that may strengthen the psychological domains of HRQoL.

Parker et al found in their sample of cancer patients that SF-12 physical score was lower that of the general population, and SF-12 mental score was comparable to that of

the general population, despite some cancer patients reporting significant depressive symptoms [48]. Other studies focused on the impact of cancer on mental health, showing that the diagnosis and treatment of cancer may be associated with anxiety and depression [49-52]. A recent review of the benefits of psychosocial oncology care stated that patients at high risk for distress are those with later stage disease, poorer prognosis, greater disease burden and perhaps younger age [53]. These subgroups are not represented in our sample. This may be why cancer occurrence seemed not to affect mental domains and one may hypothesise that the mental burden of cancer occurs along the course of the disease, with harmful medical intervention and degradation of health status [16,54-56].

The varied schedule of HRQoL measurement after cancer occurrence raises questions about the causes of the negative observed impact, including: the diagnosis itself, treatment, side effects, natural course of the cancer. HRQoL evolution as measured by the EORTC-QLQC30 before and after treatment has been assessed in a sample of female cancer patients. Before treatment, global HRQoL and emotional functioning were more affected than physical and social functioning. At the first assessment after treatment, physical, role and social functioning decreased significantly. Emotional functioning and global HRQoL improved significantly between pre-treatment and post treatment [57]. Between 3 months and 15 months after surgery for breast cancer, HRQoL of women aged 65 years or older showed significant declines for physical (difference about 10 points) and mental (difference about 3 points) functioning's [58]. Assessments of HRQoL 3 months and 1 year after surgery for breast cancer showed that all dimensions improved over time, but only social and emotional functioning showed a moderate effect size (i.e. between 0.20 and 0.50) [55]. HRQoL as measured by the SF-36 in long-term, disease-free survivors of breast cancer decreased (weakly clinically but statistically significantly) over time in Physical functioning, Role-physical, Bodily pain and General health, whereas Mental health improved over time [59].

Conclusion

The negative impact of cancer on the lives of patients was assessed in terms of HRQoL. The aspects most likely to be affected were those with a physical component, and general health perceptions. These results can thus help quantify the impact of a new cancer on ongoing HRQoL, and potentially maximise the benefit of early intervention by enabling the most affected HRQoL domains to be targeted. It would be of interest for future studies to investigate the relationship between time since diagnosis and HRQoL. Further follow-up of SU.VI.MAX to obtain more HRQoL data should help elucidate the relationship. Each cancer subject can potentially have four HRQoL measures:

one before the cancer emerges and the remainder afterwards.

Authors' contributions

S. Boini participated in the design of the study, reviewed the literature, performed the statistical analysis, and drafted the manuscript. S. Briançon designed the study, oversaw HRQoL and data collection, provided feedback and guidance on this work. FG, SH and PG participated in the design of the study, provided feedback on this work. SH, PG and S. Briançon are responsible for the SU.VI.MAX trial. All authors collaborated interactively, read and approved the final manuscript.

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