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REVIEW

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Happy thus survivor? A systematic review and meta-analysis on the association between cancer survival and positive states, emotions, and traits

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Abstract

Objectives: Traditionally, the literature investigating patient-reported outcomes in relation to cancer survival focused on negative factors such as distress. Meta-analyses in this field have provided a clear identification of negative affect that reduce cancer survival (e.g., depression). Nevertheless, positive psychological factors and especially positive affect might be equally crucial for cancer survival but have been neglected so far. While studies in this domain have been conducted, they remain less numerous and have produced mixed results.

Methods: A pre-registered systematic review and meta-analysis (https://osf.io/jtw7x) aimed at identifying the positive affect linked to mortality in cancers were conducted. Four databases (Pubmed, PsycINFO, Embase, and Cochrane Library) were searched to find longitudinal studies linking positive affect to survival in cancers. Two reviewers completed each stage of the study selection process, the data extraction, and the Quality in Prognosis Studies risk of bias assessments.

Results: Twenty-four studies involving 822,789 patients were included based on the 2462 references identified. The meta-analysis reveals that positive affect is associated with longer survival (Hazard Ratio [HR] = 0.91; 95% CI [0.86, 0.96], $z = -3.58$, $p < 0.001$) and lower mortality (Odd Ratio [OR] = 0.59; 95% CI [0.45, 0.78], $z = -3.70$, $p < 0.001$). Sub-group analyses indicated that the main predictors of survival are emotional and physical well-being, optimism, and vitality.

Conclusion: This work emphasizes the need to consider the role of affective mechanisms in patients with cancer, including their levels of well-being or optimism to provide the most favorable conditions for survival. Therefore, stronger and continuous effort to improve patients' positive affect could be particularly beneficial for their life expectancy.

Sullivan Fontesse and Valentyn Fournier are considered the first authors.

KEYWORDS
cancer, emotions, meta-analysis, mortality, optimism, positive affect, psycho-oncology, survival, systematic review

1 | INTRODUCTION

To better grasp patients' experiences regarding their disease and their well-being, patient-reported outcomes (PROs) are commonly used. In addition to the information they provide about patients' subjective quality of life, these PROs are also being studied as prognostic factors for survival in cancers.[1] For instance, the presence of a psychiatric comorbidity such as depressive disorder or adjustment disorder has been shown to predict 1-year survival status of patients with head or neck cancer.[2] In patients with lung cancer, a shorter survival was reported in those presenting a pessimistic explanatory style.[3] The abundance of research on the deleterious effect of negative affect, such as depression, on health led researchers to conduct meta-analyses that provide a clearer picture of the effect of this factor on cancer mortality. Across 51 studies, depression has been identified as increasing the risks of cancer incidence, cancer-specific mortality, and all-cause mortality.[4] As a result, multiple pathways such as biological mechanisms (e.g., inflammation), or behaviors (e.g., smoking) have been studied as potential pathways to explain the relationship between depression and cancer.[5–7] However, while PROs encompass a large spectrum of variables, most studies have focused on negative affect such as depressive mood, anxiety, or distress.[8,9]

While investigating the role of negative affect proved to be interesting and useful to patients' care, their positive counterparts tend to be neglected, although they may be equally important in cancer mortality and other clinical outcomes. This direction was thus followed by multiple studies aiming at identifying the positive affect (e.g., hope, optimism) linked to cancer survival. However, results are somewhat mixed. For example, Allison and colleagues[10] found that optimism was predictive of increased survival in patients with head and neck cancer whereas, in patients with lung cancer, Schofield and colleagues[11] found no proof of such a relationship. Contrary to expectations, another study found that, in patients with advanced malignant disease, general life satisfaction was predictive of an increased risk of mortality.[12] In the general population, a large prospective study on more than 700,000 women did not find evidence that happiness predicted cancer mortality.[13] Noteworthy, discrepancies in the observations could be explained by diversity of positive affect, measures of interest, or cancer localizations. Moreover, it should be noted that the directionality of the links between positive emotions and survival or mortality is not clear as, to the best of our knowledge, no experimental or interventional study has specifically investigated this point.

Mixed evidence has thus been found regarding the links between positive affect and cancer mortality. The overall conclusions of this field are still unclear as no systematic review and meta-analysis have been conducted on this topic. A comprehensive review of the literature is thus needed to shed light on this important field. Therefore, the main aim of the meta-analysis was to identify whether positive affect are associated with cancer survival and mortality. The secondary aims were to examine potential moderators such as cancer location, type of measures, or gender ratio. These factors will thus be used to conduct sub-group analyses to identify factors moderating the potential links between positive affect and cancer survival.

2 | METHODS

2.1 | Protocol and registration

The protocol for this systematic review and meta-analysis has been preregistered on Open Science Framework (https://osf.io/jtw7x; OSF registration DOI: 10.17605/OSF.IO/CVUFR). This work follows the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[14]

2.2 | Search strategy

Four different electronic databases were searched: Pubmed (including Medline), PsycINFO, Embase, and the Cochrane Library. The last search was conducted on the 25th of May in 2021 and included all articles comprised between this date and the oldest entry of each database. Keywords included words related to positive states, emotions, and traits (e.g., "happy", "joy") and cancer (e.g., "cancer", "Neoplasms"). Our keywords also included the type of design desired (e.g., "longitudinal", "prospective") and the outcomes ("mortality", "survival*"). The detailed search strategy in each bibliographical database is provided in the protocol on OSF (https://osf.io/jtw7x). Restrictions have been applied in search when possible: only peer-reviewed articles in English or French and only studies with human subjects.

2.3 | Inclusion and exclusion criteria

Following PICOS criteria that were the more suitable search tool for our research question (except for **Comparator**),[15] retrieved studies were eligible if (1) they recruited adult patients with cancer (any localization, any stage), before treatment, without treatment, or in curative or palliative settings or general population in which cancer mortality was measured (e.g., cohort study on the link between positive affect and mortality, including cancer mortality) (**Population**), (2) they included at least one measure of a positive emotion, state or personality trait in relation to cancer survival with any quantifiable tool (i.e., validated or not) (**Intervention—Phenomenon of Interest**), (3) they measured overall survival (**Outcome**) and (4) they were cohort studies, prospective studies, follow-up studies, randomized controlled trials, non-randomized controlled trials (**Study Type**). In addition, to be included in the meta-analysis, studies had to have comparable designs allowing the computation of valid summary effect size (ES). The use of two separate meta-analytical models

around Hazard Ratio (HR) versus Odd Ratio (OR) allowed to include the largest possible range of studies while accounting for their heterogeneity in designs and ESs. Regarding the outcome measures, the moderator analyses (such as trait vs. state) are also a safety measure that is used to ensure that the included studies are comparable.

Studies were excluded if (1) they were written in another language than English or French (studies with only the abstract was in English or French were included), and (2) the format of the article was a letter to the editor, a brief communication, a review, an editorial, a commentary, an expert opinion, a case study, a case series, a book, a book chapter, or a qualitative study; if two articles had the same dataset (same participants) or overlapping datasets (some participants are the same), one article was included (the one with the largest sample) and the other excluded.

A particular attention was paid to the measure of positive affect used. Even if many papers report measuring positive emotions, states or traits many actually measures negative affect (e.g., instead of measuring "well-being as indicated in the title of the scale, the items are related to depression). The items were thus carefully examined leading to the inclusion of the paper only if it included a scale containing at least 50% of positive items (e.g., "I am happy" is a positive item whereas "I am sad" even reverse scored is not a positive item but the absence of a negative emotion). The absence of a negative affect was also not considered as a positive affect except if the scale opposed the two concepts; for example, a study measuring pessimism will not be included except if the measure opposed optimism and pessimism on the same continuum. Supplementary Material S1 contains a table reporting all items from the scales and sub-scales of positive emotions, states, and traits of studies included in the meta-analysis. All measures of satisfaction regarding a specific topic (e.g., satisfaction with the treatment) were excluded as well as they are too dependent on the patient's evolution; a patient with high treatment satisfaction should probably be healthier which would compromise any interpretation of the results.

2.4 | Study selection process

One author (Sullivan Fontesse) extracted the references identified in the electronic databases using our search strategy. These references have been imported into Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org), a website providing a canvas and tools to support systematic reviews. The duplicates were automatically deleted. Then a first selection was made independently by two of the authors (Sullivan Fontesse and Christelle Duprez or Delphine Grynberg) based on the titles and abstracts. The eligibility of each remaining article was assessed a second time, based on the full-text screening. This second selection was also done by two authors (Sullivan Fontesse and Christelle Duprez or Delphine Grynberg or Valentyn Fournier). Disagreement was resolved by discussion with a third author (Delphine Grynberg or Christelle Duprez or Valentyn Fournier). Authors of studies (1) not reporting the link between the positive affect and survival/mortality or (2) not reporting the statistical information of this link were contacted via their email address or through ResearchGate. A reminder was also sent after a month to inform authors that inclusion of the research in the present systematic review would end after a 2-week delay. After this delay, studies with insufficient information were excluded. The articles remaining after this second selection were included in our systematic review.

2.5 | Data extraction

Two authors (Sullivan Fontesse and Christelle Duprez) independently extracted the data from the included articles using a standardized form. In this form, the authors reported the main aims of the study, the institution, the covariates controlled for in the study, the place where the data were collected, the questionnaire used for the measurement of positive affect, if the positive concept was measured in absolute terms or in opposition to its opposite, the psychometric quality of the variables of interest, when the measure of positive affect was taken relative to treatment, the frequency of measurement, the type of measurement (self or other-reported), when was the baseline measured relative to diagnostic (before or after, and how long before or after), the strategies used regarding missing data, the statistical analyses performed, the outcome (survival vs. mortality), the study design, the inclusion and exclusion criteria for participants, participants' sociodemographic status, the cancer location, the disease stage, information pertaining to patients' health, the type of treatment provided to participants (if any), the stage of treatment (if any), the presence or absence of metastases, the potential comorbidities, the time since diagnosis, and the follow-up time. One author (Pierre Gérain) extracted the statistical information necessary for the meta-analysis: the unadjusted and/or adjusted effect sizes with 95% confidence interval for survival/mortality, and other relevant statistical indices (e.g., odds ratio, sample size). Statistical information was checked by a second author (Sullivan Fontesse). Each step of the data extraction was thus reviewed by at least two persons.

2.6 | Risk of bias assessment

Given the main goal of this meta-analysis (i.e., exploring the predictive role of positive emotion, traits, and state in cancer survival), the risk of bias of each study was evaluated using the Quality in Prognosis Studies (QUIPS[16]). This tool allows for an objective rating of the quality of the prognostic research included in a systematic review. The evaluation was led by two independent coders (Sullivan Fontesse and Valentyn Fournier). Discrepancies between coders were discussed in a meeting with a third author (Delphine Grynberg).

2.7 | Statistical analysis

Hazard Ratio (HR) and its 95% confidence interval (CI) of each study were extracted when available. HR were chosen as the preferred study outcome because they provide rich information by including in

one metric the occurrence of events but also the time it took for them to happen ("events per time").[17] When unavailable the Odds Ratio (OR) were used instead. Because HR and OR are not comparable effect sizes, separate analyses were performed for summary HR and OR. When articles contained two different samples, both were included separately in the meta-analysis. When a study had multiple predictors of survival/mortality in the same sample, the most conservative indicator was chosen for the summary effect size computation.

Considering that the studies included patients with many different cancer locations and multiple measures of positive affect, the studies were expected to be highly heterogeneous and we thus used a random-effects models.[18,19] Computations were performed using the Comprehensive Meta-Analysis software.[20] The Cochrane *Q* test, T^2, I^2 and the prediction interval were used to evaluate heterogeneity between studies. Meta-regressions were conducted using the restricted maximum likelihood. Forest plots were generated using the Metafor R package.[21] The estimate of the variance of the true effect sizes and the range of effect sizes were also used. Funnel plots, Egger test, trim and fill method and the classic fail-safe method were used to detect potential publication bias.

As mentioned in the protocol, sub-groups comparisons were initially planned based on stage of cancer (early vs. advanced), cancer location, the type of treatment (curative vs. palliative), the type of assessment of the predictors (self-reported vs. reported by others), and the follow-up duration. However, the stage of cancer and cancer location presented too many different modalities to be compared. The type of treatment was not clearly reported or modalities were mixed in the study. For the follow-up time, multiple indicators were reported in the study (average, median, maximum). Not enough papers reported the mean follow-up duration to be able to run analyses based on this variable. Nevertheless, studies were still compared on other variables: the mean age of the sample, the risk of bias score, the type of report (self-reported vs. reported by others), if the positive measure was a state (i.e., situational) or a trait (i.e., dispositional), and the males/females ratio.

Univariate random meta-regressions using the restricted likelihood method were performed for both binary and continuous moderators. Multivariate meta-regressions could not be done due to the irregular reporting of descriptive information in included studies. Random-effects subgroups comparisons were performed for categorical moderators and for 2 binary moderators (univariate/multivariate and the measured outcome) to compute and compare the subgroup effect sizes. When studies reported multiple ES, only one was included in the summary effect but for the subgroup analyses, several effect sizes from a same study could be included if they belonged to distinct subgroups.

3 | RESULTS

The research strategy initially identified 3392 studies, of which 930 duplicates were detected and deleted by Covidence. A total of 2462 studies were screened based on their title and abstract. This selection led to 73 articles considered based on their full text. In the end, 24 studies meeting all the inclusion criteria have been included in our meta-analysis (see Figure 1 for the flow diagram).

3.1 | Study characteristics

In total, 822,789 participants were included in the 24 final studies. The sample size in each study ranged from 36 to 719,671. Table 1 presents a summary of the characteristics of included studies. Moreover, a table containing all the extracted information from each included study can be found in Supplementary Material S2. Studies were shown to be heterogeneous in their quality (see Supplementary Material S3 for a summary of the risk of bias evaluations).

3.2 | Effect of positive affect on survival

Regarding the HR, a total of 18 papers, one of which contained 2 subsamples, for a total of 19 effect sizes yielded a pooled HR of 0.91 (95% CI [0.86, 0,96], 95% PI [0.73, 1.12], $z = -3.58$, $p < 0.001$, $k = 19$), indicating an increase in positive affect is associated with longer survival (see Figure 2 for the forest plot). A high level of heterogeneity was found in the studies included in the meta-analysis (Q [18] = 507.17, $p < 0.001$, $I^2 = 96.45$). As regards publication bias, based on the funnel plot, an asymmetry can be observed with studies being in majority concentrated on the left side of the graph. This suggests that studies showing a harmful effect of positive emotions, states and traits might be missing from the literature. The trim and fill method simulates the addition of three studies on the right side of the funnel plot which would lead to an adjusted HR = 0.91 (95% CI [0.87, 0.97]). The Egger's test of intercept (intercept = −2.93, 95% CI [−6.12, 0.26], t[17] = 1.93, $p = 0.07$) did not reveal the presence of a publication bias. Furthermore, the classic fail-safe number revealed that 454 studies with a non-significant effect would have to be included in the meta-analysis to make the overall significant effect become non-significant. Overall, these indices do not to indicate a publication bias that would contradict the conclusion of the analysis.

Meta-regressions for the HR are reported in Table 2. The only significant moderator was the proportion of males ($b = 0.26$, $z = 2.98$, $p < 0.01$), as the effect sizes were smaller (i.e., closer to 1) when the proportion of males increased. The other moderators were not significant (risk of bias, age, type of report: self-reported vs. other, type of measure, and the type of sample). Sub-group comparisons are displayed in Supplementary Material S4. Effect sizes were not significantly different based on their univariate/multivariate nature. HR significantly differed based on the kind of scale (Q[3] = 9.98, $p = 0.019$) and the variables used to measure positive states, emotions, and traits (Q[5] = 17.81, $p = 0.003$). Indeed, the main predictors of survival are emotional and physical well-being, optimism, and vitality.

For the studies that did not provide an HR, OR were extracted instead. These 6 papers, one containing 2 subsamples, for a total of 7 effect sizes yielded a total pooled OR of 0.59 (95% CI [0.45, 0.78], 95%

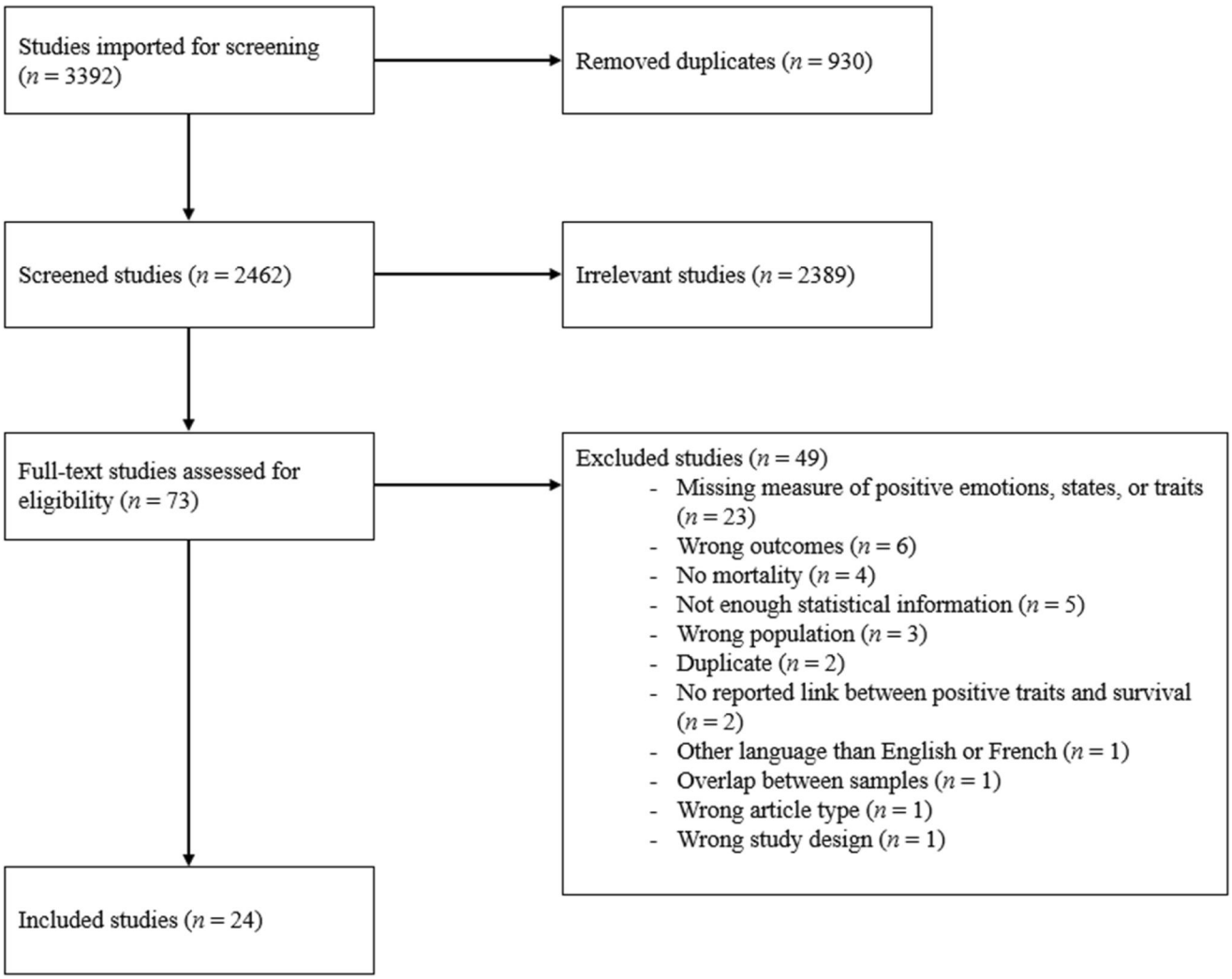

FIGURE 1 Flow diagram of the screening and selection process.

PI [0.28,1.25], $z = -3.70$, $p < 0.001$), suggesting that an increase in positive emotions, states, and traits is associated with lower mortality (Figure 3). A high level of heterogeneity was found in this sample of studies ($Q[6] = 47.62$, $p < 0.001$, $I^2 = 87.40$). Regarding the publication bias, a visual examination of the funnel plot showed an asymmetry with more studies on the left side of the graph. This asymmetry suggests that some studies showing a harmful effect of positive emotions, states, and traits and some studies showing a protective effect but with smaller effects sizes might not reach publication. Following the trim and fill suggestion of adding two studies on the right side would yield an OR of 0.85 (95% CI [0.85, 0.91]). The fail-safe indicates that 92 studies with non-significant results would be needed to render the global significant OR non-significant. The Egger's test of intercept (Intercept = −2.86 [−5.68, −0.04], SE = 1.10, $t[5] = 2.61$, $p = 0.048$) indicates the presence of a publication bias in this sample of studies. Concerning studies that reported an OR, some evidence of a publication bias has been found via the funnel plot and the Egger's test.

Meta-regressions for the OR are reported in Table 3 and did not yield any significant results. Sub-group comparisons are displayed in Supplementary Material S5. Effect sizes were significantly higher when exploring survival over mortality ($Q[1] = 25.72$, $p = 0.001$) and when focusing on univariate over multivariate effect sizes ($Q[1] = 16.17$, $p = 0.001$).

4 | DISCUSSION

This study reveals that, to the best of currently available knowledge, positive affect such as happiness, well-being, or optimism constitute protective prognostic factors regarding mortality and have a positive effect on survival duration in cancers. This effect was maintained across studies of varying quality, with different measures, and with varying samples.

Whereas most studies have focused so far on the deleterious effect of negative emotions, the objective of this meta-analysis was to counter this approach by evaluating the beneficial effect of positive affect on survival in cancer. Based on 24 papers, this review revealed that positive affect is associated with improved survival

TABLE 1 Characteristics of the 24 included studies.

First author and year	Cancer localization	*n* patients	Measure of interest	Mean age or median age*	Percentage of males	Type of measure (state vs. trait)	Patients with cancer or general population	Outcome	HR–OR
Allison et al. (2003)[10]	Head and neck	96	Dispositional optimism, DO (life orientation test)	58.3	92.7%	Trait	Cancer	Mortality	OR 0.89 (0.81, 0.99)
Anderson et al. (2014)[22]	Esophageal	836	Physical well-being (linear analog self-assessment, LASA) and emotional well-being (LASA)	64*	Not reported	State	Cancer	Survival	HR 0.69 (0.57, 0.84)
Bragstad et al. (2018)[23]	Lung cancer	44	Functional well-being (FACT-BR)	62.8	56.8%	State	Cancer	Survival	HR 0.55 (0.19, 1.58)
Butow et al. (2001)[24]	Breast	211	Physical well-being (LASA) and emotional well-being (LASA)	51	0.0%	State	Cancer	Mortality	OR 0.86 (0.42, 1.76)
Cassileth et al. (1988)[12]	Multiple	204	General life evaluation/ satisfaction	59.5	62.3%	Trait	Cancer	Survival	HR 1.50 (1.11, 2.02)
Chang et al. (2015)[25]	Multiple	873	Functional well-being	66.5	98.3%	State	Cancer	Survival	HR 1.07 (1.06, 1.09)
Coates et al. (1993)[26]	Melanoma	152	Physical well-being (LASA) and emotional well-being (LASA)	51*	68.4%	State	Cancer	Survival	HR 0.80 (0.70, 0.92)
Dodson et al. (2016)[27]	Multiple	598	Functional well-being (FACT-C) and vitality (SF-36)	53.3	46.1%	State	Cancer	Survival	HR 0.80 (0.73, 0.88)
Eton et al. (2003)[28]	Lung	573	Functional well-being (FACT)	60.6	63.0%	State	Cancer	Survival	OR 0.38 (0.28, 0.51)
Fischer et al. (2017)[29]	Melanoma	1947	Vigor (profile of mood states, POMS)	Not reported	Not reported	State	Cancer	Survival	HR 0.95 (0.93, 0.97)
Gmür et al. (2018)[30]	Liver	242	Functional well-being (FACT-Hep)	63.7*	85.1%	State	Cancer	Survival	HR 0.91 (0.88, 0.94)
Heiberg et al. (2019)[31]	Pancreatic cancer (PC) Other malignant lesions (OML)	PC = 210 OML = 109	Sense of well-being (ESAS)	PC mean age = 67.5; OML mean age = 65.8	PC = 49.3%; OML = 38.9%	State	Cancer	Survival	HR 0.99 (0.93, 1.06) HR 0.99 (0.94, 1.04)

TABLE 1 (Continued)

First author and year	Cancer localization	*n* patients	Measure of interest	Mean age or median age*	Percentage of males	Type of measure (state vs. trait)	Patients with cancer or general population	Outcome	HR–OR
Kaasa et al. (1989)[32]	Lung	102	Psychosocial well-being	Not reported	Not reported	State	Cancer	Survival	OR 0.25 (0.12, 0.52)
Kim et al. (2017)[33]	None at the beginning of the study	70,021	Optimism (life orientation test-revised)	70.1	0.0%	Trait	General population	Survival	HR 0.84 (0.74, 0.96)
Laktionov et al. (2018)[34]	Lung	102	Vitality (SF-36)	62*	65.0%	State	Cancer	Survival	HR 0.98 (0.97, 1.00)
Levy et al. (1988)[35]	Breast cancer	36	Joy	52	0.0%	State	Cancer	Survival	HR 0.63 (0.46, 0.86)
Liu et al. (2016)[13]	None at the beginning of the study	719,671	Happiness	59*	0.0%	State	General population	Survival	HR 0.78 (0.75, 0.80)
Miething et al. (2020)[36]	None at the beginning of the study	23,933	Happiness	Not reported	44.3%	State	General population	Survival	HR 1.00 (0.82, 1.21)
Moaven et al. (2019)[37]	Mucinous appendiceal	121	Functional well-being (FACT)	54.1	43.0%	State	Cancer	Survival	HR 0.95 (0.85, 1.06)
O'Mahony et al. (2010)[38]	Not reported	64	Religious well-being (FACIT-Sp, itself part of FACT)	Not reported	Not reported	State	Cancer	Survival	HR 0.41 (0.20, 0.84)
Pandit et al. (2022)[39]	Bladder	438	Vitality (SF-36)	76.3	73.5%	State	Cancer	Survival	HR 0.95 (0.91, 1.00)
Price et al. (2013)[40]	Ovarian cancer	798	Optimism (life orientation test-R)	Not reported	0.0%	Trait	Cancer	Survival	HR 0.80 (0.65, 0.98)
Shin et al. (2014)[41]	Multiple	610	Well-being (ESAS)	58.9*	53.0%	State	Cancer	Mortality	OR 0.89 (0.82, 0.98)
Stern et al. (2001)[42]	None at the beginning of the study	Depressed: 139 Not depressed: 656	Hopefulness (geriatric depression scale)	69	42.0%	State	General population	Mortality	OR 0.50 (0.22, 1.17) 0.30 (0.13, 0.67)

(HR = 0.91, OR = 0.59). Also, an additional search was conducted (from the 26 May 2021 to the 9 June 2023) which allowed to add 6 recent articles (8 samples). We specifically included those 6 additional articles because they were the only papers to specify all the needed information for meta-analysis. The results indicate that the effect of positive effect remains significant (K = 27; HR = 0.914 [0.876, 0.953], Z = −4.22, p < 001; Q[26] = 530.99, p < 0.001, I^2 = 95.10, Tau^2 = 0.09; see Figure S1_suppl in Supplementary Material S6 for the Forest plot) supporting that positive affect predict a more favorable cancer prognosis.

Regarding the initial results, they revealed that this effect was not influenced by having initially a cancer or being initially healthy, by age, or by the risk of bias. However, the effect was larger when the proportion of female was higher which could be explained by various factors such as differences in type of cancers, coping style, emotional intelligence, or physiological activity.

Concerning the relevance to consider positive affect as a significant and protective factor, the effect sizes are (inversely) comparable to the effect sizes of the deleterious effect of negative affect. For instance, depression is associated with a HR of 1.29 to breast cancer specific mortality.[4] Therefore, this meta-analysis emphasizes the necessity to raise awareness of the importance to evaluate, if not improve, positive affect, affect at early stages of cancer and continue promoting positive psychology intervention.[43] Moreover, and as further mentioned, one may consider positive affect even independently of negative one (i.e., mixed emotions).[44]

Beside the contribution of the present results, it is also important to consider the mechanisms explaining the prognostic role of those positive factors regarding cancer survival. First, it has been observed in the general population that people who report higher happiness and who are more optimistic might deploy specific health behaviors associated with longer survival and avoid hazardous behavior.[45–47] For instance, optimism is associated with healthier behaviors such as physical activity and healthy nutrition.[48] Conversely, people who experience more positive emotions can steer away more easily from risky health behaviors such as smoking or drinking alcohol than people who experience more negative emotions.[45–47]

Another explanation might be that patients who present more positive emotions have specific physiological activity favoring their survival. Indeed, past research showed that positive affect were related to specific physiological activity in patients with cancer, including inflammatory activity.[49] In addition to inflammatory activity, positive affect can impact a wide range of physiological factors such as blood pressure, cortisol levels, and immune system activity.[50,51] The physiological activity associated with positive affect could be a relevant mediator of the link found between them and reduced mortality in cancer. Future research will have to distinguish the roles of these different pathways and consider a potential synergy in their effects.

Besides behavioral and physiological mechanisms, other pathways may have the potential of explaining the reported links between positive affect and decreased mortality in cancers. First, given they have increased chances of survival, the patients with better health at baseline also report more positive affect.[45] For example, in univariate analyses, happiness has been found to be predictive of decreased cancer mortality in a large cohort of initially healthy women.[13] However, when considering the initial self-rated health and other variables related to treatment received for health disorders as well as sociodemographic and lifestyle factors, the protective effect of happiness disappeared. The health status at baseline could explain both the difference in positive affect at baseline and the differences of mortality or survival in the follow-up.

Then, negative affect are known risk factors regarding mortality in the general population[52] and cancer-specific mortality.[53] Interestingly, positive emotions cannot be confused with the absence of negative emotions. Indeed, according to Larsen and McGraw's[44] model, one can experience mixed emotions such that positive and negative affect might co-occur. Interestingly, experiencing mixed feelings might even be associated with better health.[54–56] Furthermore, according to the broaden-and-build model of positive emotions,[47] positive emotions broaden the repertoire of thoughts and actions of the person feeling them which might counteract the more narrowed thought-action repertoire associated with negative affect. People could even use positive emotions to favor the creation of social, physical, and intellectual resources, which can be used to face new challenges and difficulties.[47] All together, these two models thus highlight the importance to benefit from the complexity of the affective experience (i.e., positive and negative) and the necessity of having positive emotions.

Considering the protective effect of positive affect against mortality in cancer, creating opportunities for patients to feel better might be even more crucial than previously thought. According to a literature review by Quoidbach and colleagues,[57] interventions aimed at favoring positive emotions (e.g., gratitude or relaxation therapies) do provoke short-term and long-term gains in positive emotions. Such interventions supporting the creation of positive emotions in patients with cancer and in the general population could, in addition to directly improving their quality of life, increase survival.

4.1 | Clinical implications

To date, the research on the effects of affective factors on cancer patients' survival has mainly focused on the negative aspects. Our findings show the relevance and importance of also considering positive states, emotions, and traits. Notably, a large majority of current psychosocial interventions targets negative affective factors (e.g., stress and anxiety reduction, coping with bad news) whereas some interventions has been shown to be efficient on positive affect.[54] In the light of those results, it could be recommended to evaluate positive and negative emotions at early stage of cancer and to develop interventions targeted at the optimization of positive states, emotions, and traits (e.g., capitalizing on positive emotion, maximizing happiness, developing a positive coping style). However, it should be highlighted that interventions focusing only on positive emotions could be counterproductive if some factors are not considered (e.g., existing

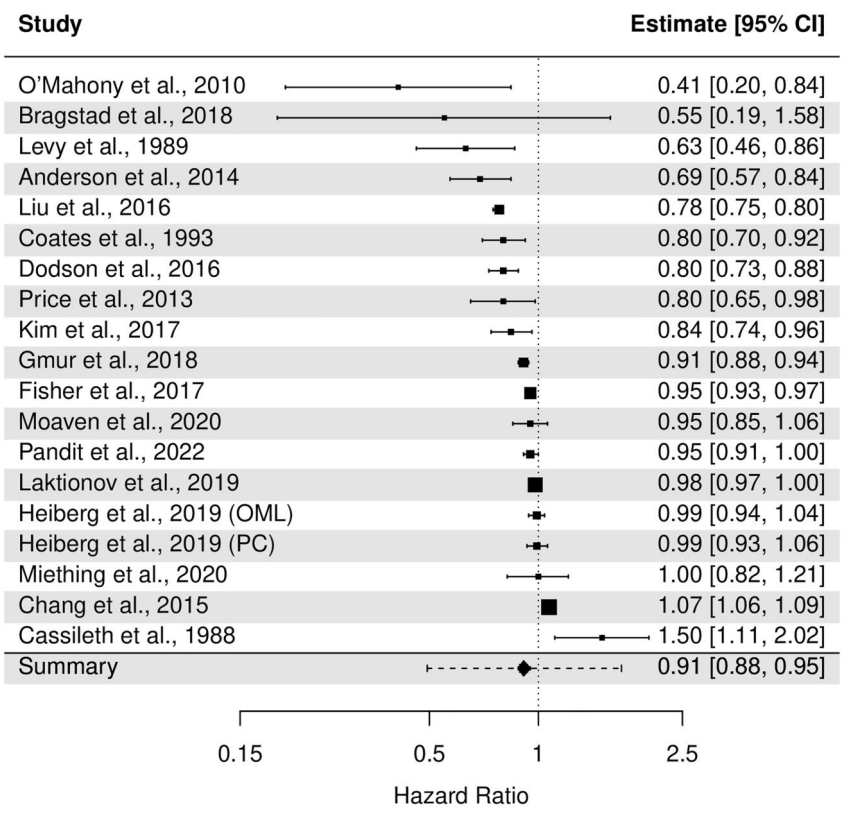

FIGURE 2 Forest plot of the association between positive affect and survival (Hazard Ratio [HR]). OML, other malignant lesions; PC, pancreatic cancer.

TABLE 2 Meta-regression for the Hazard Ratio (HR).

Grouping	Coefficient	SE	*Z*	*p*	R^2
Male proportion	0.26	0.09	2.98	0.003	0.48
Risk of bias	0.00	0.01	0.15	0.882	0.00
Age	0.01	0.01	1.09	0.274	0.02
Format (self vs. self + proxy)	0.06	0.14	0.43	0.667	0.00
Measure (state vs. trait)	−0.06	0.11	−0.57	0.570	0.00
Population (cancer patients vs. general population)	0.07	0.09	0.77	0.443	0.03

depressive symptomatology, discrepancy between perceived social expectation and actual experienced emotion[58,59]). Moreover, it is noteworthy that, because of its potential pitfalls (e.g., impaired self-efficacy, self-blame), the positive psychology is going through a paradigmatic change leading to a change of focus, from only positive aspect to a more integrated view of the emotional scope, from negative to positive.[60–62] For those reasons, it seems crucial to keep in mind that only targeting positive affect could not be sufficient, and even be deleterious.[61] In that sense, it has been shown that interventions fostering emotion regulation skills and coupling down regulation of negative affect with up regulation of positive affect are effective in enhancing psychological outcomes in breast cancer patients.[63] In the longer term, research may even focus on a beneficial effect on survival in cancer patients. In addition, psychoeducational interventions could complete those programs to raise patients' awareness on the importance of both positive and negative emotions in healthcare. These interventions might also address the question of their links with physical health and provide them with strategies to improve their emotional well-being. Developing such actions could bring powerful leverage in cancer care.

4.2 | Study limitations

Some of the initially planned sub-group comparisons such as early and later cancer stages could not be carried out for multiple reasons: lack of information in the manuscript, too many different modalities, or not enough studies representing a modality. Furthermore, heterogeneity observed across studies was high. Therefore, the empirical investigation of positive affect in relation to cancer mortality is still relatively under-developed and many aspects have still to be addressed. Our meta-analysis showed that samples which were

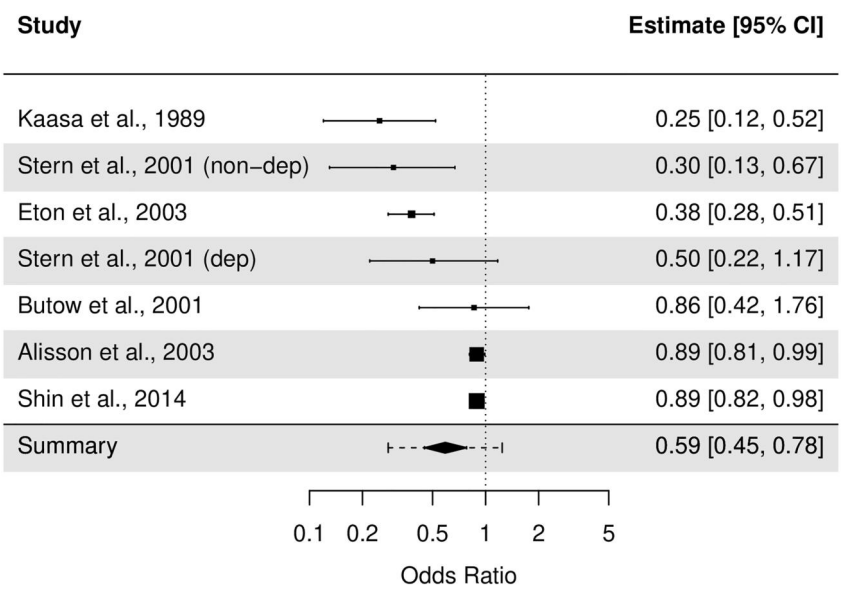

FIGURE 3 Forest plot of the association between positive affect and survival/mortality (Odd Ratio [OR]). Dep, depressed individuals; non-dep, non-depressed individuals.

TABLE 3 Meta-regression for the Odd Ratio (OR).

Grouping	Coefficient	SE	*Z*	*p*	R^2
Male proportion	0.13	0.80	0.17	0.868	0.00
Risk of bias	−0.06	0.11	−0.61	0.545	0.00
Age	−0.04	0.04	−1.01	0.310	0.09
Format (self vs. self + proxy)	NA				
Measure (state vs. trait)	−0.60	0.53	−1.12	0.263	0.02
Population (cancer patients vs. general population)	0.46	0.51	0.90	0.368	0.01

constituted of more males benefited less from the protective effect of positive affect than the samples with fewer males. This effect could be further explored in new research by focusing on cancers associated with an equal incidence in males and females and that are not sex-specific (e.g., breast cancer) and by including potential explaining mechanisms (e.g. coping style, physiological activity). Future research will also have to determine how each specific affect are related to mortality (e.g., distinguishing the effect of happiness, optimism, vitality, or well-being). Furthermore, previous research has already identified that positive emotions of different levels of arousal could have different effects.[49] The effect of level of arousal of positive emotions on mortality must thus be clarified. Tracking diversity in positive emotions (e.g., emodiversity) and in relation to negative emotions (e.g., mixed emotions) will also provide an important piece of information as some longer-lasting emotions (e.g., contentment) might be more protective than shorter-lasting ones (e.g., excitation). The diversity of positive emotions (positive emodiversity) has been shown to be associated with lower levels of inflammation independently of mean levels of positive or negative emotions and of other medical and sociodemographic variables.[64] Future research should thus follow this direction and investigate if emodiversity predict cancer survival. Besides those concepts, one could address the role of Post-Traumatic Growth (PTG).[65] Indeed, PTG is a central mechanism in cancer and in predicting higher quality of life.[66] In relation to positive affect, several studies have found a moderate correlation between PTG and optimism (Turner et al., 2017). One could thus hypothesize that PTG might be related with an increase in optimism and, in the long run, improve cancer survival. Finally, identifying the specific pathways that could explain the protective effect of positive affect and their potential bidirectional links with health status would provide key information for future interventions.

5 | CONCLUSION

Cancer patients who reported experiencing more positive affect had a longer survival duration than those with less positive affect. This meta-analysis thus emphasizes the need to systematically assess positive affect as protective factors in cancer mortality. Furthermore, while alleviating negative affect is important, promoting positive ones constitute an important complementary strategy to improve the survival of people with cancer.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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