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# The association of physician empathy with cancer patient outcomes: a meta-analysis

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## Abstract

**Objective:** In oncology, research remains unclear as to whether physician empathy is associated with patient outcomes. Our goal was to answer this question and explore potential moderators of the association.

**Methods:** In this meta-analysis on adult cancer care, we excluded randomised controlled trials, and studies of survivors without active disease or involving analogue patients. Eight databases were searched, in addition to reference lists of relevant articles and grey literature.

Two reviewers independently screened citations, extracted data, assessed risk of bias and

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graded quality of evidence by using the AXIS tool. Effect size correlations (ESr) were chosen and pooled by using a random effect model. Subgroup analyses were performed, and statistically significant variables were introduced in a meta-regression. Several methods were used to explore heterogeneity and publication biases.

**Results:** We included 55 articles, yielding 55 ESr ( $n = 12976$  patients). Physician empathy was associated with favourable patient outcomes: ESr 0.23, 95% confidence interval (CI) [0.18 to 0.27],  $z = 9.58$ ,  $p < 0.001$ . However, heterogeneity was high, as reflected by a large prediction interval, 95% CI [-0.07 to 0.49] and  $I^2 = 94.5\%$ . The meta-regression explained 53% of variance. Prospective designs and physician empathy assessed by researchers, compared with patient-reported empathy, decreased ESr. Bad-news consultations, compared with all other types of clinical encounters, tended to increase ESr.

**Conclusion:** Patient-reported physician empathy is significantly associated with cancer patient outcomes. However, the high heterogeneity warrants further longitudinal studies to disentangle the conditions under which physician empathy can help patients.

Recommendations are proposed for future research.

**Keywords:** Communication, physician empathy, cancer care, oncology, patient outcome, meta-analysis, bad news

## Introduction

Cancer patients undergo stressful events such as diagnosis, heavy treatments and side effects, the threat of or actual disease progression, uncertainty regarding the future and eventually, entry into palliative care. Several factors, such as physician empathy (PE), can help patients face these difficult times. Because there is no consensual definition of empathy, as demonstrated by numerous studies that try to address this issue<sup>e.g. 1,2</sup>, it is crucial to precisely define it when working on the topic. Considering the most used patient-reported questionnaire of PE, the CARE<sup>3</sup>, PE refers to how physicians (1) establish a good rapport with the patient by putting them at ease, actively listening and paying full attention to them (i.e. establishing rapport), (2) demonstrate a genuine interest in and a full understanding of, the patient, as well as care and compassion through a connection on a human level (i.e. the emotional process, considered most important by patients<sup>1,2</sup>) and (3) are positive, explain things clearly, help the patient to take control and make a plan of action with them (i.e. the cognitive process, which promotes patient empowerment). This definition of PE was the one used in this meta-analysis.

On a biological level, empathy is related to the hormone oxytocin<sup>4</sup> which has anti-proliferative, anti-metastatic and anti-angiogenic effects in some cancers<sup>e.g. 5</sup>. Perceived empathy, as a component of emotional support, may also be related to less inflammation<sup>6</sup>, which has a well-established role in cancer progression. On an emotional level, Neumann et al. (2009) posited that PE is supposed to help patients feel supported and improve care by better addressing their various needs, which would be more easily expressed by the patients in front of an empathetic physician<sup>7</sup>. A systematic review that investigated the links between PE and patient outcomes (PO) in oncology seemed to support this theory: PE had beneficial effects on various PO. However, there was heterogeneity in the results regarding the effect sizes and even the direction of the link: strikingly, in some studies, PE was associated with

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negative PO such as higher anxiety. Results of patient interviews suggested that an unusually high level of empathy may inadvertently convey to patients the idea that something very serious is happening and increase their already high levels of worry<sup>9</sup>. Furthermore, medical empathy has also sometimes been associated with less favourable medical outcomes, such as a decreased probability of quitting smoking in an intervention aimed at helping people to quit smoking<sup>10</sup>. This suggests that, in medical settings, empathy should not be deployed at the expense of medical priorities and warrants further investigation.

A meta-analysis was therefore needed beyond a systematic review. Indeed, conclusions based on the number of studies with significant *p* values in a systematic review cannot be relied on<sup>11</sup>. Given the divergent results found in the literature, we expected high heterogeneity in the meta-analysis, and one of our goals was to explain this heterogeneity. From previous data, we assumed that the following three variables could moderate the link between PE and PO:

1. Type of consultation. There is a dearth of studies that compare the effect of PE by treatment phase or cancer stage<sup>8</sup>. Yet, patients' sensitivity to empathy could depend on the type of consultation: the beneficial effect of PE should be stronger in bad-news consultations, in which patients' emotions may be the priority and need to be addressed, than in other less emotional contexts<sup>12</sup>. In line with this hypothesis, patients' expectations of PE have been shown to be high in bad-news contexts<sup>13</sup>.
2. The way empathy is assessed. Our previous systematic review<sup>8</sup> pointed out that patient assessment of PE was more associated with beneficial PO than other types of assessments were, such as doctor-reported empathy or empathy assessed by researchers, something that has already been verified in psychotherapy<sup>14</sup> and in a recent study in cancer care<sup>15</sup>.
3. The empathic processes. PE is often conceptualised as a whole, whereas three different processes can be identified<sup>16</sup> as previously described: (1) the process of establishing a

good rapport with the patient (2) the emotional process and (3) the cognitive process. The differentiation of the three processes may inform research. For example, establishing a good rapport and the emotional process were both associated with fewer surgical complications in patients with digestive cancer, whereas the cognitive process was not<sup>17</sup>.

To the best of our knowledge, there is no meta-analytic conclusion on whether PE is associated with PO in cancer care, and if it is, to what extent and in which conditions the association may be strongest. Our goal was to answer these questions. They are all the more important because empathy is a demanding task, especially for clinicians, who have many institutional barriers to empathy, such as time pressure and administrative load, and who are not always comfortable with patients' emotions and perspectives. Thus, it is important to motivate clinicians towards empathy by establishing the link between their empathy and PO and the conditions in which empathy may have the strongest effects. This is all the more important since communication skills training improves PE<sup>18</sup>.

## **Methods**

The analysis was conducted by following the AMSTAR 2 guidelines<sup>19</sup>.

### **Protocol and registration**

We registered the protocol prospectively on PROSPERO in November 2018 (record n° CRD42018112729).

### **Eligibility criteria**

Studies could be included if they met the following inclusion criteria:

1. Dealt with an adult oncology population at any stage, with any localisation, in curative or palliative settings, and with new or recurring cancer patients.

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2. Addressed PE, i.e. at least contained one item very similar to those of the emotional process of the Consultation and Relational Empathy (CARE) measure (i.e. the physician being interested in the patient as a whole person, fully understanding patients' concerns and showing care and compassion; items 4, 5 and 6, respectively), as this process is the core of empathy<sup>1</sup>. Therefore, articles dealing with empathy constructs but named differently (e.g. communication or compassion) could be included as long as they met these inclusion criteria (see Appendix A for search strategy). The items of the scales used to assess PE in the candidate articles were carefully considered to determine whether the article dealt with empathy as defined in these inclusion criteria.

3. Investigated *physician* empathy (surgeon, oncologist, and any medical specialist that patients met for their cancer care).

4. Involved quantitative research.

5. Assessed the association of PE with one or several PO. Outcomes could be defined as the changes that result from health care. Studies were excluded on the basis of the following exclusion criteria:

1. Studies about (a) survivors who no longer have cancer or (b) literature reviews and meta-analyses, as the data did not allow us to perform our analyses. However, their references were screened.

2. Studies about nurses or allied healthcare professionals exclusively.

3. Studies about primary care physicians, because the lack of coordination of cancer care between hospitals and community physicians sometimes makes it difficult for them to fully support their patients on their cancer care journey.

4. Studies that (a) artificially manipulated PE such as in analogue patient studies, (b) used standardised patients and (c) were about communication skill training.

## **Information sources and search**

The databases MEDLINE, PsycINFO, Academic Search Premier, Scopus, PsycARTICLES, Web of Science, Cochrane Library and Open Grey were searched. The following limiters were applied when they were available: English/French language, human studies, adult population, abstract available, peer-reviewed articles. Articles from January 1, 1990, up to November 10, 2022, were extracted. Reference lists of retained and relevant studies were hand searched.

## **Data collection, extraction and management**

A list of search terms was developed according to the literature. Different combinations of search terms were tested before extraction. The search strategy is available in Appendix A. Titles and abstracts of the retrieved studies from the search strategy and those from additional sources were screened independently by two authors (LG and CD) to identify studies that met the inclusion criteria. The full texts of these eligible studies were retrieved and independently assessed for final inclusion by two team members (LG and CD). Disagreements were discussed with one of the other two authors (SL and VC).

A standardised, pre-piloted form was used to extract data from the included studies for assessment of study quality, evidence synthesis and data. This pre-piloted form was edited, validated by the other two authors (SL and VC), and tested on 5% of studies. After it was considered satisfactory, the following data were extracted: information about the report (year of publication, author, funding), definition of PE and its measure (type and validity of the measure, empathy in a specific consultation or in general, interpretation of the score/tool), study setting, participants and sample characteristics and outcomes and their measures. Two authors (LG and CD) extracted data independently for 84% of the articles; discrepancies were identified and resolved through discussion with the other two authors (VC and SL). The

remaining 16% of articles were coded by two authors (LG and SL) and discrepancies resolved with the other two (CD and VC).

The evaluation of the quality of studies and risk of bias was assessed by using the 20-item AXIS tool<sup>20</sup>, one of the rare available tools to assess the quality and risk of bias of observational studies. For each item, the answers are yes, no, don't know/comment. The quality of studies was independently coded by two authors (LG and CD) and discussed with one of the other two authors (VC and SL) to reach consensus. A score out of 20 was calculated for each article.

## Analyses

Correlation was chosen as the effect size (ESr). A negative value indicates an unfavourable association between PE and PO (e.g. PE is associated with higher patient anxiety), whereas a positive value indicates a favourable outcome (e.g. PE is associated with higher patient satisfaction). When ESr was not directly available from studies, other ES were retrieved and transformed into Fisher's Z by CMA software (Comprehensive Meta-Analysis). When linear standardised coefficients were available, they were transformed into correlations by using the formula by Peterson and Brown<sup>21</sup>. Even though the method may not have been most appropriate for high ES, we used it because high ES are rare in the field and it is by far the most convenient method among those available. All choices and computations of ESr are explained in Appendix B. A random-model effect was chosen corresponding to the various designs and variables in the field, which makes the existence of a common ES among studies unlikely<sup>11</sup>.

Heterogeneity was explored with the prediction interval,  $Q$ ,  $T$  and  $I^2$ . Heterogeneity tests are aimed at determining whether the observed variation reflects genuine variation (i.e. heterogeneity) or is due to random error.  $Q$  tests the null hypothesis that all studies share a common ES.  $T$  is the estimation of the standard deviation of the true effects.  $I^2$  is the ratio of

true heterogeneity to total variation in observed effects. It reflects the proportion of variance that is true but, contrary to a widespread misconception, says nothing about the absolute value of this variance<sup>22</sup>. For the latter question, the prediction interval is required, which informs us about how the true effects are distributed about the mean ES, i.e. the actual dispersion of ES. In our case, it is the interval within which a new ESr would fall if a study were selected at random from the population of studies. The prediction interval would include that score 95% of the time.

Publication bias was explored by using several complementary methods<sup>22</sup>. First, the funnel plot of ES against their standard error was examined. Publication bias is likely when asymmetry exists, especially at the bottom of the plot, where small studies are represented, but it is only one possible reason for the asymmetry among many others. Egger's test and the method by Begg and Mazumdar can confirm the asymmetry with a significant *p* value. Duval and Tweedie's trim and fill method was then used to provide us with an estimate of the adjusted ES with the  $L_0$  estimator for imputing missing studies. A cumulative meta-analysis was performed, restricted to the most precise studies. It also provided an estimate of the pooled ES that can be obtained using the most precise studies.

Finally, we conducted the pre-planned subgroup analyses as recorded in Prospero (record n° CRD42018112729), with a special interest in three hypothesised moderators described in the introduction, i.e. type of consultation, the way empathy is assessed, and the empathic processes. The significant results were then added in a meta-regression in order to explore how much of the variance of the ESr could be explained by the moderators.

## Results

Our results yielded 55 studies included in the systematic review and 55 ESr (Figure 1). Descriptive statistics of the samples are provided in Appendix C. In most samples, PE was not assessed in reference to a specific encounter, but in general (47%). When empathy was related to a specific encounter, it concerned mostly bad news. Empathy was predominantly reported by patients (75%), followed by researchers using coding systems (18%). Empathy was conceptualised as a whole with the three empathic processes (i.e. establishing a good rapport, emotional and cognitive) in 42% of samples and with the emotional process only (i.e. the core of empathy) in 29% of samples. The investigated outcomes were mostly related to care (45%, e.g. patient satisfaction) or to psychological outcomes (33%, e.g. patient distress). Only 12% were physical outcomes such as the severity of symptoms. Samples were mostly cross-sectional, comprising female patients and composed of early cancer patients, with studies being performed in the United States and being funded. A detailed description of each of the included studies of the systematic review is provided in Appendix D.

### Overview of the results

The synthesis of studies is presented in Figure 2 in which the studies are sorted from the lowest to the largest ESr. The mean ESr was 0.23, 95% confidence interval (CI) [0.18 to 0.27],  $z = 9.58$ ,  $p < 0.001$  (testing the null hypothesis that ESr is 0), demonstrating that PE is significantly associated with cancer PO. As could be expected, there was a significant heterogeneity  $Q(54) = 983$ ,  $p < 0.001$ ; i.e. the true effects varied (we rejected the null hypothesis that the true effect sizes were identical in all studies), with  $I^2 = 94\%$ , meaning that 94% of the observed variation was true heterogeneity.  $T$ , the standard deviation of true effects, was 0.15. Based on  $T$ , the 95% prediction interval was [-0.07 to 0.49], so that in the population of studies, 95% of ESr fell between -0.07 and 0.49, informing us that PE can be strongly and positively associated with PO or not related to outcomes or even slightly

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associated with unfavourable outcomes. Because of this high heterogeneity, the summary ESr of 0.23 should be considered with caution, the main concern being to understand this heterogeneity from subgroup analyses and meta-regression.

### **Subgroup analyses**

Subgroup analyses are presented in Appendix E. Differences in ESr were found according to the type of empathy assessment, i.e. patient-reported empathy ( $r = 0.23$ ), showing a stronger association than coding-system assessment ( $r = 0.05$ ); the context of empathy, i.e. bad news ( $r = 0.33$ ), leading to a stronger association than any other contexts ( $r = 0.20$ ); the stage of cancer, i.e., advanced cancers ( $r = 0.30$ ), leading to a stronger association than non-advanced ( $r = 0.09$ ); and the design of studies, i.e. prospective studies ( $r = 0.07$ ), demonstrating smaller ESr than cross-sectional studies ( $r = 0.27$ ). No differences were observed according to the nature of PO (i.e. psychological, physical or care-related outcomes), the nature of empathy (i.e. empathy as a whole with the three empathic processes or not), the quality of studies (i.e. the estimated risk of bias), the bivariate vs multivariate analyses, the curative vs palliative situation, and patient-reported outcomes vs objective outcomes (i.e. outcomes not reported by patients, see Appendix E for details).

A meta-regression was then performed with the significant moderators of the subgroup analyses as candidate variables (Table 1). To avoid multicollinearity with bad news and because of 18 missing data, the variable “early vs advanced cancer” was not included in the regression. The included variables explained 53% of variance (analogous  $R^2$ ). Prospective design and coding system decreased the ESr, whereas physician-reported empathy and bad news increased it (only a trend for the latter). The result about physician-reported empathy must be taken with caution, as only three studies dealt with physician-reported empathy.

### **Publication bias and other biases**

The funnel plot (Figure 3) is asymmetric, i.e. there is a larger ES in smaller studies.

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Although Kendall's tau (Begg and Mazumdar method) did not reveal a rank correlation between ESr and sample sizes (non-significant  $p$  value), Egger's test yielded a statistically significant  $p$  value. We cannot preclude a small-study effect. More precisely, in the funnel plot, the smallest studies (i.e. high standard errors) tend to cluster toward the right side of the plot. Various reasons can explain the asymmetry, one of which is publication bias. If publication bias was indeed the reason, it would make sense to impute the missing studies and compute an adjusted ESr, which would be 0.13, 95% CI [0.08 to 0.17], using the trim and fill method. However, this result must be taken with much caution as the trim and fill method can underestimate the true positive effect when there is large between-study heterogeneity, which is the case, and when there is no publication bias<sup>23</sup>. Furthermore, the cumulative meta-analysis based on the 28 most precise studies (i.e. the half of all studies with the smaller standard errors) yielded an ESr of 0.23, 95% CI [0.17 to 0.28], identical to the final ESr for all studies, and the ESr remained the same with the inclusion of the 27 less precise studies. Hence, the cumulative meta-analysis did not indicate a small-study effect.

Taking all these results into account, a small-study effect is possible (funnel plot) but not likely (cumulative meta-analyses). If this effect existed and was due to publication bias, the true ESr would be smaller than our ESr.

As reported in Appendix B (column "ES missing"), biases were also present in the seven studies that either used stepwise regression methods, excluding non-significant effects, or did not show non-significant results or all ES<sup>24-29</sup>. However, a sensitivity analysis that excluded these studies was performed and it did not change the result. On the contrary, in two studies<sup>30,31</sup>, we entered in the meta-analysis ESr that were certainly smaller than the actual ESr (see Appendix B for explanation), but their removal (i.e. sensitivity analysis) also did not change the result.

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Finally, the quality of studies assessed using the AXIS tool was on average 14.7 with a standard deviation of 2.61, a minimum of 9 and a maximum of 20, with median = 15 (Appendix F). Of the 20 items, the most frequent issues were the lack of justification of sample sizes; the lack of information on non-responders and, when possible, the description of the non-response bias; and insufficient description of methods (including statistical methods) and basic data to describe the samples. The last issue was striking with, for example, 44% of missing data concerning the treatment aim (curative vs palliative) and 33% concerning the cancer stage (Appendix C). Many articles also did not report the number of physicians involved, and the cluster effect for physicians was not statistically accounted for (i.e. no multilevel analyses). However, as reported in the moderator analyses (Appendix E), the quality of studies did not impact the meta-analytic result. We also performed a meta-analysis with the 25 ESr extracted from studies whose quality was above the median, and this did not change the results: mean ESr = 0.22, 95% CI [0.15 to 0.29], and prediction interval 95% CI [-0.12 to 0.51].

## Discussion

This is the first meta-analysis to assess the association between PE and cancer PO. PE was associated with favourable PO with an ESr of .23. Considering the field of PE rather than an arbitrary threshold, the ESr of .23 is much higher than what was found in a previous meta-analysis on PE<sup>32</sup> in various medical contexts in which the standardised mean difference between empathic and non-empathic physicians was .18 on various PO. Indeed, our ESr of .23 would correspond to a standardised mean difference of 0.47. To give further perspective, a meta-analysis performed in psychotherapies found a correlation between psychotherapists' empathy and PO of .28<sup>14</sup>. Although the latter correlation is higher than ours, the difference is not too large.

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Most important, heterogeneity was high, with a prediction interval (95% CI) from -0.07 to 0.49. Even if this heterogeneity was rather well explained by the subgroup analyses and the meta-regression, efforts should continue to understand the conditions under which empathy can help patients. As hypothesised, PE was most strongly associated with PO in bad news and with advanced patients. Accordingly, empathy should be a priority in these contexts. However, because of the high emotional load of bad news, physicians may be tempted to hide themselves behind medical issues in order to avoid addressing patients' emotions, as well as their own. Thus, physicians need to first regulate their own emotions in order to remain emotionally available for patients without becoming distressed themselves<sup>33</sup>. Indeed, medical empathy implies a genuine concern for patients along with a willingness to support them but not a *sharing* of their emotions, which would be distressing and is not what is expected by the patients themselves<sup>1</sup>. Another important result was that the strongest association between PE and PO was for patient-reported assessments of empathy. On the one hand, the results of the PE-PO link, between empathy assessed by patients, physicians, or researchers cannot be attributed to the way empathy is assessed, since empathy is not defined and measured in the same way in these different groups. On the other hand, patient-reported empathy was expected to have the strongest effect, because the effect of empathy on patients could not occur if the empathy was not felt or perceived by the patients themselves. Furthermore, patient-reported outcomes share variance with patient-reported PE as both variables are reported by patients. This can explain the larger associations in patient-reported empathy compared to coding systems. This result might be amplified with "patient satisfaction" as outcome as in two<sup>26,34</sup> out of the seven articles that dealt with "patient satisfaction", satisfaction comprised items very close to empathy. However, the fact that empathy coded by researchers showed no association with PO raised some concerns for research and clinical recommendations. Indeed, it means that the current tools used by researchers do not well

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grasp the elements of empathy that are important for patients and thus PO. According to patients<sup>1,2</sup>, the most important elements of empathy are relationship sensitivity (i.e. general sensitivity, listening, care and compassion) and a focus on the whole person (i.e. attention to what matter most to patients, understanding and attention to emotions). However, the coding systems, mostly the Roter Interaction Analysis System in the 10 samples that used coding systems in this meta-analysis, are mainly oriented to how physicians respond to patients' emotions, and therefore may not detect other important elements such as a genuine interest in patients. Furthermore, three intertwined elements may ameliorate the predictive power of coding systems: (1) the timing of empathy within the consultation, (2) the function of physician behaviour (why the physicians behave the way they do, what is their *intention*?) and (3) patients' reaction to physicians' behaviour. Regarding the timing of empathy, the study of Eide et al. (2003)<sup>34</sup> showed that empathy is associated with patient satisfaction only in the counselling phase of the consultation and not in the history taking or examination phase of the consultation. Future studies should consider the timing of empathy. Regarding the function of physician behaviour, even if patients disclose some emotions, their need may be to receive medical information and not to have their emotions addressed *immediately*. If physicians grasp this patient need and do not respond to patient emotion purposely but take time to clarify medical points, they might be deemed not empathic by coding systems, whereas they would be from the patient's perspective. Finally, the patient's reaction to physician response to their emotion should be the first point of attention. Indeed, it will be the best assessment of whether physician response was relevant for the patient. The physician's response to the patient's emotions is not a sufficient indicator of the PE. Empathy cannot be well assessed by using pre-formatted theories about what is empathic or not. For example, naming an emotion and praising patients are coded as empathetic in the NURSE coding system whereas in cases of bad news, it is deemed as inappropriate<sup>13</sup> respectively because the emotion is obvious and

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because patients feel so bad that praise does not fit their psychological state. Therefore, the patient's reaction, rather than only the physician's behaviour, will be of help to assess PE in a more iterative and realistic manner. In this regard, artificial intelligence may be a precious tool in the future to code this iterative process along with non-verbal (e.g. prosodic features) and physiological reactions (e.g. cortisol secretion) of both clinicians and patients<sup>35</sup>. Physician gender should also be considered, as a recent study showed that verbal empathy statements were linked to higher patient satisfaction only when the physician was male<sup>36</sup>.

We did not find any differences in the ESr according to the nature of empathy. Only the studies that comprised *at least* the emotional process of empathy (i.e. a genuine interest in and a full understanding of the patient, genuine care and compassion) were included in the meta-analysis. Thus, the emotional process seems to be most important for patients, regardless of the presence of the other two processes (establishing a good rapport and the cognitive process). Furthermore, the three processes are highly correlated<sup>16</sup> so that in most cases, it is likely that the emotional process occurs with the other two even if the latter two are not assessed. However, for future research, we still recommend considering the precise nature of empathy in order to inform theory and practice about the processes that might be most helpful for patients according to the medical context. For example, a study by Lelorain et al. (2018)<sup>37</sup> revealed that in bad news consultations, emotional and relational processes of empathy predicted a *higher* risk of death whereas the cognitive process did not. Although this result needs to be replicated, it suggests that in specific contexts, too much emotional empathy can convey hopelessness to patients. In distinguishing between the different types of empathy, however, other distinctions might prove more useful, such as that between perspective taking or emotional resonance. Moreover, what we have called "cognitive empathy" can be criticized as being not empathy but patient empowerment.

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Finally, the 12 prospective studies revealed a lower ESr than the cross-sectional studies did. Some methodological issues could explain this result. With the exception of two studies that assess patients across the cancer trajectory<sup>29,38</sup>, all the other prospective studies tested the association between PE in a specific encounter or period and PO 3 or 6 months later. So many things can happen and be heard by patients in a 3- or 6-month period of cancer that it is difficult to assume an impact of PE on PO during such a long time. However, should this result be confirmed in future longitudinal research by using a rigorous method, it would call into question the assumed causality of the link between PE and PO. Indeed, we assume that PE can alleviate PO, but the reverse might be true: the patient's physical and psychological well-being may also influence their perception of PE. PE and PO might also be independent, but both affected by a third variable such as patient personality or attachment. In order to properly clarify the causality, longitudinal studies with several assessments of PE and patients' state at key points in the cancer pathway (e.g. diagnosis, treatment, end of treatment, recurrence, entry into palliative care) are warranted. The *change* of the perceived empathy by patients during the disease trajectory may also be informative and has not yet been explored. For example, if a physician who was deemed very empathetic at the beginning turned out to be less empathetic at recurrence, PO could be severely affected despite a rather high average level of empathy.

### **Clinical implications**

Empathy can no longer be considered a mere "bonus" in patient care. Our findings show that it is a real necessity for patient health, especially for advanced patients or in bad news. In 13 studies, the ESr was higher than .40, showing the large effect empathy can have on patients. Therefore, empathy training should be better developed in medical education, fully integrated into clinical training, and started at the beginning of medical education and continue throughout it. As bad news is emotionally difficult to handle for physicians, emotion

regulation training is required to help them to cope with bad news. Nurses could be more involved in the delivery of bad news for the benefit of patients and physicians. In addition, patients' perceptions of empathy, rather than external assessments of empathy, should be the gold standard. Therefore, physicians could ask patients for feedback on their perceptions of communication and empathy. In this way, they could immediately clarify emotional misunderstandings and become more attuned to patients' needs.

### **Limitations and perspectives**

The lack of information provided in the studies hinders the test of moderators. In particular, the aim of treatments (palliative or curative), the cancer stage, patients' ethnicity and marital status, and information about the physician(s) such as gender or medical specialties are crucial pieces of information to record. Environmental information (e.g. workload, bureaucracy) could also inform the PE-PO link. Another limitation is the over-representation of women in the samples. Only 9% of samples included a large majority of male patients. Future studies with men are warranted to make sure that the results of this meta-analysis remain valid for men. The inclusion of more minorities, patients with a lower education and isolated patients is also warranted, as PE is particularly expected and important for these individuals. Finally, interesting perspectives would be gained from studies using mixed methods (quantitative and qualitative data). Interviews with patients would be insightful to understand how they rate the empathy of their physician(s) and would provide data on the specific elements patients consider to form their judgement. Related to this last comment, it must be acknowledged that the empathy concept presents important challenges in medical settings. It is likely that patients judge their physicians to be empathetic when they are kind, thoughtful and thorough. Even in the CARE questionnaire, only two out of the 10 items really bear on empathy ("fully understand your concerns" and "showing care and

compassion”). Thus, it is possible that our meta-analysis pertains as much to the physician's kindness and caring as it does to their empathy in the purest sense.

## Conclusion

At a time when cancer care is becoming more and more technical, robotised and organised into increasingly narrower specialties, PE is of utmost importance. Indeed, this radical change of medicine should not be at the expense of patient care. In the midst of medical imaging, cutting-edge medical advances and a growing variety of medical practitioners, which inevitably complexifies coordination and continuity of care, patients more than ever need empathy and support. The results of the meta-analysis show that this claim for empathy is not a humanistic fad, but a real need for patient health and quality of care.

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## Appendix A. Electronic database search strategy

Database	Keywords	Limiters
Academic Search Premier, PsycINFO, PsycARTICLES	(Cancer (ab) OR oncolog* (ab) OR palliat* (ab)) AND (doctor* (ab) OR physician* (ab) OR nurse* (ab)) AND (empath* (ab) OR communication (ab) OR compassion (su) OR caring (su) OR perspective taking (ab) OR role taking (ab)) AND patient* (ab)	French or English; 01/1990 to 11/2022; Adults; Humans; Peer-reviewed.
COCHRANE LIBRARY	((cancer (ab) OR oncolog* (ab) OR palliat* (ab)) AND (doctor* (ab) OR physician (ab) OR nurse* (ab)) AND (empath* (ab) OR communication (ab) OR caring (ab) OR compassion (ab) OR perspective taking (ab) OR role taking (ab)) AND patient*(ab) AND outcome*	01/1990 to 11/2022; Words variations not searched
MEDLINE	(cancer OR oncolog* OR palliat*) AND (doctor* OR physician* OR nurse*) AND (empath* OR communication OR caring OR compassion OR relation* OR perspective-taking OR role-taking )  (cancer [Title/Abstract]OR oncolog* [Title/Abstract]OR palliat*[Title/Abstract]) AND (doctor* OR physician* OR nurse*) AND (empath* [Title/Abstract]OR communication [Title/Abstract]OR caring [Title/Abstract]OR compassion [Title/Abstract]OR relation* [Title/Abstract]OR perspective-taking [Title/Abstract]OR role-taking)	Age: 19+; French or English; 01/1990 to 06/2018; Humans; Abstract available.  Age: 19+; French or English; From July 2018 to November 2022; Humans; Abstract available.
OPEN GREY	(Cancer (ab) OR oncolog* (ab) OR palliat* (ab)) AND (doctor* (ab) OR physician* (ab) OR nurse* (ab)) AND (empath* (ab) OR communication (ab) OR compassion (ab) OR caring (ab) OR relation* (ab) OR perspective taking (ab) OR role taking (ab)).	No limiters.
SCOPUS	((cancer (ab) OR oncolog* (ab) OR (palliat* (ab)) AND (doctor* (ab) AND physician* (ab) OR nurse* (ab)) AND (empath* (ab) OR communication (ab) OR relation* (ab) OR perspective-taking (ab) OR role-taking (ab) AND patient* AND outcome*	1990-2018; French or English; Review conference paper; Article in press; Conference Review; Short Survey
WEB OF SCIENCE	((cancer (tp) OR oncolog* (tp) OR (palliat* (tp)) AND (physician* (tp) OR nurse* (tp)) AND (empath* (tp) OR communication (tp) OR compassion (tp) OR perspective-taking (tp)) AND patient* AND outcome*  ((((TI=(cancer OR oncolog*))) AND AB=((physician* OR doctor* OR radiolog* OR surgeon*))) AND AB=(empath* OR communication OR compassion)) AND AB=(patient*)) AND ALL=(outcome)	1990-2018; French or English; Article; Review; Proceedings paper; Meeting abstract; Book review.  From July 2018 to November 2022; French or English; Article; Review;

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Note. The keyword “Nurses” was used to avoid missing studies that included both physicians and nurses but with separate analyses for each profession (Von Essen et al., 2002; von Gruenigen et al., 2006).

## Appendix B. Choices made in the case of multiple effect sizes (ES) and ESr (effect size correlation) computations

Study identification	Outcomes or ES in the publication	Decision: chosen outcome or detail of computation	Justification of the decision (if needed)	ES missing (i.e. non-significant results not reported in the paper or simple effects for a significant interaction)	Controlled variables	Available data → Computations and/or ES used to obtain correlations (ESr) in CMA. If necessary, the data entry mode in CMA is specified between quotation marks. → If done, “correction for dichotomisation” is added
Albrecht et al., 1999 <sup>39</sup>	Accrual in RCT			No	No	Means and SDs of 2 dimensions of empathy “Connection” and “Physician responsiveness to patient’s concerns” are given for each group of “non-accrued” and “accrued” patients (Table 3 of the article) “Independent groups (means, SD)”
Arora & Gustafson, 2009 <sup>40</sup>	Trust in a longitudinal survey with ES reported at baseline, 2-month and 5-month FU	5-month FU	Most distance time retained	No	Patients’ age, race, income, education, living status and insurance status, days since diagnosis, stage of cancer, type of	Standardised regression coefficient (Table 2) transformed into correlation. Corrected for dichotomisation

					surgery before baseline, receipt of adjuvant therapy before baseline, and trust at 2 months	
<b>Cao et al., 2017</b> <sup>41</sup>	Hope (psychological outcome) Trust in physician (care-related outcome)	Hope	Psychological issues are prioritised over care-related issues	No	Education, health, income, support from family, information support, personalised disclosure, discussion of multiple treatment plans, and key disclosure person	Hierarchical multiple regressions with standardised coefficients (Table 3) transformed into correlation Corrected for dichotomisation of empathy
<b>Chen et al., 2008</b> <sup>30</sup>	BC knowledge			Yes, simple effects of an interaction not fully reported (i.e. standard errors are missing)	Age, sex, education, married, regular source of care, health, comorbidity, treatments, and various variables related to BC knowledge	Unstandardised multiple regression coefficient with SE (Table 4). “Raw differences (independent groups) SE” Corrected for dichotomisation of empathy
<b>Chen et al., 2022a</b> <sup>42</sup>	Psychological distress Self-care efficacy (i.e. positive attitude, stress reduction and decision making)	Average of the 2 ES	Homogeneous outcomes related to psychological issues	No	No	Standardised B for self-care efficacy (Table 3) and OR and 95%CI for distress (Table 4)

<b>Chen et al., 2022b</b> <sup>43</sup>	Anxiety and depression	Average of the 2 ES	Homogeneous outcomes related to psychological issues	No	No	Correlations (Table 2)
<b>Dong et al., 2014</b> <sup>44</sup>	Trust, satisfaction, authentic self-representation (i.e. how patient is genuine in the expression of concerns and questions), and anxiety.  Empathy is assessed by using both a patient-reported measure and a coding system.	Anxiety  Coding system	Psychological issues over care-related issues  Coding is prioritised, as there are fewer researches using coding systems.	No	Radiation therapist experience	Unstandardised regression coefficients with SD (multilevel analysis in Table 5 and descriptive statistics in Table 3)
<b>Eide et al., 2003</b> <sup>34</sup>	Correlation between empathy and satisfaction during: <ul style="list-style-type: none"> <li>- the history-taking phase of the consultation</li> <li>- the clinical examination phase of the consultation</li> <li>- the counselling phase of the consultation</li> </ul>	ES during the counselling phase. ES could be given for each phase of the consultation, but it is not clear whether empathy is delivered in only one phase of the consultation, which	Empathy is tested in interaction with the consultation phase Empathy was: <ul style="list-style-type: none"> <li>- not associated with satisfaction during history taking</li> <li>- negatively associated during clinical examination</li> <li>- positively association</li> </ul>	No	No	Correlations (Table 3)

		precluded independence of observations	during the counselling phase			
<b>Ernstman et al., 2017</b> <sup>38</sup>	Global HRQoL and all functional domains of QoL of the QLQ-C30	Global HRQoL	It summarises all information	No	Risk of progression, comorbidity, age, live with someone and time points within patients (multilevel analyses)	Unstandardised group-mean centred coefficients at the patient level (longitudinal multilevel analysis in Table 3). Standardisation is performed with the retrieved SD in Table 2, and then B are transformed into correlations.
<b>Ernstman et al., 2019</b> <sup>45</sup>	Prostate-specific HRQoL subscales: incontinence aid, urinary symptoms, bowel symptoms, hormonal treatment-related symptoms, sexual activity and sexual functioning	Average	Homogeneous outcomes related to physical functioning	No	Charlson index of comorbidities, age, live with someone, risk of cancer progression	Unstandardised group-mean centred coefficients at the patient level (longitudinal multilevel analysis in Table 2).
<b>Farin &amp; Nagl, 2013</b> <sup>24</sup>	FACT scales and SF-12 physical and mental components at the end of rehabilitation and at 6-month FU. However, all results are not available, as the authors chose a stepwise method of variable inclusion (no ES available at 6-month FU). ES reported are for social well-being, functional well-being and mental component of the SF-12.	Change in functional well-being between the start and the end of rehabilitation	Physical outcomes (i.e. functional well-being here) prioritised over psychological outcomes.	Yes	Various sociodemographic, medical and psychological variables	Unstandardised coefficients at the patient level (multilevel analysis in Table 4). Standardisation is performed with the retrieved SD in Tables 2 and 3, then B is transformed into one correlation
<b>Fröjd &amp; Von Essen, 2006</b> <sup>25</sup>	Satisfaction with the consultation Hope to live a good life despite the disease	Satisfaction	Hope data not reported as non-significant	Yes	No	Values and <i>t</i> test with <i>df</i> for empathy between patients who found the consultation “very satisfying” vs

						“satisfying” (p. 376 in the text). R is then computed from <i>t</i> test and <i>df</i> .
<b>Geessink et al., 2018</b> <sup>46</sup>	Patients’ perception of involvement in the decision-making process			Yes, due to backward procedures + SD of empathy not provided		Impossible to compute ESr due to backward procedures and lack of SD: not included in the meta-analysis
<b>Gehenne et al., 2021</b> <sup>17</sup>	Severity of medical and surgical complications after esogastric surgery (No complication vs minor or major complications)	Major complications	The impact of major complications is stronger for patients	No	Age, gender, distress, obesity, tumor differentiation, tobacco, alcohol, physical status and type of surgical approach	OR and 95%CI (Table 3)
<b>Grant et al., 2000</b> <sup>47</sup>	Accrual in RCT			No	No	Means and SD of empathy for both groups: declined or agreed to trial (Table 2). “Independent groups (means, SD)”
<b>Grassi et al., 2015</b> <sup>48</sup>	Incidence of nausea Impact of nausea on life	Average of the 2 ES	Homogeneous outcomes related to physical well-being	No	Age, sex, age, chemotherapy, distress, coping, and patient perception of physician attitude as only interested in medical issues	OR and 95% CI (Online Table 2). “OR, lower and upper limits, CI”.
<b>GroB et al., 2015</b> <sup>49</sup>	Fear of recurrence, ES: - high empathy vs poor empathy - very high empathy vs poor empathy	Average of the 2	Backward regression analyses were	No	Age, sex, education, employment	Standardised regression coefficients (Table 2)

			used. In the final model, only 'very high empathy' still remained. However, before the reduced final model, a full model presented all ES. We used the full model to average the 2 ES.		status, social support, recurrence and secondary tumour, duration of consultation and comprehensibility of information	
<b>Ishikawa et al., 2002a</b> <sup>†50</sup>	Emotional expression Information giving Question asking	Average of the 3	Homogeneous outcomes about patient expression during consultation	No	No	Correlations (Appendix A)
<b>Ishikawa et al., 2002b</b> <sup>†51</sup>	Satisfaction with the medical interview			No	Age, sex, education, physical status, family presence, length of consultation and whether examination results were received	Z scores (Table 5) are transformed into ESr by using $r = \sqrt{(z^2/N)}$
<b>Kuroki et al., 2013</b> <sup>52</sup>	Satisfaction with diagnosis			No	No	P-values and sample size (Table 3)

<b>Lelorain et al., 2018a</b> <sup>†12</sup>	One single outcome, emotional QoL (eQoL), but 6 ES reported for the link between empathy and eQoL: <ul style="list-style-type: none"> <li>- in BN for 3 types of patients: patients with low, middle, and high emotional skills</li> <li>- in FU for the same 3 types of patients</li> </ul>			No	No	Correlations retrieved from our own database
<b>Lelorain et al., 2018b</b> <sup>†37</sup>	Overall patient survival			No	Age, sex, education, financial situation, type and severity of cancer, comorbidities, genetic mutations, metastases, emotional distress and emotional skills	Adjusted Cox Proportional Hazard Model for overall survival (Table 3)
<b>Lin et al., 2014</b> <sup>53</sup>	Stage-appropriate treatment			No	No	Raw data given in Table 2 allowing computation of OR that are transformed in Fisher's Z by CMA
<b>Loge et al., 1997</b> <sup>54</sup>	Satisfaction with diagnosis			No	No	Correlation is given in the text (p. 880).
<b>Mack et al., 2009</b> <sup>55</sup>	Patient-reported psychological states, i.e. feeling depressed, terrified about the future, psychological symptoms, emotional acceptance of terminal illness, existential well-being Emotional-based coping, avoidant coping, active coping	Average of all these ES to compute a "Global HRQoL" score	The idea of this study is to give a picture of patients' state at the end of life. The average gives a global	No	No	Correlations (pp. 5 and 6)

	Functional status Caregiver-rated quality of patient death		picture of the link between empathy and patient-related variables.			
<b>Maly et al., 2004</b> <sup>56</sup>	Questioned the surgeon Perceived final decision-maker as himself or herself	Average of the 2 ES to create “Participation in treatment-decision making”		No	Financial adequacy, education, cancer stage, comorbidity and social support. Surgeon effect (multilevel analyses)	OR and CI (Table 4)
<b>Martinez et al., 2016</b> <sup>57</sup>	Only one outcome, but an ES relates to the oncologist and another to the surgeon	Average of the 2 ES	There is no reason to prioritise one type of physician over another one	No	Race, education, comorbidities, age, self-reported health status, cancer stage, treatment, hormonal receptor status, hospitals (2 hospitals), communication style preference	Estimates and SE in Tables 2 and 3 for dichotomised empathy using the median; hence, corrected for dichotomisation
<b>Neumann et al., 2007</b> <sup>†58</sup>	Non-significant paths are <i>not</i> available, which biases the results.  <i>Direct</i> effects available for the links between physician empathy and patient “desire for more information” (DFMI):	Indirect effects are retained.	Only psychological issues are available: Depression and socio-emotional-cognitive QoL	Yes	Social support, patient-perceived busyness of physicians and nurses, and all variables listed in the left cell of this	Standardised regression coefficients (Table 6)

	<ul style="list-style-type: none"> <li>- from physician about findings and treatment options</li> <li>- from physician about side effects and medication</li> <li>- about health promotion</li> </ul> <p><i>Indirect</i> effects available:</p> <ul style="list-style-type: none"> <li>- PE -&gt; DFMI about findings and treatment options -&gt; depression</li> <li>- PE -&gt; DFMI about findings and treatment options -&gt; QoL socio-emotional-cognitive</li> <li>- PE-&gt; DFMI about health promotion -&gt; depression</li> <li>- PE-&gt; DFMI about health promotion -&gt; depression</li> <li>- QoL socio-emotional-cognitive</li> </ul>				row (desire for information, etc.)	
<b>Neumann et al., 2011</b> <sup>59</sup>	<p>Compared with the reference class ‘no unmet needs’, odds of patients being in 1 of the 4 possible classes, i.e., patients have:</p> <ol style="list-style-type: none"> <li>1. psychosocial unmet information needs</li> <li>2. medical unmet information needs</li> <li>3. both psychosocial and information unmet needs</li> <li>4. psychosocial unmet information needs, especially about social issues</li> </ol>	Average of the 4 ES		No	No (medical and sociodemographic variables are considered, but in separate models)	OR, Wald and <i>p</i> -value (Table 6) Coefficients are retrieved (log OR) and SE also using Wald = $(B/SE)^2$ “OR log and SE log”



<b>Nielsen et al., 2013</b> <sup>60</sup>	Decision self-efficacy Self-efficacy for coping with cancer	Average	Homogenous in psychological outcomes	No		Standardised regression coefficients (Table 3) transformed into correlations
<b>Ong et al., 2000</b> <sup>26</sup>	Physical distress, psychological distress, global QoL Global satisfaction Visit-specific satisfaction Two time points, after 1 week (T1) and 3 months (T2)	Visit-specific and global satisfaction	Non-significant ES are missing. Available correlations are for visit-specific satisfaction and global satisfaction at T2 (average of the 3 available ESr).	Yes		Correlations (Table 1)
<b>Pozzar et al., 2021</b> <sup>61</sup>	HRQoL total score and all subscales Symptom burden	HRQoL total score		No	No	Standardised regression coefficients (Table 3) transformed into correlations
<b>Ptacek &amp; Ptacek, 2001</b> <sup>62</sup>	Satisfaction with BN delivery			No	Other items of the patient-centred factor of the patient-reported questionnaires (items not given due to non-statistical significance)	OR and 95% CI (Table 2) Corrected for dichotomisation of satisfaction
<b>Roberts et al., 1994</b> <sup>63</sup>	Psychological distress			No	Psychiatric history and premorbid life stressors	Correlation (Table 2)

<b>Schofield et al., 2003</b> <sup>27</sup>	Satisfaction, anxiety and depression related to: <ul style="list-style-type: none"> <li>- Diagnosis disclosure</li> <li>- Prognosis discussion</li> <li>- Treatment options</li> </ul> and for each theme (e.g. diagnosis disclosure) at baseline, 4 months and 13 months	Anxiety and depression at 13 months	Empathy is not a candidate variable for prognosis and treatments (reasons unclear for this choice in the publication). Prioritisation of psychological issues over care: satisfaction not retained. Longer time prioritised	Unsure due to unclear reasons (see left cell)	No	Scores of anxiety and depression for empathic vs non-empathic physicians (Table 1) and <i>p</i> -value in the text (p. 54)
<b>Senft et al., 2018</b> <sup>64</sup>	Oncologist-patient centeredness, trust in oncologist, confidence in recommended treatments	Average of trust and confidence	Homogenous in care outcomes. Oncologist-patient centeredness is an outcome in the study, whereas it must be a predictor in the meta-analysis and therefore discarded.	No	No	Correlations (Table 3)
<b>Sikavi &amp; Weseley, 2017</b> <sup>65</sup>	Trust in oncologist Satisfaction with the oncologist Medication adherence	Average the 3 ES	Homogeneous in care outcomes	No	No	Correlations (Table 2)

<b>Siminoff et al., 2000</b> <sup>66</sup>	Patient knowledge about treatments and decisional regrets	Average	Homogeneous in care outcomes. However, average is unfortunate, as it hides that empathy is associated with fewer regrets (i.e. <i>favourable</i> outcome) but also with less knowledge (i.e. <i>unfavourable</i> outcome)	No	No	Raw data: number of patients whose knowledge is correct for empathic vs non-empathic physician (Table 2) and number of patients with and without regret for empathic vs non-empathic physicians (Table 3)
<b>Simmons &amp; Lindsay, 2001</b> <sup>67</sup>	Adherence			No	No	OR, SE, Wald (Table 1)
<b>Singer et al., 2016</b> <sup>68</sup>	Acute, emerging or chronic psychiatric conditions and psychiatric conditions at any point in time between surgery and completion of adjuvant treatment	Average of all ES		No	Age, education, employment status, partnership status, QoL, cancer in family or own history, somatic comorbidity, Nottingham Prognostic Index (i.e. assessment of the risk of dying)	OR and 95% CI (Table 3)

<b>Smith et al., 2011</b> <sup>69</sup>	Post-consultation anxiety, decisional conflict, satisfaction with (a) decision, (b) consultation and (c) doctors' shared decision-making skills	Anxiety	Psychological outcomes prioritised over care outcomes	No	No	Correlations (Table 4)
<b>Step et al., 2009</b> <sup>28</sup>	Communication involvement and decision regret	Average	Care outcomes	Yes. We averaged the 2 correlations, whereas the hypothesised theory was a mediation model (empathy-> more patient involvement-> fewer regrets), but data are not presented for mediations as they "did not support the mediation hypothesis".	No	Correlations (Table 4)
<b>Takayama et al., 2001</b> <sup>31</sup>	Satisfaction with the encounter Anxiety	Anxiety	Psychological outcomes prioritised over care-related outcomes	No	Sex, age and education level	<i>P</i> -values and <i>n</i> given (Figure 1). Exact <i>p</i> -values not given so that <i>p</i> -values are set to .05, which is likely to underestimate the actual ES.
<b>Takayama &amp;</b>	Participation in consultation			No	No	Correlations (Table 5)

<b>Yamazaki, 2004<sup>70</sup></b>						
<b>Tomai &amp; Lauriola, 2022<sup>71</sup></b>	Trust in physician			No	No	Correlations (Table 6)
<b>Trevino et al., 2014<sup>72</sup></b>	Suicidal ideation			No	No	OR and 95% CI (Table 1) Corrected for dichotomisation of the empathy score
<b>Trudel et al., 2014<sup>29</sup></b>	All dimensions of HRQoL	Average	However, in multivariate analyses, only significant predictors were retained and presented. They concerned sexual functioning and arm symptoms.	Yes	Time (longitudinal data), clinical data, age, education, marital status, family income, social support, disease stage and type of treatment, and dimensions of communication with the physician	Exact <i>p</i> -values and <i>n</i> (Table 1)
<b>Von Essen et al., 2002<sup>73</sup></b>	Every scale of the EORTC QLQ C-30 and anxiety and depression	Average	Average of those ES to compute a “Global HRQoL” score	No	No	Correlations (Table 4)
<b>Von Gruenigen et al., 2006<sup>74</sup></b>	Severity of symptoms during palliative chemotherapy			No	No	Correlations (in the text)
<b>Westendorp et al., 2021<sup>75</sup></b>	Patient information recall (i.e. treatment options, aims of treatment and side effects)			No	No	Unstandardised coefficients (Table 3) and SD in Table 2

						and in the text p. 1111 for empathy
<b>Yanez et al., 2012<sup>76</sup></b>	HRQoL in Latinas and non-Latinas (i.e. White) patients at time 2 (mental and physical) + BC concerns and emotions	Average		No	No	Correlations (Table 3)
<b>Yang et al., 2018a<sup>77</sup></b>	Anxiety, self-efficacy, perception of being stigmatised, and natural killer (NK) cells	NK cells	Physical outcomes prioritised	No	No	Correlations (Table 4)
<b>Yang et al., 2018b<sup>78</sup></b>	Self-efficacy, perception of being stigmatised, and natural killer (NK) cells	NK cells	Physical outcomes prioritised	No	No	Correlations (Table 4)
<b>Zachariae et al., 2003<sup>79</sup></b>	Satisfaction with personal contact Satisfaction with handling of medical aspects Change in total distress, self-efficacy and perceived control after the consultation	Average of the 3 ES about distress, self-efficacy and perceived control	Psychological outcomes prioritised over care-related outcomes	No	No	Correlations (Table 2)
<b>Zhou et al., 2019<sup>80</sup></b>	Thought of dropping out and intention to complete the clinical trial Patient trusts that researcher knows what is best for them	Average of the 3 ES	Homogeneous in care outcomes.	No	No	<i>t</i> statistics and correlation (Tables 1 and 4)

*Note.* The tables indicated in the last column are the tables of the original publications. † Neumann et al., 2007 and 2011, Ishikawa et al., 2002a and 2002b, Ernstmann et al., 2017 and 2019, as well as Lelorain et al., 2018a and 2018b are two analyses of the same samples, so that we present the results all publications here, but have included only Neumann et al., 2011, Ishikawa et al., 2002b, Ernstmann et al., 2017 and Lelorain et al., 2018a in the meta-analysis to comply with the rule of independence of observations. A sensitivity analysis revealed that these choices did not change the results. When needed, unstandardised coefficients were transformed into standardised coefficients by using the formula “standardised coefficient = (unstandardised coefficient × standard deviation of X)/standard deviation of Y)” or into partially standardised for dichotomous predictors (i.e. only standardization of Y). When primary studies used artificial dichotomisation of a continuous variable, a correction was

performed as recommended by Card (2016, page 136). Card NA. *Applied Meta-Analysis for Social Science Research*. Reprint edition. The Guilford Press; 2016. When only multivariate results were available, this was recorded and tested as a moderator (see Appendix E). When studies included more than one time-point assessment, data collected at the furthest time-point were collected. When several outcomes were reported, ES for outcomes of the same nature were averaged. For example, depression and anxiety outcomes could be averaged, as they both represent psychological outcomes. When outcomes of different natures were provided, physical issues were prioritised over psychological issues, and the latter over care-related issues. This hierarchy was chosen in order to maximise the less frequent outcomes in the literature so that we had enough data for the less frequent outcomes to test the nature of the outcome as a moderator. When HRQoL and physical outcomes were both present, HRQoL was chosen to prioritize general outcomes over specific ones. When studies reported several results according to the way empathy was assessed, the same logic was applied: first doctor-reported empathy, then observer-reported empathy, then patient-reported empathy. When empathy was tested in a significant interaction with another variable, if available, the ES were reported for the different categories of the independent variable (e.g. ES reported for men and women separately).

BC = breast cancer, CI = confidence interval, CMA = Comprehensive Meta-Analysis software, DFMI = desire for more information, EORTC = European Organisation for Research and Treatment of Cancer, eQoL = emotional quality of life, ES = effect size, ESr = effect size correlations, FACT = Functional Assessment of Cancer Therapy, FU = follow-up, HRQoL = health-related quality of life, NK = natural killer, OR = odds ratio, PE = physician empathy, QLQ-C30 = European Organisation for Research and Treatment of Cancer Core Quality of Life questionnaire, QoL = quality of life, RCT = randomised controlled trial, SE, standard error, SF-12 = Medical Outcomes Study, Short Form Health Survey.

Accepted

## Appendix C. Overview of the included samples or studies

Characteristics	n (%)
<b>Context of empathy (n = 55)</b>	
Overall, i.e., assessment not related to a specific encounter	26 (47)
BN consultation	10 (18)
Diagnosis	6 (11)
Disease progression	3 (5)
Not specified	1 (2)
FU consultation	6 (11)
Consultation about treatments	10 (18)
Accrual in an RCT	3 (5)
Initial discussion after diagnosis	3 (5)
Adjuvant therapy	2 (4)
Radiotherapy education session	1 (2)
BN and FU without possibility of disentanglement	4 (7)
<b>Type of empathy assessment (n = 55)</b>	
Patient reported	41 (75)
Physician reported	3 (5)
Researchers using coding systems	10 (18)
Patient reported and coding	1 (2)
<b>Nature of empathy (n = 55)</b>	
Emotional process only	16 (29)
Emotional and cognitive processes	7 (13)
Emotional and relational processes	9 (16)
All 3 processes	23 (42)
<b>Nature of the outcome (n = 55)</b>	
Care related	27 <sup>†</sup> (45)
Patient satisfaction	8
Trust in the physician and/or treatments	4
Participation in the consultation	3
Knowledge	2
Information recall	1
Stage-appropriate treatment	1
Regrets about treatments	3
Unmet information needs	1
Treatment adherence	1
Accrual in RCT/intention to remain in RCT	3
Psychological	20 <sup>†</sup> (33)
Distress/anxiety	13
Self-efficacy	2
Hope	1
Fear of recurrence	1
Suicidal idea	1
Psychiatric comorbidities	1
Depression	1
Physical	7 (12)
Sexual functioning and arms symptoms	1
Changes in functional well-being	1
Incidence and impact of nausea on life	1

Severity of symptoms	1
Natural killer cells	2
Major complications after surgery	1
Health-related quality of life	6 (10)
<b>Design of the samples (n = 55)</b>	
Cross-sectional	43 (78)
Prospective	12 (22)
<b>Treatments (n = 55)</b>	
Curative only	24 (44)
Palliative only	2 (4)
Some palliative (i.e., 29% to 38% of patients)	5 (9)
Unknown	24 (44)
<b>Stage of cancer (n = 55)</b>	
No advanced patients at all	9 (16)
Some advanced patients (stage III/IV;metastases)	22 (40)
Advanced patients only	6 (11)
Unknown	18 (33)
<b>Type of cancer (n = 55)</b>	
100% BC	16 (29)
Miscellaneous with a majority of BC	10 (18)
Miscellaneous without a majority of BC	12 (22)
100% Prostate	2 (4)
100% Endocrine	1 (2)
100% Lung	2 (2)
100% Skin	1 (2)
100% Endocrine gastrointestinal	1 (2)
100 % Ovarian, peritoneal, endometria, vaginal	2 (2)
100% Colon	1 (2)
100% Esophagus or stomach	1 (2)
100% Gastrointestinal	1 (2)
100% Male BC	1 (2)
Unknown	4 (9)
<b>Physicians (n = 55)</b>	
One single physician but with different specialties within the same sample (e.g., surgeon, oncologist, GP)	10 (18)
Oncologist	19 (35)
“Physician’s empathy” without more information about the physician	6 (11)
Radiotherapist	1 (2)
Urologist	1 (2)
Surgeon	6 (11)
Physicians, i.e., patients are invited to refer to “physicians” and not to one physician in particular	9 (16)
Research doctor (i.e., the doctor who presented a clinical trial to patients)	1 (2)
Oncologists	2 (4)
<b>Female patients (n = 55)</b>	
0%	3 (5)
0% to 30%	2 (4)
30% to 50%	14 (25)
50% to 90%	16 (29)

90% to 100%	20 (36)
<b>Major ethnicity in the country (n = 55)</b>	
0%	6 (13)
0% to 30%	0
30% to 50%	1 (2)
50% to 90%	11 (21)
90% to 100%	6 (9)
Unknown	31 (55)
<b>Patients who are co-habiting or married (n = 55)</b>	
50% to 75%	21 (38)
>75%	13 (24)
Unknown	21 (38)
<b>Funded studies (n = 55)</b>	
No	9 (16)
Yes	44 (80)
Unknown	2 (4)
<b>Countries of recruited patients<sup>‡</sup></b>	
USA	20 (36)
Germany	6 (13)
Australia	3 (6)
Japan	3 (6)
Denmark	2 (4)
China	5 (9)
Sweden	2 (4)
Norway	2 (4)
France	2 (4)
New Zealand	1 (2)
Netherlands	2 (4)
Italy	2 (4)
Spain	1 (2)
Austria	1 (2)
Canada	1 (2)
United Kingdom	1 (2)

*Note.* † Some studies included more than a single outcome. ‡The sum is more than 55, as some samples come from different countries. BC = breast cancer, BN = bad news, FU = follow-up, GP = general practitioner, RCT = randomised controlled trial.

## Appendix D. Summary of included studies

Study country	Who assessed empathy?	Empathy test, reliability and dimension	Participants: number of patients (% of women)/physicians Type and number of physicians; patients' ethnicity and marital status are given when available	Type of cancer/% of advanced cancer (described according to available information) Ethnic minorities	Nature of the outcomes → Classification	Does empathy refer to a specific encounter?	Longitudinal or prospective design?	ESr <sup>§</sup> (standard error)	Interaction tested
Albrecht et al., 1999 <sup>39</sup> USA	Researchers	Ad hoc (a coding system coined "Moffitt Accrual Analysis System" was developed by the authors: "Connectedness/closeness, warm relationships between physician and patient" "Responsiveness to patients' concerns", Kappa average = .67) ER	48 (76%) / 12 oncologists 94% White patients	Unknown/ Unknown	Accrual to RCT → Care	Yes, about the proposed RCT	No	0.48 (0.12)	No

<b>Arora &amp; Gustafson, 2009<sup>40</sup></b> USA	Patients	Ad hoc (2 questions about physician emotional support, $\alpha$ not provided) EE	246 (100%) 74% White and 82 live with someone	BC/20% stage III and IV	Trust in the physician → Care	No	No	0.51 (0.07)	No
<b>Cao et al., 2017<sup>41</sup></b> China	Patients	Ad hoc (4 questions: During the diagnosis, my doctor “encouraged me to have confidence”, “comforted me”, “told me stories of cancer survivors”, “told me how to face the disease”, $\alpha = 0.85$ ) EC	192 (57%)/100	Lung (33.3%), BC (39.1%), other (26%)/39.6% “late stage”	Hope → Psy	Yes, diagnosis	No	0.31 (0.07)	No
<b>Chen et al., 2008<sup>30</sup></b> USA	Patients	Ad hoc (3 questions: How often did your doctors “allow you to express all of your feelings?”, “show extreme compassion and caring?”, and “listen very carefully to you?”, $\alpha = .91$ ) RE	909 (100%)/participants were directed to answer regarding their “breast cancer doctors” 31% White patients, 49% married	BC/Stages unknown but no metastatic patients	BC knowledge → Care	No	No	0.16 (0.04)	Yes, physician empathy statistically interacted with patient self-efficacy in the communication with physician. Empathy was of greatest benefit for women with low self-efficacy. Unfortunately, standard errors were not given for simple effects, and

<b>Chen et al., 2022a<sup>42</sup> China</b>	Patients	Empathy sub-dimension of the Physician-Patient Communication Scale (PPCS) $\alpha$ between 0.73 and $\alpha = 0.86$ EE	219 (61.6%)/ Nurses and physicians/81 % married	Gastrointestinal cancers (liver, gastric, esophageal, colorectal cancers) (42.47% Stage IV tumor).	Distress -> Psy	Patients complete questionnaires after a chemotherapy session, but empathy seems to be assessed in general	No	0.04 (0.068)	so we used 0.16 (0.04), i.e. the main general effect of empathy No
<b>Chen et al., 2022b<sup>43</sup> China</b>	Patients	Communication Assessment Tool (e.g., “let me talk without interruptions”, “showed care and concern”) $\alpha = .92$ REC	199 (22% of women;92% married)	Lung cancer (32% stage III and 68% stage IV and)	Anxiety/depression → Psy	No	No	0.28 (0.065)	Yes, a three-way interaction is significant for both anxiety and depression. For patients with low levels of disease understanding and low perceived-empathy, symptom burden is associated with anxiety ( $B = 1.10, p < 0.001$ ) whereas

<b>Dong et al., 2014<sup>44</sup></b> <b>Australia</b>	Researchers	Ad hoc derived from previous work of Stewart et al. Six items are defined to observe how physicians introduce the consultation (1 item), inquire and respond to patients' feelings (4 items) and inquire about patients' understanding (1 item). Inter-rater reliability from .80 to .84	55 (46% of women; 59% live with someone)/10 radiation therapists	BC (23%), prostate (16%), gynaecological (11%) colorectal (11%), other (39%)/Unknown	Anxiety change post consultation → Psy	Yes, radiotherapy education session	Yes, anxiety assessed before and just after the consultation	0.33 (0.12) Unfavourable direction	for a high level of perceived empathy, the association is not significant ( $B = 0.18, p = 0.54$ ). Same pattern for depression No
<b>Eide et al, 2003<sup>34</sup></b> <b>Norway</b>	Researchers	RIAS (psychosocial exchange cluster, interrater reliability .73) EC	36 (44%)/4 oncologists	Urological (39%), gastrointestinal (17%), head and neck (22%), BC (17%), other (5%)/42%	Satisfaction with consultation and physician → Care	Yes, a regular outpatient consultation	No	0.33 (0.16)	Yes, this effect, 0.33, only when empathy was present during the counselling phase of consultation, no effect when empathy occurred in the "history" phase of the consultation and a

				with relapse or advanced cancers					deleterious effect when empathy occurred in the “exam” phase of the consultation
<b>Ernstmann et al., 2017<sup>38</sup></b> <b>Germany</b>	Patients	Cologne Patient Questionnaire (4 dimensions: devotion, $\alpha = .86$ ; support, $\alpha = .89$ ; information, $\alpha = .89$ ; and shared decision-making, $\alpha = .76$ ) REC	1772 (0%) 82% live with someone	Prostate (100%)/newly diagnosed	→ HRQ oL	No	Yes, longitudinal over 3 years	0.12 (0.03)	No
<b>Ernstmann et al., 2019<sup>45†</sup></b> <b>Germany</b>	Patients	Cologne Patient Questionnaire (4 dimensions: devotion; support; information; and shared decision-making).	1772 (0%) 82% live with someone/private urologists	Prostate (100%)/newly diagnosed	→ HRQ oL	No	Yes, longitudinal over 3 years	Unable to compute ESr (as standard deviations are not reported)	No
<b>Farin &amp; Nagl, 2013<sup>24</sup></b> <b>Germany</b>	Patients	Ad hoc (3 questions: The physician (1) was empathic and understanding, (2) explained everything concerning my symptoms in a way I understood and (3) arranged the proper therapies for me, $\alpha = .86$ )	312 (100%)	BC (100%)/5% at stage IV	Change in functional well-being between the start of rehabilitation and 6 months after the end of rehabilitation → Phy	No	Yes, start of, end of, and 6 months after rehabilitation	0.21 (0.05)	No

<b>Fröjd &amp; Von Essen, 2006<sup>25</sup> Sweden</b>	Physicians	EC 9 questions from Parlet et al., 1997 (e.g. initiates discussions about patients' concerns, encourages them to talk about their feelings, concludes interviews with an agreed plan of action, manages collusion, $\alpha = .91$ ) EC	69 (51%) 72% married or cohabiting/11	Endocrine (100%)/unknown	Satisfaction with the consultation → Care	Yes, diagnosis consultation	No	0.27 (0.12)	No
<b>Gehenne et al., 2021<sup>17</sup> France</b>	Patients	Emotional process of the CARE measure (items 4-6) $\alpha = .92$ EE	256 (16.8%) 67% married/referring cancer physician	Esophagus or stomach cancer/No advanced cancers.	Severity of medical and surgical complications: → Phy	No	No	0.045 (0.021)	No
<b>Grant et al., 2000<sup>47</sup> USA</b>	Patients	A revised version of the Communicator Style Measure. Empathy was grasped through 3 dimensions: friendly, communicative and attentive physicians, $\alpha$ not given) ER	126 (47%)/oncologists, radiologists and surgeons	Various types of cancer (% not available)/100% "very serious diseases" but without	Accrual to RCT → Care	Yes, consultation in which RCT is proposed	No	0.22 (0.08)	No

<b>Grassi et al., 2015<sup>48</sup></b> <b>Italy, Spain, Austria</b>	Patients	Patient Satisfaction Questionnaire – Supportive Dimension, $\alpha = .82$ REC	302 (60%)	further precisions Gastrointestinal (36%), BC (31%)/52% metastatic	Incidence and impact of nausea on life → Phy	No	Yes, before and 5 days after chemotherapy	0.02 (0.01)	No
<b>GroB et al., 2015<sup>49</sup></b> <b>Germany</b>	Patients	CARE scale (Mercer et al., 2004), $\alpha = .95$ REC	152 (43%), 65% married/44 oncologists	Colon (100%)/11% with recurrence or secondary tumour	Fear of recurrence → Psy	Yes, first private practice consultation after the diagnosis	Yes, before and within 3 days after the consultation	0.13 (0.10) Unfavourable direction	No
<b>Hoffstädt et al., 2020<sup>15†</sup></b> <b>The Netherlands</b>  (same sample as Westendorp et al., 2021 <sup>75</sup> )	Patients and clinicians	Patient-perceived empathy: a single 0-100 visual analogue scale (“to what extent you felt that the clinician demonstrated empathy in the conversation”) Clinician-reported empathy: the same with the question “How much empathy did you express during the consultation?”	41 (100%)/12 oncologists 66% married, 86% Dutch, 12% western immigrant, 2% non-western immigrant patients	Breast (100%)	Anxiety pre-post	Yes, first consultations in which the incurable diagnosis was discussed, or evaluative follow-up consultations which included		Unstandardized <i>B</i> for patient-perceived empathy: -0.67, 95% CI [-1.3 to -0.03], $p = 0.04$ ; For clinician-perceived own empathy: -0.34 [-1.00 to 0.31], $p = 0.31$	No

<b>Ishikawa et al., 2002a</b> <sup>50†</sup> <b>Japan</b>	Researchers	RIAS (physician emotional responsiveness: show concern, reassurance, self-disclosure, empathy, interrater reliability 0.76) EC	140 (60%)/12 internists and surgeons	Unknown Unknown	Patient expression during consultation → Care	test- results: Yes, with examination results received in 72%	No	0.23 (0.08)	No
<b>Ishikawa et al., 2002b</b> <sup>51†</sup> <b>Japan</b>	Researchers	RIAS (physician emotional responsiveness: show concern, reassurance, self-disclosure, empathy, interrater reliability 0.76) EC	140 (60%)/12 internists and surgeons	Unknown Unknown	Satisfaction with the clinical interview → Care	Yes, with examination results received in 72%	No	0.20 (0.08) Unfavourable direction	No
<b>Kuroki et al.</b> <sup>52</sup> , <b>2013</b> <b>USA</b>	Patients	Communication Assessment Tool (patient-centred factors and communication skills, $\alpha$ not given) REC	100 (100%, 52 married and 90 White)/100 (58 gynaecologists, 26 gynaecological oncologists, 8 primary care physicians, 7 other, 1 non-physician)	Uterine (71%), ovarian, peritoneal (20%), cervical, vulvar or vaginal (11%)/6% with metastases	Satisfaction with diagnosis → Care	Yes diagnosis	No	0.32 (0.10)	No

<b>Lelorain et al., 2018a<sup>12</sup>, Bad-news subsample France and Germany</b>	Patients	CARE (Mercer et al., 2004), $\alpha = .95$ REC	112 (32%) 73% live with someone/22 (82% oncologists, 18% others)	Thoracic (70%), digestive (30%)/37% at stage IV	Emotional QoL → Psy	Yes, bad news (88% change of treatment because of drug resistance, 4% relapse and 8% end of active treatment)	No	0.006 (0.09) for patients with low emotional skills 0.29 (0.11) for high emotional skills	The interaction between empathy and the type of consultation and patients' emotional skills is considered here; hence 4 ESR for the same study (see the row below too)
<b>Lelorain et al., 2018a<sup>12</sup>, follow-up subsample France and Germany</b>	Patients	CARE (Mercer et al., 2004), $\alpha = .95$ REC	174 (32%) 86% live with someone/22 (82% oncologists, 18% others)	Thoracic (59%), digestive (41%)/31% at stage IV	Emotional QoL → Psy	Yes, follow-up consultation (no bad news)	No	0.25 (0.08) for low patient emotional skills 0.05 (0.09) for high patient emotional skills	Yes, see preceding
<b>Lelorain et al., 2018b<sup>37</sup></b>	Patients	CARE (Mercer et al., 2004), $\alpha = .95$ REC	179 (32%) 76% live with someone/ 5 oncologists	Thoracic /31% at stage IV	Survival → Phy	Yes, follow-up and bad news consultations	Yes, prospective (censorship at 3 years)	In bad news, HR = 1.06, 95% CI [1.01-1.12], i.e. unfavourable outcome (empathy predicted a higher risk of death)	Yes, interaction between empathy and type of consultation. Furthermore, in bad news consultations, only the

								In follow-up, HR = 0.96, 95% CI [0.90-1.03]	“listening/compassion” dimension of empathy (items 1 to 6 from the CARE questionnaire) predicted a higher risk of death, whereas the “
<b>Lin et al., 2014<sup>53</sup></b> USA	Patients	Ad hoc questions developed previously for physician support (showed care about me, warm and friendly, used simple language, encouraged asking questions, α not provided) (Nelson et al., 2011) REC	352 (52%) 55% White and 55% married/lung cancer physicians	Lung (100%)/24% metastatic	Stage-appropriate treatment → Care	No	No	0.24 (0.16)	No
<b>Loge et al., 1997<sup>54</sup></b> Norway	Patients	One single ad hoc item (physician perceived as personally interested) EE	497 (30%)	BC (26%), gastrointestinal (26%), reproductive system (14%), hematopoietic (9%), head and neck	Satisfaction with diagnosis → Care	Yes, diagnosis	No	0.20 (0.04)	No

				(9%)/32% metastatic					
<b>Mack et al., 2009<sup>55</sup></b> USA	Patients	The Human Connection scale developed for the purpose of the study, $\alpha = .90$ REC	217 (53%) 85% White, 65% married	Gastrointestinal and thoracic (n not available)/100% metastatic	Multiple outcomes averaged → HRQoL	No	No	0.16 (0.07)	No
<b>Maly et al., 2004<sup>56</sup></b> USA	Patients	Ad hoc, based on Feher & Maly, 1999. Surgeons' Emotional support (14 items, $\alpha = 0.70$ ) and partnership-building efforts (1 item) ER	209 (100%) 64% White, 52% married/surgeons	BC (100%)/9.2% $\geq$ stage III	Participation in treatment decision-making → Care	No		0.07 (0.07)	No
<b>Martinez et al., 2016<sup>57</sup></b> USA	Patients	Modified Healthcare Climate Questionnaire (6 items, $\alpha = 0.94$ for the surgeon and 0.95 for the medical oncologist) REC	2286 for surgeons, 1507 for oncologists (100%)/oncologists and surgeons	BC (100%)/0% at stage IV	Subjective decision quality → Care	No	No	0.19 (0.02)	No
<b>Neuman et al., 2007<sup>58</sup>‡</b> Germany	Patients	CARE scale (Mercer et al., 2004), $\alpha = .95$ REC	323 (48%) 79% live with a partner/"the physician primarily responsible	BC (34%), skin (21%), prostate (17%), oesophagus (11%), other	Depression, socio-emotional-cognitive QoL → Psy	No	No	0.20 (0.06)	No

<b>Neuman et al., 2011<sup>59‡</sup></b> <b>Germany</b>	Patients	CARE Scale (Mercer et al., 2004), $\alpha = .95$ REC	323 (48%) 79% live with a partner	(17%)/14% relapse Same as Neumann et al., 2007	Medical and psychosocial unmet information needs → Care	No, but assessment refers to “Your hospital stay”	No	0.41 (0.13)	No
<b>Nielsen et al., 2013<sup>60</sup></b> <b>Denmark</b>	Patients	Revised version of the Physician-patient Relationship Inventory (Zachariae et al., 2001), $\alpha = .94$ ER	188 (60%) 76% married or living with a partner/oncologists	BC (31%), lung (14.6%), gastrointestinal, (11.5%) urogenital (15%), head and neck (8.4%), other (19.5%)/palliative (29%)	Self-efficacy both regarding decision-making and coping with cancer → Psy	No	No	0.31 (0.07)	No
<b>Ong et al., 2000<sup>26</sup></b> <b>The Netherlands</b>	Researchers	RIAS (“Social behavior”, “Verbal attentiveness”, “Showing concern” and “Friendliness/warmth”, interrater reliability 0.68 to 1) ER	96 (83%)/5 medical oncologists and 6 gynaecologists)	BC, bladder, skin, testis, liver, pancreas, oesophagus, colon, gynaecology	Visit satisfaction → Care	Yes, initial oncology consultation for discussion of possible treatment	Yes, assessment before the consultation, after 1 week and after 3 months	0.11 (0.10)	No

<b>Pozzar et al., 2021<sup>61</sup></b> USA	Patients	Patient-Centered Communication in Cancer Care (six subscales: exchanging information, fostering healing relationships, making decisions, recognizing emotions, self-management, managing uncertainty) $\alpha = 0.76$ .	176 (100%)/176 physicians (81% gynecologic oncologists)/86% white and 62% married.	gical (n not available)/unknown 100% ovarian cancer/65% advanced cancer (stage III, IV or recurrent).	HRQoL → Phy	No	No	0.42 (0.063)	No
<b>Ptacek &amp; Ptacek, 2001<sup>62</sup></b> USA	Patients	Ad hoc items “The doctor tried to empathize with what I was feeling” and “The doctor took into account my personality and emotionality when s/he delivered the news”, $\alpha$ not given EE	120 (42%) 97% White /more than 50 physicians who represented 7 specialties, 26% surgeons, 24% urologists, 10% family physicians	More than 10 cancer sites with 26% BC, 20% prostate, and 17% lung/unknown	Satisfaction with bad-news delivery → Care	Yes, bad-news consultation	No	0.49 (0.18)	No
<b>Roberts et al., 1994<sup>63</sup></b> USA	Patients	Cancer Diagnostic Interview Scale (18 items, $\alpha = 0.92$ ) REC	100 (100%) 72% married/surgeon	100% newly diagnosed	Psychological distress → Psy	Yes, the interview of diagnosis	No	0.46 (0.10)	No

			ons (n not available)	BC/unkno wn		and treatment options			
<b>Schoefiel d et al., 2003<sup>27</sup> Australia</b>	Patients	Ad hoc items adapted from Butow et al., 1996: “Doctor willing to discuss patients’ feeling” (yes/no) and “doctor was reassuring” (yes/no), $\alpha$ not given EE	131 (40%) 75% married or in a relationship/unknown	100% skin/10% with lymph node involveme nt	Anxiety and depression → Psy	Yes, diagnosis	Yes, baseline at 3.8 months on average after diagnosis, 4 months later, and 13 months post diagnosis	0.16 (0.09)	No
<b>Senft et al., 2018<sup>64</sup> USA</b>	Coding and patients	RIAS average of “warmth, cheerfulness and attentiveness”, $\alpha = .93$ . Patient-perception of Patient-Centeredness Scale (Stewart et al., 2000), $\alpha = .81$ REC	74 (93%) 100% Black patients/15 oncologists	BC (87%), colorectal (8%), lung (5%)/unkn own	Trust in oncologists and in recommende d treatments → Care	Yes, initial consultati on about treatment	No	0.19 (0.13)	No
<b>Sikavi et al., 2017<sup>65</sup> USA</b>	Patients	Perceived physician supportiveness using Patient Affective Index (Galassi et al., 1992), $\alpha = .81$ EE	118 (100%) 59% White/oncolo gists (n unknown)	BC (100%)/10 % stage IV	Trust in and satisfaction with the oncologists and medical adherence → Care	No	No	0.68 (0.05)	No

<b>Siminoff et al., 2000<sup>66</sup></b> USA	Researchers	RIAS (affective physician utterances) EE	50 (100%) 84% White and 68% married/15 oncologists	BC (100%)/0	Knowledge about treatments and decisional regret → Care	Yes, about treatments (post-surgical care and adjuvant therapy)	Yes, immediately after the clinical encounter and a follow-up at 3 months after initial assessment	0.08 (0.16)	No
<b>Simmons &amp; Lindsay, 2001<sup>67</sup></b> UK	Patients	Empathic understanding (Barrett-Lennard, 1962) EE	74 (76%)/2 oncologists	BC (46%), colorectal (30%), bladder (22%)/58 % node-positive	Treatment adherence → Care	No	Yes, assessment between the first and sixth postoperative day and then completion of treatment retrieved from medical records	0.00 (0.00)	No
<b>Singer et al., 2016<sup>68</sup></b> Germany	Patients	"Doctor facilitation" of the Patient Involvement in Care Scales (PICS) EC	628 (100%)/unkn own	BC (100%) No metastatic or recurrent or bilateral disease	Psychiatric comorbidities during cancer → Psy	Probably not, but information unclear	Yes, T1 before surgery, T2 = 1 month later, T3 = after completion	0.09 (0.05)	No

							of adjuvant treatment		
<b>Smith et al., 2011<sup>69</sup></b> <b>Australia and New Zealand</b>	Researchers	Response to Emotional Cues and Concerns, RECC (Butow et al., 2002) and 9-item facilitating behavior scale, inter-rater agreement .68-0.91 EE	55 (100%)/11 medical oncologists, 6 radiation oncologists, 3 surgical oncologists	BC (100%) 100% early BC	Post-consultation anxiety → Psy	Yes, about treatments	No (anxiety is assessed after the consultation )	0.43 (0.11) Unfavourable direction	No
<b>Step et al., 2009<sup>28</sup></b> <b>USA</b>	Researchers	Confirming messages (reassurance, acknowledgment or shared humour), emotional talk (Siminoff Communication Content and Affect program, Siminoff et al., 2006) and non-verbal interpersonal closeness or warmth called “immediacy” (i.e. with 3 subdimensions: fluency, $\alpha = .67$ ; directness, $\alpha = .62$ ; and inclusion, $\alpha = .71$ ) EC	179 (100%) 74% married and 83% White/24 oncologists	BC (100%) 100% stages I, II and III	Communication involvement during the consultation and decisional regret 3 months later → Care	Yes, about adjuvant therapy decision	Yes 3-month post consultation	0.16 (0.08)	No
<b>Takayama &amp; Yamaza</b>	Researchers	RIAS (psychosocial information giving, social talk, verbal	86 (100%)/5 surgeons	BC (100%) examination	Participation during the consultation	Yes	No	0.09 (11)	No

ki,  
2004<sup>70</sup>  
Japan

attentiveness,  
partnership building)  
REC

n results  
with  
favourable  
or no  
examination:  
77%;  
unclear or  
unfavourable:  
8%  
and  
unknown  
15%

→ Care

<b>Takayama et al., 2001<sup>31</sup></b> <b>Japan</b> <b>Bad-news subsample</b>	Patients	Creation of a 30-item scale with 4 factors: acceptable ( $\alpha = .90$ ), patient-centred ( $\alpha = .90$ ), attentive ( $\alpha = .73$ ) and facilitative ( $\alpha = .76$ ) REC	138 (67%) for the whole sample but only 10 in bad news/9 oncology internists and 4 oncology surgeons	BC (50.3%), gastric (30.6%), lung (15%), other (4.1%), recurrent status or metastatic (44.9%)	Post-consultation anxiety → Psy	Yes	No	0.63 (0.23)	Yes, hence two lines for this study: bad news vs follow-up
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<b>Takayama et al., 2001<sup>31</sup></b> <b>follow-up subsample</b>	Patients	See preceding	See preceding and 41 in follow-up	See preceding	See preceding	Yes	No	0.31 (0.15)	
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<b>Tomai &amp; Lauriola, 2022<sup>71</sup>, study 2, Italy</b>	Patients	Emotional dimension of the Healthcare Provider Social Support (HPSS), emotional support (i.e. physically expressing affection, listening to you talk about your feelings, interest and concern for your well-being, let you know s/he understands your mood and concerns, present and heartened you in a stressful situation for you ( $\alpha=0.92$ ) EE	69 (57.9%)	21.7% stomach, colon, rectal, 30.4% breast, 11.6% skin, 17.4% lung, 1.4% kidney, bladder, 5.8% male genitals, 11.6% other/8.7 stage III and 21.7% stage IV	Trust in the physician → Care	No	No	0.65 (0.071)	No
<b>Trevino et al., 2014<sup>72</sup> USA</b>	Patients	Human Connection Scale ( $\alpha = .89$ ) REC	93 (69%) 87% White and 58% married/49 oncologists	BC (34%), brain (16%), leukaemia/lymphoma (11%), soft tissue (9%), other (30%), 51.6% metastatic	Suicidal ideation → Psy	No	No	0.37 (0.16)	No

Accepted

<b>Trudel et al., 2014<sup>29</sup></b> <b>Canada</b>	Patients	Socio-emotional dimension ( $\alpha = .92$ ) of the Medical Communication Competence Scale (Cegala et al., 1998) EE	85 (100%) 67% living with someone/the surgeon at T1 ant T3 and the radiation oncologist at T2	BC (100%) 100% stage I or II	Sexual functioning and arm symptoms → Phy	Yes, follow-up consultations across the disease trajectory	Yes, T1 between diagnosis and surgery, T2 halfway through radiotherapy, T3 at follow-up	0.24 (0.10)	No
<b>Von Essen et al., 2002<sup>73</sup></b> <b>Sweden</b>	Patients	Doctor's interpersonal Skills dimension ( $\alpha = .88$ ) of the Comprehensive Assessment of Satisfaction with Care (CASC, Brédart et al., 1998) REC	85 (43%) 78% married/unknown	Endocrine gastrointestinal (100%) Unknown	EORTC QLQ C-30, anxiety and depression → HRQoL	No	No	0.31 (0.10)	No
<b>Von Gruenin et al., 2006<sup>74</sup></b> <b>USA</b>	Patients	Quality of care dimension ( $\alpha = .83$ ) of the Quality of End-of-Life care and Satisfaction with Treatment scale (Sulmasy et al., 2002) ER	31 (100%) 69% married and 82% White/oncologists (n unknown)	Ovarian/pe ritoneal (79%), endometri a (18%), vaginal (3%) recurrent cancer (100%)	Symptoms severity (pain, shortness of breath, nausea/vomiting, weakness and drowsiness) → Phy	No	Yes, after the diagnosis of cancer recurrence and 1 week later	0.09 (0.19)	No
<b>Westendorp et al.,</b>	Researchers	Coding of audio recorded consultations, by 2 researchers:	41 (100%)/12 oncologists	Breast (100%)	Correct information	Yes, first consultations	No	0.38 (0.14)	No

2021<sup>75</sup>,  
Netherlands

coding scheme addressed the number and content of the oncologist-expressed empathic behaviors i) Naming, Understanding, Respecting, Supporting, Exploring, ii) showing interest in the patient and her feelings, not just the disease, iii) not interrupting the patient (only “negative” was coded); and iv) other. – methods is described in Van Vliet et al., 2019 EE

66% married, 86% Dutch, 12% western immigrant, 2% non-western immigrant patients

recall percentage  
→ Care

in which the incurable diagnosis was discussed, or evaluative follow-up consultations which included test-results: good evaluation (58%), uncertain (27%), bad results (15%)

<b>Yanez et al., 2012<sup>76</sup></b> USA Latina subsample	Patients	Consumer Assessment of Healthcare Providers and Systems survey ( $\alpha = .89$ ) (Hargraves, Hays, & Cleary, 2003) REC	326 Latina (100%)/surgeons (n unknown)	BC (100%) stage I-III (100%)	→ HRQ oL	No	No	0.10 (0.06)	No
<b>Yanez et al., 2012<sup>76</sup></b>	Patients	Consumer Assessment of	168 non-Latina White (100%)/surge	BC (100%)	→ HRQ oL	No	No	0.10 (0.08)	No

<b>USA White subsample</b>		Healthcare Providers and Systems survey ( $\alpha = .89$ ) (Hargraves, Hays, & Cleary, 2003) REC	ons (n unknown)	stage I-III (100%)					
<b>Yang et al., 2018a<sup>77</sup> China</b>	Physicians	Jefferson Scale of Physician Empathy, $\alpha = .87$ (Hojat et al., 2001) ER	175 (0%) 87% married/unknown	Prostate (100%) Metastases (46%)	Natural killer subset → Phy	No	No	0.51 (0.06)	No
<b>Yang et al., 2018b<sup>78</sup> China</b>	Physicians	Jefferson Scale of Physician Empathy, $\alpha = .87$ (Hojat et al., 2001) ER	256 (0%)/256 physicians from 58 hospitals 86% married	Male BC unknown	Natural killer → Phy	No	No	0.65 (0.04)	No
<b>Zachariae et al., 2003<sup>79</sup> Denmark</b>	Patients	Physician-patient relationship Inventory (Pederson et al., 2001; Zachariae et al., 2001). Empathy, consisted of 4 items (e.g. 'The physician may have understood my words but not my feelings'), $\alpha = .82$ EE	454 (66%)/31 doctors, 13 specialists in oncology and 18 junior doctors in different training positions, 13 male and 18 female doctors	Unknown, 30% life-prolonging and 8% palliative	Change in total distress, self-efficacy and perceived control after the consultation → Psy	Yes, 11% newly diagnosed, chemotherapy 25%, radiotherapy 5%, specific problems 19%, routine 40%	Yes, assessment before and just after the consultation	0.16 (0.05)	No
<b>Zhou et al., 2019<sup>80</sup> USA</b>	Patients	Relation development (i.e., expressing care and concern) of an adapted version of the	92 (48%) 82% married, 90% White	Hematologic (22%), breast, gynecologic	Thought of dropping out and intention to complete	No but patients had to think	No	0.26 (0.09)	No

Medical  
Communication  
Competence Scale  
(Cegala, Coleman and  
Turner, 1998)  
 $\alpha = .96$   
The adaptation is that  
patients refer to the  
*research* doctor  
EE

cal,  
perineal  
(15%),  
multiple  
myelomas  
(14%),  
melanoma  
s (11%),  
urology  
(4%), lung  
(3%),  
digestive  
(3%),  
missing  
data

the clinical  
trial + trust  
that the  
research  
doctor knows  
what is best  
for the  
patient  
→ Care

about the  
research  
doctor

*Note.* <sup>§</sup>ESr = effect size correlation between physician empathy and patient outcome; see Appendix B for the justification of the ESr chosen or computed. <sup>†</sup> Neumann et al., 2007 and 2011, Ishikawa et al., 2002a and 2002b, Ernstmann et al., 2017 and 2019, Lelorain et al., 2018a and 2018b, as well as Hoffstädt et al., 2020 and Westendorp et al., 2021 are two analyses of the same samples, so that we present the results of all publications here, but have included only Neumann et al., 2011, Ishikawa et al., 2002b, Ernstmann et al., 2017, Lelorain et al., 2018a and Westendorp et al., 2021 in the meta-analysis to comply with the rule of independence of observations.

BC = breast cancer, Care = care-related outcome(s), CARE = Consultation and Relational Empathy, CASC = Comprehensive Assessment of Satisfaction with Care, Researchers = researchers use a coding system to assess an encounter, EC = emotional and cognitive empathy, EE = emotional empathy, ER = Emotional and Rapport, EORTC = European Organisation for Research and Treatment of Cancer, HRQoL = health-related quality of life, Phy = physical outcome(s), PICS = Patient Involvement in Care Scales, Psy = psychological outcome(s), QLQ-C30 = Quality of Life Questionnaire-Core 30, QoL = quality of life, RCT = randomised controlled trial, REC = all three dimensions of empathy (i.e. rapport, emotional and cognitive dimensions), RECC = Response to Emotional Cues and Concerns, RIAS = Roter Interaction Analysis System.

**Hypothesised moderators declared on Prospero (record n° CRD42018112729, [https://www.crd.york.ac.uk/prospero/display\\_record.php?RecordID=112729](https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=112729))**

**Results of group analyses using mixed-effects models (i.e. random within groups and fixed between groups; a common among-study variance component across subgroups is assumed)**

Early vs advanced cancer (i.e. stage IV or metastases; however, sometimes the available information was “stage  $\geq 3$ ” or “advanced cancer” without any further information. In these cases, it was considered “advanced”).

**Q(2) = 7.09,  $p = 0.03$**

- No patients with advanced cancer at all ( $n = 9$ ):  $r = 0.09$  [-0.06 to 0.23],  $z = 1.18$ ,  $p = 0.24$
- Advanced cancers ( $n = 28$ , including 6 samples with 100% patients with advanced cancer, 19 between 10% and 78%, and 3  $\leq 10\%$ ):  $r = 0.30$  [0.22 to 0.38],  $z = 6.94$ ,  $p < 0.001$
- Unknown ( $n = 18$ ):  $r = 0.19$  [0.09 to 0.30],  $z = 3.56$ ,  $p < 0.004$

The link between physician empathy and patient outcome is stronger in samples with patients with advanced cancer than in samples without,  $z = 2.53$ ,  $p = 0.01$

Curative vs palliative treatments

**Q(3) = 4.05,  $p = 0.26$ , but caution is required due to the small number of samples with palliative treatments**

- Curative treatments only ( $n = 24$ ):  $r = 0.19$  [0.12 to 0.25],  $z = 5.57$ ,  $p < 0.001$
- Some palliative treatments ( $n = 5$  with 29% to 38% palliative patients):  $r = 0.22$  [0.07 to 0.36],  $z = 2.81$ ,  $p = 0.005$
- Palliative only ( $n = 2$ ):  $r = 0.14$  [-0.13 to 0.38],  $z = 1.03$ ,  $p = 0.31$
- Unknown ( $n = 24$ ):  $r = 0.28$  [0.21 to 0.35],  $z = 7.56$ ,  $p < 0.001$

BN consultations (e.g. diagnosis, transition to palliative care, recurring cancer) vs other contexts (see below for more details)

**Q(1) = 5.96,  $p = 0.02$**

- Empathy in BN consultations ( $n = 11$ , including 6 with diagnosis, 3 with disease progression and 1 not specified):  $r = 0.33$  [0.24 to 0.42],  $z = 6.49$ ,  $p < 0.001$
- All other contexts ( $n = 44$ ):  $r = 0.20$  [0.15 to 0.25],  $z = 8.38$ ,  $p < 0.001$

General empathy measures vs empathy measures about a specific encounter. In the latter case, the context is specified.

**Q(4) = 14.22,  $p = 0.007$**

- Empathy in BN consultations ( $n = 10$ , including 6 with diagnosis, 3 with disease progression and 1 not specified):  $r = 0.33$  [0.23 to 0.42],  $z = 6.15$ ,  $p < 0.001$
- Empathy in FU consultations ( $n = 6$ ):  $r = 0.16$  [0.01 to 0.29],  $z = 2.15$ ,  $p = 0.03$
- Overall assessment of empathy ( $n = 26$ ):  $r = 0.26$  [0.20 to 0.31],  $z = 8.50$ ,  $p < 0.001$

- Consultations in which treatments are discussed (n = 9, including 3 related to the accrual/intention to stay in an RCT, 3 to the initial discussion shortly after diagnosis, 2 to adjuvant therapy and 1 to radiotherapy education):  $r = 0.10$  [-0.02 to 0.21],  $z = 1.61$ ,  $p = 0.11$
- BN and FU (without possibility of disentanglement, n = 4):  $r = 0.08$  [-0.08 to 0.24],  $z = 1.02$ ,  $p = 0.31$

The nature of medical staff (e.g. surgeons vs oncologists) **Q(8) = 20.33,  $p = 0.01$**

- Empathy from *one* single doctor but with different specialties within the same sample (e.g. surgeon, oncologist, GP) (n = 10):  $r = 0.22$  [0.12 to 0.32],  $z = 4.32$ ,  $p < 0.001$
- Oncologist's empathy (n = 19):  $r = 0.20$  [0.14 to 0.27],  $z = 5.70$ ,  $p < 0.001$
- Oncologists' empathy (n=2):  $r = 0.35$  [0.16 to 0.51],  $z = 3.58$ ,  $p < 0.001$
- Physician's empathy without more information about the physician (n = 6):  $r = 0.35$  [0.24 to 0.45],  $z = 5.83$ ,  $p < 0.001$
- Radiotherapist's empathy (n = 1):  $r = -0.33$  [-0.60 to 0.02],  $z = -1.85$ ,  $p = 0.06$
- Urologist's empathy (n = 1):  $r = 0.12$  [-0.12 to 0.35],  $z = 0.96$ ,  $p = 0.34$
- Surgeon's empathy (n = 6):  $r = 0.13$  [0.02 to 0.24],  $z = 2.29$ ,  $p = 0.02$
- Research doctor (n=1):  $r = 0.26$  [-0.04 to 0.52],  $z = 1.69$ ,  $p = 0.09$
- Physicians' empathy, i.e. patients are invited to refer to "physicians" and not to one physician in particular (n = 9):  $r = 0.26$  [0.16 to 0.35],  $z = 5.27$ ,  $p < 0.001$

**The empathy of one particular physician vs the empathy of several physicians, Q(1) = 1.62,  $p = 0.20$**

- Physician's empathy (n = 44):  $r = 0.21$  [0.16 to 0.26],  $z = 8.18$ ,  $p < 0.001$
- Physicians' empathy (n=11):  $r = 0.28$  [0.19 to 0.37],  $z = 5.70$ ,  $p < 0.001$

The type of assessment of the independent variable **Q(3) = 22.93,  $p < 0.001$**

(empathy measure): self-report, patient-report, observer coding such as RIAS

- Coding system (n = 10):  $r = 0.05$  [-0.06 to 0.16],  $z = 0.85$ ,  $p = 0.40$
- Self-reported by physician (n = 3):  $r = 0.51$  [0.37 to 0.64],  $z = 6.12$ ,  $p < 0.001$
- Patient-reported (n = 41):  $r = 0.23$  [0.19 to 0.28],  $z = 9.37$ ,  $p < 0.001$
- Patient-reported and coding (n = 1):  $r = 0.19$  [-0.17 to 0.51],  $z = 1.03$ ,  $p = 0.31$

Patient-reported empathy showed a stronger association than coding systems did:  $z = 2.95$ ,  $p = 0.003$

Doctor-reported empathy showed a stronger association than coding systems did:  $z = 4.73$ ,  $p < 0.001$  but caution because only 3 studies with physician-reported empathy

Physician-reported empathy showed a stronger association than patient-reported empathy:  $z = 3.44, p < 0.001$  but caution because only 3 studies with physician-reported empathy

### The nature of empathy

To be coded as emotional process, at least one item related to a genuine interest in the patient as a whole or to a full understanding of patients' concerns or to genuine care and compassion should be present in the measure. To be coded as relational process, at least one item of physician careful listening or physician warm attitude towards the patient should be present in the measure. To be coded as cognitive process, at least one item of patient's empowerment by physician should be present in the measure.

### Q(3) = 2.74, $p = 0.43$

- Emotional process only (n = 16):  $r = 0.24$  [0.14 to 0.33],  $z = 4.59, p < 0.001$
- Emotional and cognitive processes (n = 7):  $r = 0.16$  [0.01 to 0.30],  $z = 2.06, p = 0.04$
- Emotional and relational processes (n = 9):  $r = 0.31$  [0.18 to 0.43],  $z = 4.64, p < 0.001$
- All 3 processes (n = 23):  $r = 0.21$  [0.12 to 0.29],  $z = 4.79, p < 0.001$

### The nature of the design (prospective vs cross-sectional)

### Q(1) = 18.26, $p < 0.001$

- cross-sectional (n = 43):  $r = 0.27$  [0.23 to 0.31],  $z = 11.77, p < 0.001$
- prospective (n = 12):  $r = 0.07$  [-0.01 to 0.15],  $z = 1.72, p = 0.09$

### Whether the ESr comes from a bivariate analysis or a multivariate analysis with some covariates

### Q(1) = 2.32, $p = 0.13$

- bivariate (n = 39):  $r = 0.26$  [0.19 to 0.32],  $z = 7.26, p < 0.001$
- multivariate with covariates (n = 16):  $r = 0.16$  [0.06 to 0.26],  $z = 3.03, p = 0.002$

### RoB of the retrieved studies, using AXIS coding for the assessment of RoB<sup>†</sup>

### Point estimate in Fisher's Z: -0.006 [-0.04 to 0.02], $z = -0.35, p = 0.73$

### The nature of the outcome, i.e. psychological (e.g. coping), care (e.g. satisfaction with care), physical (e.g. symptoms, functioning) and HRQoL

### Q(3) = 4.20, $p = 0.24$

- Care-related outcomes (n = 24):  $r = 0.28$  [0.20 to 0.37],  $z = 6.04, p < 0.001$
- Psychological outcomes (n = 18):  $r = 0.15$  [0.04 to 0.26],  $z = 2.66, p = 0.008$
- Physical outcomes (n = 7):  $r = 0.27$  [0.11 to 0.42],  $z = 3.29, p = 0.001$
- HRQoL (n = 6):  $r = 0.20$  [0.24 to 0.36],  $z = 2.22, p = 0.026$

### Patient-reported outcome (PRO) vs not PRO<sup>†</sup>.

### Q(1) = 0.91, $p = 0.34$

- PRO (n = 45):  $r = 0.22$  [0.16 to 0.27],  $z = 6.96, p < 0.001$
- Not PRO, n = 10: accrual in RCT (n = 2), cancer-related knowledge (n = 3), stage-appropriate treatment, treatment adherence, complications after surgery, natural killer cells (n = 2);  $r = 0.28$  [0.16 to 0.40],  $z = 4.38, p < 0.001$

*Note.* n is the number of samples and not always the number of studies, as several studies comprised different samples. <sup>†</sup>As AXIS coding gives a continuous score, meta-regression is used here instead of a group analysis. BN = bad news, ESr = effect size correlations, FU = follow-up, GP = general practitioner, HRQoL = health-related quality of life, RCT = randomised controlled trial, RIAS = Roter Interaction Analysis System, RoB = risk of bias. All scores in brackets are 95% confidence intervals. <sup>†</sup>This analysis was not planned but suggested by a reviewer of the article.

Appendix F. Assessment of the risk of bias for studies included in the systematic review or meta-analysis, using AXIS Tool

Albrecht et al. (1999) <sup>39</sup>	Were the aims/objectives of the study clear?	+
	Was the study design appropriate for the stated aims?	+
	Was the sample size justified?	-
	Was the reference population clearly defined?	+
	Was the sample frame taken from an appropriate population base so that it closely represented the target population under investigation?	?
	Was the selection process likely to select subjects who were representative of the reference population under investigation?	?
	Were measures undertaken to address and categorise non responders?	+
	Were the risk factor and outcome variables measured appropriate to the aims of the study?	+
	Were the risk factor and outcome variables measured correctly using instruments that had been trialled, piloted or published previously?	?
	Is it clear what was used to determine statistical significance and / or precision estimates? (eg, p values, CI)	+
	Were the methods (including statistical methods) sufficiently described to enable them to be repeated?	-
	Were the basic data adequately described?	-
	Does the response rate raise concerns about non-response bias?	?
	If appropriate, was information about non-response bias described?	+
	Were the results internally consistent?	-
	Were the results for the analyses described in the methods, presented?	+
	Were the author's discussions and conclusions justified by the results?	-
	Were limitations discussed?	+
	Were there any funding sources or conflicts of interest that may affect the author's interpretation of the results?	?
	Was ethical approval or consent of participants attained?	-
	Number of « + » per Study	9
	Number of « ? » per study	5
	Number of « - » per study	6

Arora & Gustafson <sup>40</sup> (2009)	+	+	-	+	+	+	+	+	+	?	+	+	+	+	+	+	+	+	+	?	+	17	2	1
Cao et al. (2017) <sup>41</sup>	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	?	+	17	1	2
Chen et al. (2008) <sup>30</sup>	+	+	+	+	+	+	?	+	?	+	-	+	+	+	+	+	+	+	+	?	-	15	3	2
Chen et al. (2022a) <sup>42</sup>	+	+	+	+	+	?	+	+	+	+	+	?	?	?	+	+	+	+	+	?	+	15	5	0
Chen et al. (2022b) <sup>43</sup>	+	+	+	+	+	+	?	+	+	+	+	+	?	?	+	+	+	+	+	+	+	17	3	0
Dong et al. (2014) <sup>44</sup>	+	+	-	+	+	+	+	+	?	+	+	+	+	+	+	+	+	+	+	+	+	18	1	1
Eide et al. (2003) <sup>34</sup>	+	+	?	+	+	?	-	+	+	+	+	+	?	+	?	+	+	+	+	?	+	14	5	1
Ernstmann et al. (2017) <sup>38</sup>	+	+	+	+	?	?	?	+	+	+	+	+	?	?	+	+	+	+	+	?	+	14	6	0
Ernstmann et al., (2019) <sup>45</sup>	+	+	+	+	?	?	?	+	+	+	+	+	?	?	+	+	+	+	+	+	+	15	5	0
Farin & Nagl (2013) <sup>24</sup>	+	+	?	+	+	?	+	+	+	+	+	?	+	+	+	+	+	+	+	?	+	16	4	0



Fröjd & Von Essen (2006) <sup>25</sup>	+	+	-	+	+	+	+	+	+	?	+	+	-	+	+	+	+	+	-	+	+	16	1	3
Gehenne et al., (2021) <sup>17</sup>	+	+	+	+	+	?	?	+	+	+	+	+	?	-	+	+	+	+	+	+	+	16	3	1
Grant et al. (2000) <sup>47</sup>	+	?	-	?	+	?	-	+	+	+	?	-	?	?	+	+	+	+	?	-	+	9	7	4
Grassi et al. (2015) <sup>48</sup>	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	?	+	+	?	+	+	16	2	2
Groß et al. (2015) <sup>49</sup>	+	+	+	+	?	?	-	+	+	+	?	-	?	-	?	+	+	+	?	+	+	11	6	3
Ishikawa et al. (2002b) <sup>51</sup>	+	+	?	+	?	?	+	+	+	+	-	-	+	-	+	+	+	+	+	?	+	13	4	3
Kuroki et al. (2013) <sup>52</sup>	+	+	?	+	-	-	+	+	+	+	-	?	+	+	-	+	+	+	?	+	+	13	3	4
Lelorain et al. (2018a) <sup>12</sup>	+	+	+	+	+	+	-	+	+	+	+	+	?	?	+	+	+	+	+	+	+	16	3	1
Lelorain et al. (2018b) <sup>37</sup>	+	+	+	+	+	+	-	+	+	+	+	+	?	?	+	+	+	+	+	+	+	17	2	1
Lin et al. (2014) <sup>53</sup>	+	+	?	+	+	+	?	+	+	+	+	+	+	-	+	+	+	+	+	+	+	17	2	1



Loge et al. (1997) <sup>54</sup>	+	+	?	+	?	?	?	?	-	+	-	+	+	+	?	+	+	+	?	-	10	7	3
Mack et al. (2009) <sup>55</sup>	+	+	-	+	+	?	?	+	?	+	?	-	?	?	+	+	+	+	?	+	11	7	2
Maly et al. (2004) <sup>56</sup>	+	+	?	+	+	+	+	+	?	+	+	+	+	+	+	+	+	+	?	+	17	3	0
Martinez et al. (2016) <sup>57</sup>	+	+	+	+	?	?	?	+	+	+	+	?	+	+	?	+	+	+	?	+	14	6	0
Neumann et al. (2011) <sup>59</sup>	+	+	?	+	+	?	?	+	+	+	+	+	?	+	+	+	+	+	?	+	15	5	0
Nielsen et al. (2013) <sup>60</sup>	+	+	+	+	+	?	+	+	+	+	+	?	?	+	+	+	+	+	?	+	16	4	0
Ong et al. (2000) <sup>26</sup>	+	+	?	+	?	?	+	+	+	+	+	-	+	+	+	+	+	+	?	+	15	4	1
Pozzar et al., (2021) <sup>61</sup>	+	+	-	+	-	-	+	+	+	+	+	+	?	?	+	+	+	+	+	+	15	2	3
Ptacek & Ptacek (2001) <sup>62</sup>	+	+	+	+	?	?	-	+	?	?	?	-	?	-	-	?	+	+	+	+	9	7	4
Roberts et al. (1994) <sup>63</sup>	+	+	+	+	+	+	-	+	+	-	+	?	?	-	+	+	?	+	?	?	12	5	3



Schofield et al. (2003) <sup>27</sup>	+	+	?	+	?	?	-	+	+	+	?	+	+	+	+	+	+	+	?	+	14	5	1
Senft et al. (2018) <sup>64</sup>	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	20	0	0
Sikavi & Weseley, (2017) <sup>65</sup>	+	+	+	+	?	?	-	+	+	+	+	?	?	-	+	+	+	+	+	-	13	4	3
Siminoff et al. (2000) <sup>66</sup>	+	+	?	+	+	+	-	+	-	+	-	-	+	+	+	+	+	+	+	?	14	2	4
Simmons & Lindsay (2001) <sup>67</sup>	+	?	?	+	+	+	?	?	?	+	-	-	+	+	+	?	+	-	+	-	10	6	4
Singer et al. (2016) <sup>68</sup>	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	?	+	?	+	16	2	2
Smith et al. (2011) <sup>69</sup>	+	+	?	+	+	+	-	+	+	+	?	-	?	-	+	+	+	+	+	+	14	3	3
Step et al. (2009) <sup>28</sup>	+	+	?	+	?	?	?	+	?	+	+	-	?	-	?	+	+	+	?	?	9	9	2
Takayama et al. (2001) <sup>31</sup>	+	+	+	+	?	+	-	+	+	+	+	-	+	?	?	+	+	+	?	+	14	4	2
Takayama et al. (2004) <sup>70</sup>	+	+	+	+	+	+	?	+	+	+	+	-	+	+	+	+	+	+	?	+	17	2	1



Tomai and Lauriola (study 2, 2022) <sup>71</sup>	+	+	-	+	+	+	?	+	?	+	+	-	+	+	+	+	+	+	?	+	15	3	2
Trevino et al. (2014) <sup>72</sup>	+	+	+	+	+	+	-	+	+	+	+	+	?	+	+	+	+	+	?	+	17	2	1
Trudel et al. (2014) <sup>29</sup>	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?	+	+	?	+	18	2	0
Von Essen et al. (2002) <sup>73</sup>	+	+	-	+	+	?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	18	1	1
von Gruenigen et al. (2006) <sup>74</sup>	+	+	-	+	+	?	+	+	+	+	+	+	?	+	+	+	+	+	+	+	17	2	1
Westendorp et al., 2021 <sup>75</sup>	+	+	-	+	+	+	+	+	?	+	+	?	?	+	?	+	+	+	+	+	15	4	1
Yanez et al. (2012) <sup>76</sup>	+	+	?	+	+	+	+	+	+	+	-	-	+	-	+	+	+	+	+	-	15	1	4
Yang et al. (2018a) <sup>77</sup> advanced prostate cancer	+	+	+	+	+	+	-	+	+	+	?	+	?	?	+	+	+	+	+	+	16	3	1
Yang et al. (2018b) <sup>78</sup> male breast cancer	+	+	+	?	+	+	+	+	+	+	+	?	+	+	?	+	+	+	+	+	17	3	0

Zachariae et al. (2003) <sup>79</sup>	+	+	+	+	+	+	+	+	?	+	-	-	+	+	?	+	+	+	?	+	15	3	2
Zhou et al. (2019) <sup>80</sup>	+	+	+	+	+	?	-	+	?	+	+	?	?	-	+	+	+	+	+	+	14	4	2
Number of « + » per column	52	50	25	50	37	27	23	50	36	50	35	23	27	30	39	47	49	50	22	42			
Number of « ? » per column	0	2	15	2	13	23	14	2	14	1	7	10	25	11	9	4	2	0	30	3			
Number of « - » per column	0	0	12	0	2	2	15	0	2	1	10	19	0	11	4	1	1	2	0	7			

Note. ‘+’ indicates a low risk of bias, ‘-’ indicates a high risk of bias, and ‘?’ indicates an unclear risk of bias, as defined using the AXIS tool items described below.

AXIS tool item	Coding choices explanations
Were the aims/objectives of the study clear?	1 = yes 0 = No ? = don't know/unclear
Was the study design appropriate for the stated aims?	1 = yes 0 = No ? = don't know/unclear

Was the sample size justified?	1 = yes if there was an a priori sample size calculation OR an a posteriori power calculation OR large number of subjects (N > 1000 by example) OR, in case of regressions, at least 5 subjects by variable 0 = No ? = don't know/unclear
Was the reference population clearly defined?	1 = Yes if by example, it appeared from the introduction section that the study was conducted in an oncology setting, and with which type of patients (e.g., newly diagnosed) 0 = No ? = don't know/unclear
Was the sample frame taken from an appropriate population base so that it closely represented the target population under investigation?	1 = yes / 0 = No / ? = don't know/unclear
Was the selection process likely to select subjects that were representative of the reference	1 = yes / 0 = No / ? = don't know/unclear
Were measures undertaken to address and categorize non responders?	1 = Yes if there was at least an indication of the non-response rate and differences between respondents and non-respondents or at least indications about reasons for refusal) 0 = No ? = don't know/unclear
Were the risk factor and outcome variables measured appropriate to the aims of the study?	1 = yes 0 = No ? = don't know/unclear
Were the risk factor and outcome variables measured correctly using instruments that had been trialled, piloted or published previously?	1 = yes 0 = No ? = don't know/unclear
Is it clear what was used to determine statistical significance and / or precision estimates? (eg, p values, CI)	1 = yes 0 = No ? = don't know/unclear
Were the methods (including statistical methods) sufficiently described to enable them to be repeated?	1 = yes 0 = No

	? = don't know/unclear
Were the basic data adequately described?	1 = Yes if there was information about age AND gender AND disease severity (e.g. stage) AND tumor localization AND time since diagnosis 0 = No ? = don't know/unclear
Does the response rate raise concerns about non-response bias?	1 = No / 0 = Yes / ? = don't know/unclear (we used this inverse coding comparing to the original AXIS coding indications)
If appropriate, was information about non-response bias described?	1 = Yes if there was at least a sentence about non-response rate 0 = No ? = don't know/unclear
Were the results internally consistent?	1 = Yes if variables kept the same names all along the article, numbers add up correctly e.g. 20 participants, 14 men and 7 women) and do not change throughout the text, no selective reporting) 0 = No ? = don't know/unclear
Were the results for the analyses described in the methods, presented?	1 = yes 0 = No ? = don't know/unclear
Were the author's discussions and conclusions justified by the results?	1 = yes 0 = No ? = don't know/unclear
Were limitations discussed?	1 = yes 0 = No ? = don't know/unclear
Were there any funding sources or conflicts of interest that may affect the author's interpretation of the results?	1 = yes 0 = No ? = don't know/unclear Personal note: it was very difficult to detect a conflict of interest based solely on article information
Was ethical approval or consent of participants attained?	1 = yes 0 = No if no mention of ethics appeared in the article

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? = don't know/unclear

**Table 1.** Meta-regression explaining ESr

Covariates	Unstandardised coefficient	95% Lower limit	95% Upper limit	p-Value
Intercept	0.25	0.19	0.30	< 0.001
Prospective design	-0.14	-0.23	-0.05	0.002
Empathy assessment <sup>†</sup> :				
Coding system	-0.14	-0.25	-0.04	0.009
Physician-reported	0.32	0.16	0.47	< 0.001
Patient & coding <sup>‡</sup>	-0.05	-0.38	0.27	0.75
Bad news	0.09	-0.01	0.19	0.09

*Note.* Reference groups are cross-sectional design, patient-reported assessment, and all other contexts except for bad news, <sup>†</sup> $Q(3) = 24.34, p < 0.001$ ; <sup>‡</sup>Note that only one study assessed empathy both via patient-reported measure and coding system. Analogous  $R^2 = 53\%$ . Test of the model, i.e. test that all coefficients are zero:  $Q(5) = 50.02, p < 0.001$ . Goodness of fit, i.e. test that unexplained variance is zero:  $Q(49) = 377, p < 0.001$ .

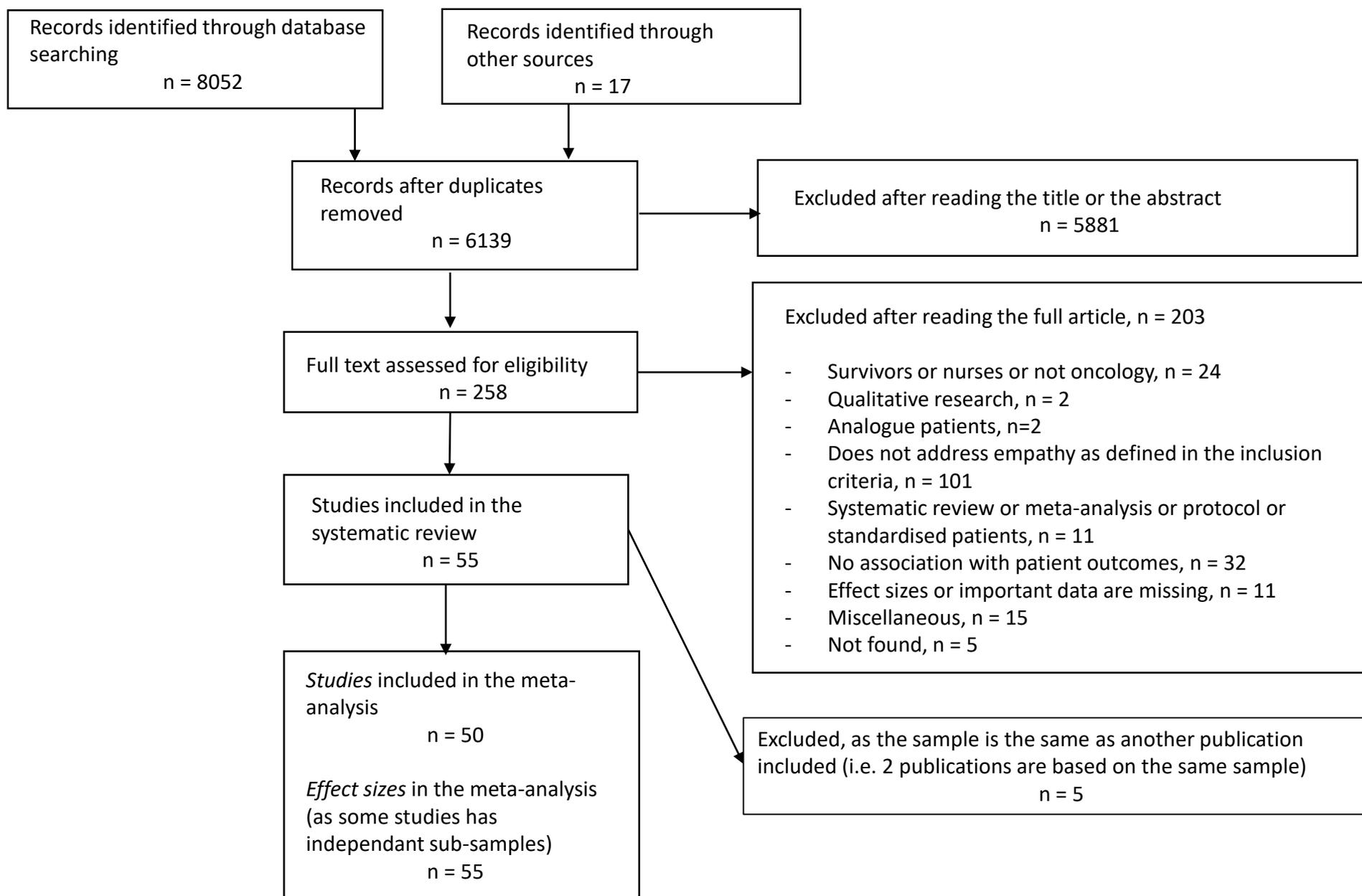
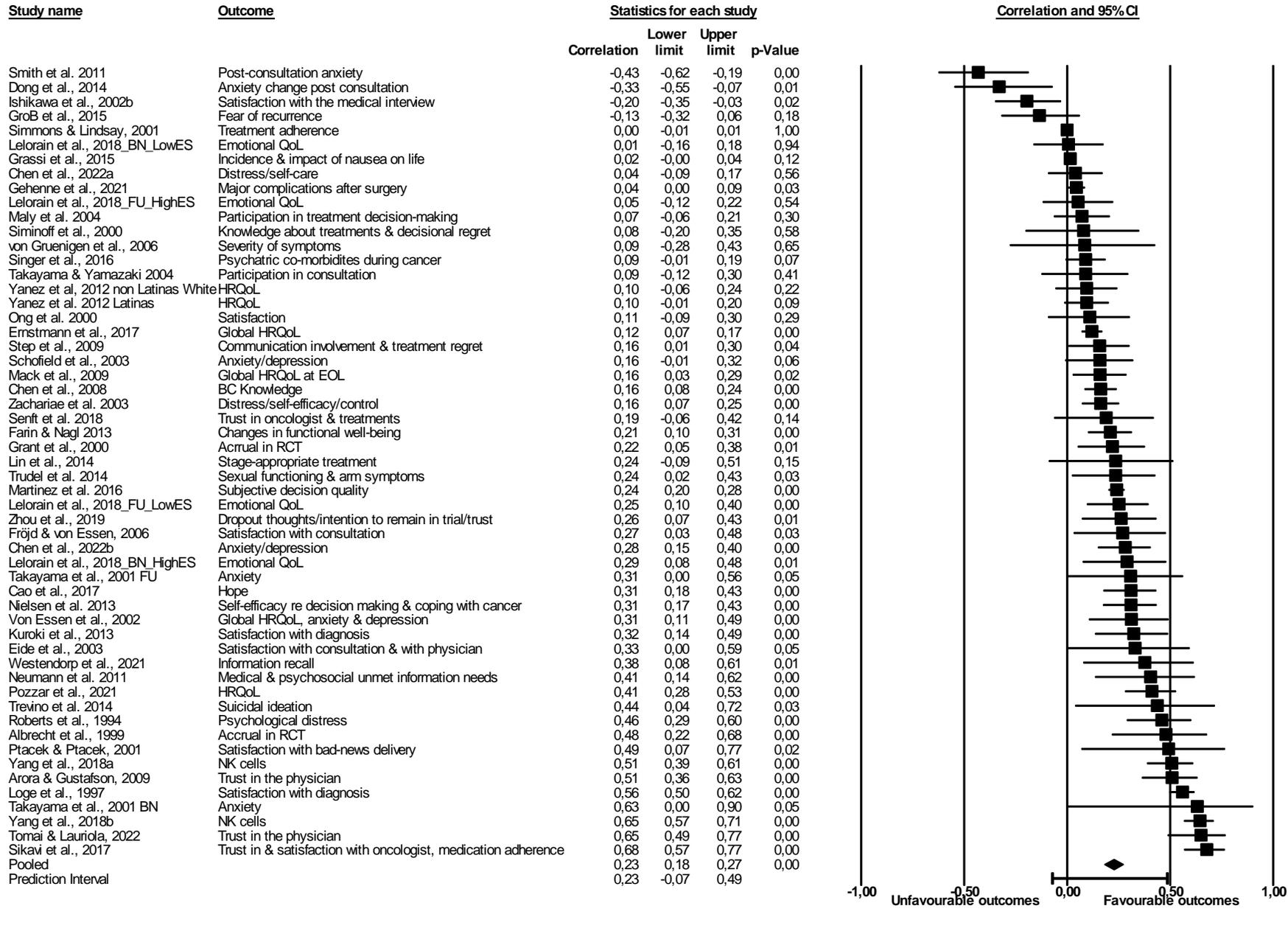


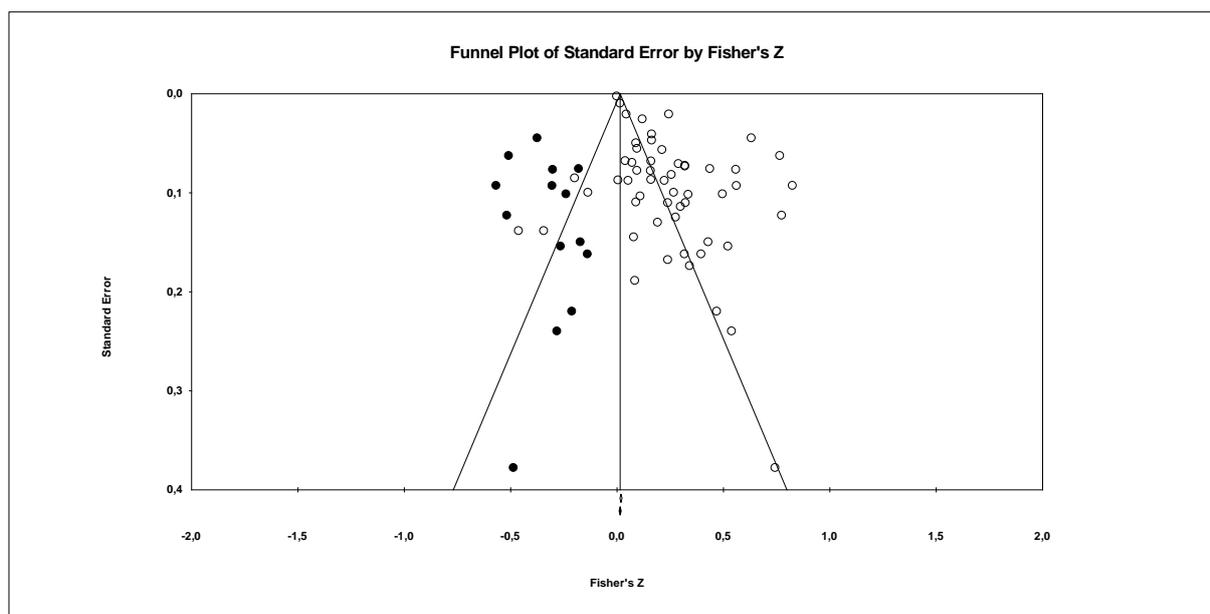
Figure 1. Flow diagram of the selection procedure

Figure 2. Forest plot of the correlations between physician empathy and patient outcomes



Note. BC = breast cancer, BN = bad news,, EOL = end of life, ES = patient emotional skills, FU = follow-up, HRQoL = health-related quality of life, NK = natural killer, QoL = quality of life, RCT = randomised controlled trial

Figure 3. *Funnel Plot of Standard Error by Fisher's Z*



*Note.* White dots represent the studies of the meta-analysis, and black dots ( $n = 14$ ) represent the studies that would be needed to correct for asymmetry if it were due to publication bias.