Screening and Stepped Care Targeting Psychological Distress in Patients With Metastatic Colorectal Cancer: The TES Cluster Randomized Trial

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ABSTRACT

Background: This study evaluated the effectiveness of a screening and stepped care program (the TES program) in reducing psychological distress compared with care as usual (CAU) in patients with metastatic colorectal cancer starting with first-line systemic palliative treatment. **Patients and Methods:** In this cluster randomized trial, 16 hospitals were assigned to the TES program or CAU. Patients in the TES arm were screened for psychological distress with the Hospital Anxiety and Depression Scale and the Distress Thermometer/Problem List (at baseline and 10 and 18 weeks). Stepped care was offered to patients with distress or expressed needs, and it consisted of watchful waiting, guided self-help, face-to-face problem-solving therapy, or referral to specialized mental healthcare. The primary outcome was change in psychological distress over time, and secondary outcomes were quality of life, satisfaction with care, and recognition and referral of distressed patients by clinicians. Linear mixed models and effect sizes were used to evaluate differences. **Results:** A total of 349 patients were randomized; 184 received the TES program and 165 received CAU. In the TES arm, 60.3% of the patients screened positive for psychological distress, 26.1% of which entered the stepped care program (14.7% used only watchful waiting and 11.4% used at least one of the other treatment steps). The observed low use of the TES program led us to pursue a futility analysis, which showed a small conditional power and therefore resulted in halted recruitment for this study. No difference was seen in change in psychological distress over time between the 2 groups (effect size, -0.16 ; 95% CI, -0.35 to 0.03 ; $P>.05$). The TES group reported higher satisfaction with the received treatment and better cognitive quality of life (all $P<.05$). **Conclusions:** As a result of the low use of stepped care, a combined screening and treatment program targeting psychological distress in patients with metastatic colorectal cancer did not improve psychological distress. Our results suggest that enhanced evaluation of psychosocial concerns may improve aspects of patient well-being.

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Background

Cancer diagnosis and treatment are often associated with elevated levels of psychological distress,^{1,2} which may cause poorer quality of life (QoL), reduced adherence to treatment, and potentially a poorer prognosis.^{3–5} Routine screening for distress is recommended by a number of major cancer organizations, with the assumption that identification of elevated levels of distress will result in increased uptake of psychosocial services and reduction in distress.^{2,6} Psychosocial interventions and social support for patients with diagnosed distress have been shown to be

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effective,^{7–11} but so far no conclusive evidence shows that the combination of screening and subsequent treatment of distress actually improves patient outcomes (supplemental eAppendix 1 and eTable 1, available with this article at JNCCN.org). It has been suggested that for screening programs to be effective, they should be designed to target and follow up on patients' actual needs in order to direct patients to appropriate psychosocial services.^{12,13} In line with these suggestions, we developed the TES program, which combines targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care–oriented approach (S) to create optimal conditions for a screening and treatment program targeting psychological distress. The goal of this cluster randomized trial (CRT) was to assess the effectiveness of the TES program in improving psychological distress compared with care as usual (CAU) in patients with metastatic colorectal cancer (mCRC) starting with first-line systemic palliative treatment. Secondary goals were to assess effects of the TES program on QoL, patient satisfaction with care offered, actual recognition and management of distressed patients by clinicians, and evaluation of the cost-effectiveness of the TES program compared with CAU.

Patients and Methods

Study Design and Population

This study was a multicenter CRT approved by the medical ethics committee of VU University Medical Center and registered in the Netherlands Trial Register (NTR4034). An extensive description of the study protocol was published previously.¹⁴ All procedures were in accordance with the ethical standards of the medical ethics committees and with the Helsinki declaration.

Patients were recruited from the medical oncology departments of 16 participating hospitals in the Netherlands between July 2013 and October 2016. Eligible patients had a diagnosis of mCRC, were scheduled to start palliative treatment with first-line chemotherapy, and had a life expectancy of >3 months. Exclusion criteria were age <18 or >85 years, insufficient command of the Dutch language, recent psychotherapy (in the past 3 months, at least one session every 2 weeks), and severe psychopathology (ie, mental illnesses that required [acute] inpatient treatment). All patients provided informed consent.

Randomization and Blinding

In this CRT, hospitals were selected as the unit of randomization to avoid contamination of treatment between groups. The randomization procedure was performed by a blinded statistician before patient recruitment. Blinding of patients, oncologists, nurses, and psychologists was not possible, owing to the nature of the intervention. Statistical analyses were performed blindly.

TES Program and CAU

Patients in the hospitals assigned to the TES arm were screened for psychological distress by a trained nurse/clinical nurse specialist before the start of treatment (0 weeks) and 10 and 18 weeks thereafter. Screening was performed using the Hospital Anxiety and Depression Scale (HADS)¹⁵ and Distress Thermometer/Problem List (DT/PL).^{16,17} Scores of ≥ 13 on the HADS¹⁵ or ≥ 5 on the DT¹⁶ were seen as indicators of elevated psychological distress. After reviewing the distress scores with the patient, the trained nurses offered treatment in the form of stepped care to patients scoring above the cutoff scores of either screening tool and to those expressing the need for receiving psychosocial care. The steps included (1) watchful waiting, (2) a guided self-help program via the Internet or a booklet, (3) face-to-face problem-solving treatment offered by a trained nurse, and (4) referral to specialized psychosocial services or prescription of psychotropic medication.^{14,18} A diagnostic evaluation and needs assessment were performed by a psychologist after patients completed step 2 or at step 4 for patients who were immediately referred to specialized psychosocial services without participating in the previous steps. In contrast, in the hospitals assigned to CAU, distress was identified by oncologists and nurses on an ad hoc basis only. For these patients, nonstandardized regular care was delivered in the form of advice or referral to other services. Three hospitals assigned to CAU introduced screening for psychological distress. Contrary to the TES program, screening in these hospitals was used as a stand-alone tool, without standardized follow-up and algorithms to guide triage. Patients from these 3 hospitals were excluded in a sensitivity analysis (see later discussion).

Outcomes

In both treatment arms, outcome measures were collected at baseline (T0), shortly after start of treatment (T1), and after 10 (T2), 24 (T3), and 48 (T4) weeks. The primary outcome was the difference in course of distress measured with the HADS¹⁹ between treatment arms over time. The HADS is a 14-item self-assessment scale for measuring distress, with a total score that ranges from 0 to 42.^{15,20} Secondary outcomes were differences in the course over time in QoL, assessed with the functioning scales and global score of the EORTC QoL of Cancer Patients questionnaire (EORTC QLQ-C30, version 3.0),²¹ patients' evaluation of psychosocial care assessed with the Client Satisfaction Questionnaire-8,²² and actual recognition and referral related to psychological distress by clinicians in both treatment arms assessed by data extracted from medical records. Results on cost-effectiveness will be reported elsewhere.

Sample Size

The sample size calculation was based on the effectiveness of screening and treatment in all patients in the TES group,

including those who were not offered or did not use stepped care after screening. The expected proportion of patients in the TES group treated for psychological distress was 33%,¹ in whom an effect size (ES) of $d=0.54$ was expected.²³ The remaining 67% of patients without treatment had an expected ES of $d=0$. The overall expected ES was therefore $d=0.18$. To show this effect on the primary outcome measure (ie, HADS) using a longitudinal design with 4 follow-up measurements, setting the within-subject correlation at $\rho=0.3$, $\alpha=0.05$ (2-tailed), and power $(1-\beta)=0.80$, a total of 302 patients was needed in each group. Assuming an intracluster correlation of 0.005,²⁴ a total of 715 patients was needed (ie, 359 in each group).

Statistical Analyses

Analyses were based on the intention-to-treat principle. Descriptive statistics were used to describe the baseline values of demographic and clinical variables in both arms. Linear mixed model (LMM) analyses were conducted to evaluate the differences in psychological distress and secondary outcomes between the TES and CAU arms. Both discrete time and linear time models were conducted. The LMMs considered 3 levels: measurements of individuals at the lowest level, individuals at the second level, and hospitals at the highest level. In the discrete time models, fixed effects were estimated for the 4 time indicators, for the 4 group-by-time 2-way interaction terms, and for disease progression that we added as a covariate. In the linear time model, fixed effects were estimated for time, the group-by-time 2-way interaction term, and for progression as a covariate. It should be noted that no main effect for group membership was estimated, thus correcting for baseline differences between the 2 intervention groups.²⁵ At the second level, error terms within persons were allowed to be correlated according to an unstructured covariance matrix, whereas at the highest level, a random intercept for hospitals was used. Cohen's formula was used to calculate ESs from the estimated differences, using pooled pretest SDs.²⁶ LMM analyses handle missing observations caused by dropout under the missing-at-random assumption. A sensitivity analysis was performed excluding patients enrolled in the 3 hospitals assigned to CAU that offered routine screening for psychological distress. For all statistical analyses, $P<.05$ was considered statistically significant. Data were analyzed using SPSS Statistics, version 22 (SPSS Inc.) and STATA, version 15 (StataCorp LLP).

Results

In-Between Futility Analysis

After recruitment of 321 patients, the observed proportion of patients receiving active treatment (not

including watchful waiting) in the TES group was 8.7% (95% CI, 5.1%–13.7%), instead of the initially expected proportion of 33%. The low uptake of active treatment resulted in a decrease of the expected ES. An unplanned futility analysis showed that with the planned number of 715 patients, the conditional power would be small (power, 0.11; supplemental eTable 2). The planned power of 0.80 would require recruitment of an unrealistic number of patients ($n=33,318$). To prevent burdening additional patients in palliative treatment, the Medical Ethics Committee recommended closing the study for further patient entry and reporting results on those already included.

Study Population

Medical oncology departments in 16 participating hospitals in the Netherlands consented to participate and were allocated to either the TES program ($n=8$) or CAU ($n=8$). No hospital dropped out during the study. The first patient was enrolled on July 29, 2013, and the final assessment of the last patient was performed on October 20, 2017. Of 393 patients meeting the inclusion criteria and willing to participate, 349 participated in the study: 184 in the TES arm and 165 in the control arm receiving CAU (Figure 1). After 48 weeks of follow-up (T4), 110 patients (59.8%) in the TES arm and 87 patients (52.7%) in the CAU arm completed the outcome assessment. During the study, 98 patients died (47 [25.5%] in the TES group and 51 [30.9%] in the CAU group; $P=.263$).

At baseline, the TES and CAU groups were comparable regarding sociodemographic and most clinical characteristics (Table 1 and supplemental eTable 3). Patients in the TES arm received prior treatments for their metastases more often than those receiving CAU (27.7% vs 15.2%, respectively), and presented with peritoneal lesions more frequently (31.0% vs 20.0%, respectively) (supplemental eTable 3). Mean HADS scores at baseline were lower in patients assigned to the TES arm than in those assigned to the CAU arm (supplemental eTables 3 and 4). The EORTC QLQ-C30 at baseline showed better scores for role functioning and social functioning in the TES group. When baseline characteristics were compared between patients who completed the study and those who dropped out before the last assessment, we observed that completers had better ECOG performance status scores and were more often men (all $P<.05$; data not shown).

TES Intervention

According to protocol, 552 screenings had to be performed and subsequently evaluated by clinical nurse specialists in the 184 patients enrolled in the TES arm (ie, 3 screenings per patient). A total of 480 screenings and

Figure 1. CONSORT diagram: study flowchart. Patients who did not complete an assessment were kept in the analysis and handled as missing observations.

Abbreviations: CAU, care as usual; TES, targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care-oriented approach (S).

evaluations (87.0%) were accomplished in the hospitals assigned to TES. Of the 72 screenings not accomplished, 35 were the result of patient drop-out due to disease progression or death and the remaining 37 were missed (6.7%) (Figure 2).

Of 184 patients in the TES arm, 111 (60.3%) screened positive for elevated distress as assessed by the HADS or the DT/PL on at least one of the screenings (Figure 2). A total of 46 patients (25.0%) entered stepped care after

screening, and 2 without elevated distress scores entered after expressing the need for psychosocial care; 27 (14.7%) used only watchful waiting and 21 (11.4%) used at least one of the other steps (Table 2). Overall, a total of 62 interventions were used by these 48 patients. Step 1 (watchful waiting) was used most frequently by 38 patients; of those, 3 chose to undergo watchful waiting for a second time. Two patients entered step 2 (self-help intervention), but neither actually started the program

Table 1. Baseline Patient Characteristics

	Total Group (N=349) n (%)	TES Program (n=184) n (%)	CAU (n=165) n (%)
Mean age (SD), y	66.1 (10.2)	66.25 (9.8)	65.84 (10.6)
Sex			
Male	224 (64.2)	113 (61.4)	111 (67.3)
Female	125 (35.8)	71 (38.6)	54 (32.3)
ECOG PS			
0	82 (23.5)	48 (26.1)	34 (20.6)
1	105 (30.1)	71 (38.6)	34 (20.6)
2	11 (3.2)	6 (3.3)	5 (3.0)
Missing	151 (43.3)	59 (32.1)	92 (55.8)
Primary CRC tumor location			
Right-sided	107 (30.7)	62 (33.7)	45 (27.3)
Left-sided	239 (68.5)	121 (65.8)	118 (71.5)
Missing	3 (0.9)	1 (0.5)	2 (1.2)
Chemotherapy regimen			
Capecitabine	72 (20.6)	36 (19.6)	36 (21.8)
CAPOX	240 (68.8)	124 (67.4)	116 (70.3)
FOLFOX	24 (6.9)	17 (9.2)	7 (4.2)
Other	10 (2.9)	6 (3.3)	4 (2.4)
Missing	3 (0.9)	1 (0.5)	2 (1.2)
Marital status			
Married/Domestic partnership	256 (73.4)	133 (72.3)	123 (74.5)
Unmarried/Divorced/Widowed	89 (25.5)	49 (26.6)	40 (24.2)
Missing	4 (1.1)	2 (1.1)	2 (1.2)
Education			
Low	19 (5.4)	10 (5.4)	9 (5.5)
Middle	223 (63.9)	122 (66.3)	101 (61.2)
High	101 (28.9)	49 (26.6)	52 (31.5)
Missing	6 (1.7)	3 (1.6)	3 (1.8)
Currently working			
Yes	81 (23.2)	39 (21.2)	42 (25.5)
No/Retired	264 (75.6)	143 (77.7)	121 (73.3)
Missing	4 (1.1)	2 (1.1)	2 (1.2)
Time from diagnosis of primary tumor until start of study			
<1.5 mo	116 (33.2)	52 (28.3)	64 (38.8)
1.5–10.0 mo	114 (32.9)	66 (35.9)	48 (29.1)
>10.0 mo	116 (33.2)	65 (35.3)	51 (30.9)
Missing	3 (0.9)	1 (0.5)	2 (1.2)
Distress			
Mean HADS score (SD)	9.52 (6.6)	8.8 (6.5)	10.3 (6.7)

(continued on next page)

Abbreviations: CAPOX, capecitabine/oxaliplatin; CAU, care as usual; CRC, colorectal cancer; FOLFOX, leucovorin/5-fluorouracil/oxaliplatin; HADS, Hospital Anxiety and Depression Scale; PS, performance status; QLQ-C30, QoL of Cancer Patients questionnaire; QoL, quality of life; TES, targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care-oriented approach (S).

Table 1. Baseline Patient Characteristics (cont.)

	Total Group (N=349) n (%)	TES Program (n=184) n (%)	CAU (n=165) n (%)
Mean QoL (EORTC QLQ-C30) scores (SD)			
Physical functioning	74.4 (20.6)	76.0 (20.9)	72.6 (20.2)
Role functioning	64.3 (30.7)	68.3 (28.9)	59.8 (32.0)
Emotional functioning	77.1 (18.9)	78.3 (18.1)	75.9 (19.8)
Cognitive functioning	88.9 (15.4)	89.8 (14.2)	88.0 (16.5)
Social functioning	76.2 (25.8)	79.3 (23.8)	72.8 (27.5)
Global QoL	63.0 (21.8)	64.9 (22.0)	60.9 (21.3)

Abbreviations: CAPOX, capecitabine/oxaliplatin; CAU, care as usual; CRC, colorectal cancer; FOLFOX, leucovorin/5-fluorouracil/oxaliplatin; HADS, Hospital Anxiety and Depression Scale; PS, performance status; QLQ-C30, QoL of Cancer Patients questionnaire; QoL, quality of life; TES, targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care-oriented approach (S).

due to disease progression. Step 3 (face-to-face problem-solving treatment) was provided to 1 patient, and 18 patients were referred to specialized psychosocial care (step 4).

Effectiveness of the TES Program

Means and SDs (observed scores) of the HADS scores and secondary outcomes are summarized in supplemental eTable 4. No evidence of an intervention effect on HADS scores was seen at any time point (discrete time model; all $P > .05$; ES, $|d| \leq 0.16$) (Table 3, Figure 3). Similarly, the course of distress over time did not differ between patients in the TES and CAU arms (linear time model; $P = .093$; ES, $|d| = 0.16$) (Table 3, Figure 4). For the course of secondary end points between groups over time, a positive effect on

patient satisfaction ($P = .003$) and cognitive functioning ($P = .010$) was seen in the intervention arm (Table 3). Symptoms of distress were recognized by clinicians in 79 patients (42.9%) in the TES group and in 62 (37.6%) in the control group ($P = .309$). Additionally, no between-group difference was found regarding referral of distressed patients by clinicians ($P = .264$), which was reported for 30 patients (16.3%) in the TES group and 20 (12.1%) in the control group (Table 3, supplemental eTable 4).

Sensitivity analysis conducted in 269 patients (ie, excluding patients in the CAU arm from the 3 hospitals that provided screening) showed the robustness of the primary findings. No evidence of an intervention effect on HADS scores at any time point (discrete time models; all $P > .05$; ES, $|d| \leq 0.12$) or on the course of distress over time (linear time model; $P = .479$; ES, $d = 0.08$) was found (data not shown).

Discussion

This CRT showed no evidence that screening for distress and offering treatment if needed improved psychological distress in patients with mCRC. The course of distress did not differ among patients assigned to the TES group

Figure 2. Distress screening with Hospital Anxiety and Depression Scale and the Distress Thermometer/Problem List in the TES arm. Abbreviation: TES, targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care-oriented approach (S).

Table 2. Stepped Care in TES Arm

Stepped Care	TES Arm (N=184) n (%)
Watchful waiting*	27 (14.7)
Active stepped care treatment	21 (11.4)
Self-help program	2 (1.1)
Problem-solving treatment	1 (0.5)
Specialized psychosocial care	18 (9.8)
Total patients using stepped care	48 (26.1)

Abbreviation: TES, targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care-oriented approach (S).

*27 patients used watchful waiting only. In addition, 11 patients used watchful waiting in combination with another step.

Table 3. Differences in Primary and Secondary Outcomes Between Arms, From LMM Analyses

	Discrete Time Model			Linear Time Model		
	Test Statistic	P Value	Effect Size ^a (d)	Test Statistic	P Value	Effect Size ^a (d)
Primary outcome						
Distress (HADS)						
3 wk	$z = -0.54$	.590	-0.04			
10 wk	$z = -1.07$	.283	-0.10			
24 wk	$z = -1.17$	.240	-0.12			
48 wk	$z = -1.62$	.104	-0.16	$z = -1.68$	.093	-0.16
Secondary outcomes						
Physical functioning (EORTC QLQ-C30)						
10 wk	$z = 2.72$	.006				
24 wk	$z = 0.28$	.779	0.03			
48 wk	$z = 1.39$	.164	0.17	$z = 1.27$	.204	0.15
Role functioning (EORTC QLQ-C30)						
10 wk	$z = 0.94$	.345	0.10			
24 wk	$z = -0.22$	.826	-0.02			
48 wk	$z = 0.48$	.630	0.06	$z = 0.30$	.767	0.04
Emotional functioning (EORTC QLQ-C30)						
10 wk	$z = 0.72$	.474	0.07			
24 wk	$z = 1.02$	.306	0.12			
48 wk	$z = 1.35$	.178	0.17	$z = 1.36$	.175	0.17
Cognitive functioning (EORTC QLQ-C30)						
10 wk	$z = 1.98$	.048	0.23			
24 wk	$z = 2.61$	.009	0.34			
48 wk	$z = 2.09$	.037	0.31	$z = 2.58$	.010	0.37
Social functioning (EORTC QLQ-C30)						
10 wk	$z = 1.33$	.182	0.13			
24 wk	$z = 0.66$	.507	0.08			
48 wk	$z = -0.40$	.689	-0.05	$z = -0.51$	.613	-0.06
Global functioning (EORTC QLQ-C30)						
10 wk	$z = 1.61$	.107	0.17			
24 wk	$z = -0.16$	.870	-0.02			
48 wk	$z = 1.74$	.083	0.21	$z = 1.44$	.149	0.17
Patient satisfaction ^b (CSQ-8)						
24 wk	$z = 0.89$	.371	0.08			
48 wk	$z = 2.98$	.003	0.31	$z = 2.99$	.003	0.31
Recognition distress by clinicians						
79 (42.9%) vs 62 (37.6%)	$z = -1.02$	.309	0.11			
Referral distress by clinicians						
30 (16.3%) vs 20 (12.1%)	$z = -1.12$	.264	0.12			

Abbreviations: CSQ-8, Client Satisfaction Questionnaire-8; HADS, Hospital Anxiety and Depression Scale; LMM, linear mixed model; QLQ-C30, QoL of Cancer Patients questionnaire.

^aEffect size obtained by standardizing the group-by-time interaction term from the LMM using the pooled within-group SDs.

^bOutcome variables were administered at 10, 24, and 48 weeks only and corrected for differences at 10 weeks.

Figure 3. Predicted means of HADS score (with error bands) in the TES group (intervention) versus CAU arm (control) at the different time points in weeks from a linear mixed models analysis using a discrete time model.

Abbreviations: CAU, care as usual; HADS, Hospital Anxiety and Depression Scale; TES, targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care-oriented approach (S).

versus the CAU group. Previous studies already revealed that screening alone is not enough to improve distress²⁷ (supplemental eAppendix 1), but they suggested that screening when followed with further assessment of specific needs and appropriate referral and treatment could lead to improvement in patient outcomes.^{12,13} However, our results show that the combination of screening, triage, and referral to appropriate services did not result in better distress outcomes.

The absence of effect of this combined approach is most likely due to the low use of stepped care in the intervention group. In the TES arm, 26.1% of patients entered the stepped care program, with only 11.4% using genuine active treatment to address psychological distress and 14.7% using only watchful waiting. The low uptake of care, despite a rather high rate of distressed patients, is consistent with findings in other studies showing low acceptance rates of psychological treatment ranging from 3% to 10%.^{28–31} Empiric evidence is accumulating that an elevated level of distress does not equate to the need for support.^{16,30,31} Some patients needing psychological support show no signs of distress, whereas others with elevated levels of distress do not report unmet needs.³² Our results further underscore these findings and challenge the assumption that screening for distress helps ensure identification of patients in need of support.^{31,33} Alternatively, developing valid indicators of need for psychological treatment is an urgent research priority.³⁰

Patients assigned to the TES group reported higher satisfaction with care and better cognitive function than those assigned to the CAU group. Additionally, patients in the TES arm tended to have better QoL scores over time than those in the CAU group, although this was not statistically significant. A plausible explanation is that

Figure 4. Predicted means of HADS score (with error bands) in the TES group (intervention) versus CAU arm (control) over time in weeks from a linear mixed models analysis using a linear time model.

Abbreviations: CAU, care as usual; HADS, Hospital Anxiety and Depression Scale; TES, targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care-oriented approach (S).

enhanced discussion of psychosocial concerns by nurses and oncologists improves well-being in patients with mCRC. It was previously suggested that, rather than implementing screening, patients could simply be asked whether they would like to discuss any psychosocial concerns with oncologic or psychosocial staff, regardless of their level of distress.³⁴ Indeed, patients' emotional well-being and QoL outcomes have been shown to improve after solely evaluating psychological issues with staff.³⁵

Our study had some limitations. First, the observed low use of the stepped care program led us to pursue the futility analysis, resulting in halted recruitment. The low uptake of psychological treatment, which is consistent with findings in other studies (see earlier discussion), resulted in a small overall ES of routine screening and subsequently offering treatment if indicated. Our results show that only a very large trial would be sufficiently powered to detect the small overall effect. One might question the clinical relevance of such a modest effect. Second, it has been shown that the HADS is effective in detecting clinically significant elevations of distress in oncology populations,¹⁵ it was recently shown that a range of psychosocial concerns are not covered by the HADS.³⁶ However, our study used the DT/PL in addition to the HADS, and trained nurses evaluated all screening results with patients, allowing detection of additional patients in need of psychosocial care not identified by the HADS or the DT/PL. Furthermore, 60% of patients in the TES arm were identified as having elevated distress, which is considerably higher than percentages reported in previous studies^{16,37}; however, this could have been partly the result of the relatively low cutoff that was set for the HADS score (≥ 13); reported cutoff scores on the HADS vary greatly among studies in cancer settings (from ≥ 10 to ≥ 16).³⁸

Another possible limitation could be the homogeneity of our study population. Cancer type-specific characteristics (eg, average age at disease onset, disease course, and associated physical impairment) may influence patients' level of distress and their response to supportive psychological interventions. However, the combination of screening followed by a subsequent treatment program has also not been found to improve patient outcomes in patients with different tumor types or stages (supplemental eAppendix 1).

Strengths of our study were that it was conducted in 16 oncology departments at different hospitals and a cluster random design was used, which minimized the risk of contamination. Furthermore, we created optimal conditions for a standardized screening and referral program, with marked contrasts between the intervention and CAU arms. Our findings showed that 89% of planned screenings and evaluations were indeed performed, indicating successful intervention delivery in the TES arm.³⁹ The high protocol adherence enhanced the likelihood of finding differences in distress over time between the arms. Of the 8 hospitals assigned to CAU, 3 offered routine screening for psychological distress (without standardized follow-up and algorithms to guide triage), and the sensitivity analysis excluding patients enrolled in these hospitals yielded results similar to those in the primary analysis, thereby strengthening our conclusion and confirming its robustness. Another strength of this trial was the timing and multiple time points of screening (eg, at start of treatment and after 10 and 18 weeks). Previous intervention studies

offering screening and subsequent treatment were designed to screen and treat directly at diagnosis²⁹ or only once,⁴⁰ whereas the importance of monitoring emotional problems and distress over time has been highlighted.⁴¹

Conclusions

Due to the low uptake of active treatment in the TES group, we found no evidence that screening for distress and offering subsequent treatment improve psychological distress. Our findings, however, suggest that enhanced discussion of psychosocial concerns may improve aspects of patient well-being.

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Supplemental online content for:

Screening and Stepped Care Targeting Psychological Distress in Patients With Metastatic Colorectal Cancer: The TES Cluster Randomized Trial

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eTable 1: Characteristics and Outcomes of the Included Randomized Controlled Trials

eTable 2: Conditional Power and Required Number of Patients to Obtain Power of 0.80

eTable 3: Extended Baseline Patient Characteristics

eTable 4: Mean Observed Scores for Outcomes

eAppendix 1: Review: Evaluation of Distress Screening on Psychological Well-Being

eTable 1. Characteristics and Outcomes of Included Randomized Controlled Trials

Reference	Primary Outcome	Secondary Outcomes	Study Design	Sample	Measures	Results	Conclusions	Comments
Braeken et al, ¹ 2013	Distress	QoL	Cluster randomized trial at the level of radiotherapists, with 2 intervention and 2 control groups Intervention groups were screened twice: before the first consultation and at the end of radiotherapy Potential referral for psychosocial support was based on the SIPP scores and judgment concerning patient's needs All patients had distress and QoL assessment at 3 and 12 mo	N=568: control, n=300; intervention, n=268 Patients with different types of cancer, no distant disease starting radiotherapy Baseline distress on GHQ-12: 2.89 vs 3.16 in control vs intervention groups, respectively (P=.53)	HADS, GHQ-12, EORTC QLQ-C30 Screening tool: SIPP	No significant difference in distress between control and intervention groups at 3 and 12 mo (P=.19 and P=.12, respectively) Distress on GHQ-12 in control vs intervention groups, respectively: 2.85 vs 2.74 at 3 mo, and 2.14 vs 1.96 at 12 mo	No effect on psychosocial well-being	An additional baseline assessment was conducted in 1 experimental group and 1 control group to check for potential premeasurement effect on the intervention outcomes
Geerse et al, ² 2017	QoL	Distress, patient satisfaction	Intervention group: 5 screening moments, followed by face-to-face discussion with nurse, and referral for patients with high scores or expressed need All patients had QoL, distress, and satisfaction assessment at 1, 7, 13, and 25 wk after randomization	N=223: control, n=113; intervention, n=110 Patients with newly diagnosed stage Ib-IV or recurrent lung cancer Baseline global QoL score: 57.7 vs 59.2 in control vs intervention group	EORTC QLQ-C30, EQ-5D, HADS, PSQ-III Screening tool: DT/PL	No significant difference was found in the mean change global QoL score (-2.4; 95% CI, 12.1-7.2; P=.61) or in the other patient-reported outcomes	No effect on psychosocial well-being	Substantially higher dropout rate than originally anticipated led to an interim analysis Based on interim analysis results, study inclusion was stopped early at 223 patients because not even a trend toward a significant effect in primary outcome was found
Hollingsworth et al, ³ 2013	Mood state	QoL, satisfaction with care, costs	Intervention group: patients completed assessment in a face-to-face meeting with radiographer/nurse, during which potential solutions were discussed, including referrals during second week of treatment Outcomes for all patients were collected at baseline and 1, 6, and 12 mo	N=220: control, n=112; intervention, n=108 Patients with primary solid tumor diagnosis undergoing outpatient chemotherapy or radiotherapy Mean total POMS score at baseline was 35 in both groups	POMS, EORTC QLQ-C30, EQ-5D, TPVCSQ Screening tool: DT/PL	No evidence of an intervention effect on the total POMS score at 12 mo or over the 12-mo follow-up Comparison of total POMS scores at 12 mo (estimate, -5.16; 95% CI, -10.36 to 0.04; P=.052) provided weak evidence of higher (worse) POMS scores in the DT/PL group	No effect on psychosocial well-being	No formal triage criteria were implemented; the DT/PL was used as a needs assessment rather than as a triage tool

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Abbreviations: CES-D, Center for Epidemiologic Studies-Depression Scale; DIS, Diagnostic Interview Schedule; DT/PL, Distress Thermometer/Problem List; EQ-5D, EuroQol 5 Dimensions questionnaire; GAS, Generalized Anxiety Screener; GHQ-12, 12-item General Health Questionnaire; GHS, German Health Survey; QLQ-C30, QoL of Cancer Patients questionnaire; HADS, Hospital Anxiety and Depression Scale; H&N35, Head and Neck module; LES, Life Experiences Survey; LWMAT, Locke-Wallace Marital Adjustment Test; PHQ-9, Patient Health Questionnaire 9; POMS, Profile of Mood States; PSI, Psychiatric Symptom Index; PSQ-III, Patient Satisfaction Questionnaire III; QoL, quality of life; SIPP, Screening Inventory of Psychosocial Problems; SSQ, Social Support Questionnaire; TPVCSQ, Trent Patient Views of Cancer Services Questionnaire.

eTable 1. Characteristics and Outcomes of Included Randomized Controlled Trials (cont.)

Reference	Primary Outcome	Secondary Outcomes	Study Design	Sample	Measures	Results	Conclusions	Comments
Maunsell et al, ⁴ 1996	Distress	QoL, including depression, anxiety, physical health, return to usual activities, employment, marital satisfaction	Intervention group: 12 monthly telephone screenings; patients with high distress were contacted by social worker within 2 wk All patients had telephone follow-up at baseline and 3 and 12 mo	N=250: control, n=127; intervention, n=123 Women newly diagnosed with first primary breast cancer, no distant disease; mean baseline distress, mean PSI of 20.5	PSI, GHQ, LES, LWMAT, DIS, SSQ, employment Screening tool: GHQ	No significant difference in distress and control groups ($P=.65$) Distress changes: mean PSI, 20.4 to 13.5 in intervention group and 20.7 to 14.6 in control group Distress level in both groups decreased over time ($P\leq.001$)	No effect on psychosocial well-being	All patients received brief psychosocial intervention from social worker at initial treatment; this may have obscured an effect of the intervention
Singer et al, ⁵ 2017	Referral to psychosocial services and distress	Uptake of outpatient care	Cluster randomized trial at the level of wards: 7 in the control arm and 6 in the intervention arm Intervention comprised screening for distress, consultation between doctor and patient regarding the patient's need for services, and provision of services All patients had assessment of well-being at the beginning and end of their hospital stay and at 3 and 6 mo after baseline	N=1,012: control, n=570 (7 wards); intervention, n=442 (6 wards) Patients treated for cancer in the wards At the beginning of their hospital stay, mean HADS distress scores were 10.2 in the control group and 11.4 in the intervention group	HADS, referral to psychosocial services, GHS Screening tool: PHQ-9, GAS-7	22% of patients in the intervention group were referred to services and 3% to standard care (odds ratio, 10.0; $P<.001$) Well-being 6 mo after baseline was 9.5 in the intervention group ($n=341$) and 9.4 for the control group ($n=234$) ($\beta = -0.3$; $P=.71$)	No effect on psychosocial well-being	
van der Meulen et al, ⁶ 2018	Depressive symptoms	QoL, worry of cancer	Intervention consisted of screening and nurse-guided follow-up lasting ~20 min 3 or 4 times during 12 mo All patients had assessment at baseline and at 6 and 12 mo	N=110: control, n=57; intervention, n=53 Patients with head and neck cancer Baseline depressive scores were 12.4 in the control group and 11.8 in the intervention group	CES-D, EORTC QLQ-C30, EORTC QLQ-H&N35, Cancer Worry Scale Screening tool: DT/PL	Depressive symptoms, health-related QoL, and worry of cancer were not significantly different in the treatment groups	No effect on psychosocial well-being	Feasibility trial

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Abbreviations: CES-D, Center for Epidemiologic Studies–Depression Scale; DIS, Diagnostic Interview Schedule; DT/PL, Distress Thermometer/Problem List; EQ-5D, EuroQol 5 Dimensions questionnaire; GAS, Generalized Anxiety Screener; GHQ-12, 12-item General Health Questionnaire; GHS, German Health Survey; QLQ-C30, QoL of Cancer Patients questionnaire; HADS, Hospital Anxiety and Depression Scale; H&N35, Head and Neck module; LES, Life Experiences Survey; LWMAT, Locke-Wallace Marital Adjustment Test; PHQ-9, Patient Health Questionnaire 9; POMS, Profile of Mood States; PSI, Psychiatric Symptom Index; PSQ-III, Patient Satisfaction Questionnaire III; QoL, quality of life; SIPP, Screening Inventory of Psychosocial Problems; SSQ, Social Support Questionnaire; TPVCSQ, Trent Patient Views of Cancer Services Questionnaire.

eTable 1. Characteristics and Outcomes of Included Randomized Controlled Trials (cont.)

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eTable 2. Conditional Power and Required Number of Patients to Obtain Power of 0.80

Proportion Receiving Distress Treatment in TES Program (%)	Conditional Power With n=715	Number Needed (Experimental + Control Groups) for Power of 0.80
5%	0.06	251,088
8.7% ^a	0.11	33,318
10%	0.13	20,716
13.7% ^b	0.21	7,548
15%	0.24	5,746
15.4% ^c	0.25	5,318
20%	0.39	2,552
25%	0.56	1,432
33%	0.80	716
35%	0.84	640

Abbreviation: TES, targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care-oriented approach (S).

^aObserved proportion of patients treated for psychologic distress.

^bUpper limit of the 95% CI of the observed proportion treated.

^cUpper limit of the 99% CI of the observed proportion treated.

eTable 3. Extended Baseline Patient Characteristics

	Total Group (N=349) n (%)	TES Program (n=184) n (%)	CAU (n=165) n (%)
Mean age (SD), y	66.1 (10.2)	66.25 (9.8)	65.84 (10.6)
Sex			
Male	224 (64.2)	113 (61.4)	111 (67.3)
Female	125 (35.8)	71 (38.6)	54 (32.7)
ECOG PS			
0	82 (23.5)	48 (26.1)	34 (20.6)
1	105 (30.1)	71 (38.6)	34 (20.6)
2	11 (3.2)	6 (3.3)	5 (3.0)
Missing	151 (43.3)	59 (32.1)	92 (55.8)
Primary tumor location			
Right-sided	107 (30.7)	62 (33.7)	45 (27.3)
Left-sided	239 (68.5)	121 (65.8)	118 (71.5)
Missing	3 (0.9)	1 (0.5)	2 (1.2)
RAS status			
WT	62 (17.8)	31 (16.8)	31 (18.8)
MT	86 (24.6)	49 (26.6)	37 (22.4)
Missing	201 (57.6)	104 (56.5)	97 (58.8)
Chemotherapy regimen			
Capecitabine	72 (20.6)	36 (19.6)	36 (21.8)
CAPOX	240 (68.8)	124 (67.4)	116 (70.3)
FOLFOX	24 (6.9)	17 (9.2)	7 (4.2)
Other	10 (2.9)	6 (3.3)	4 (2.4)
Missing	3 (0.9)	1 (0.5)	2 (1.2)
Use of monoclonal antibodies			
Yes	230 (65.9)	117 (63.6)	113 (68.5)
No	116 (33.2)	66 (35.9)	50 (30.3)
Missing	3 (0.9)	1 (0.5)	2 (1.2)
Mean number of comorbidities (SD)	2.33 (1.83)	2.44 (1.86)	2.21 (1.78)
Marital status			
Married/Domestic partnership	256 (73.4)	133 (72.3)	123 (74.5)
Unmarried/Divorced/Widowed	89 (25.5)	49 (26.6)	40 (24.2)
Missing	4 (1.1)	2 (1.1)	2 (1.2)
Education			
Low	19 (5.4)	10 (5.4)	9 (5.5)
Middle	223 (63.9)	122 (66.3)	101 (61.2)
High	101 (28.9)	49 (26.6)	52 (31.5)
Missing	6 (1.7)	3 (1.6)	3 (1.8)

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Abbreviations: CAPOX, capecitabine and oxaliplatin; CAU, care as usual; FOLFOX, leucovorin/5-fluorouracil/oxaliplatin; HADS, Hospital Anxiety and Depression Scale; HIPEC, hyperthermic intraperitoneal chemotherapy; MT, mutant type; PS, performance status; QLQ-C30, QoL of Cancer Patients questionnaire; QoL, quality of life; RFA, radiofrequency ablation; TES, targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care-oriented approach (S); WT, wild type.

eTable 3. Extended Baseline Patient Characteristics (cont.)

	Total Group (N=349) n (%)	TES Program (n=184) n (%)	CAU (n=165) n (%)
Currently working			
Yes	81 (23.2)	39 (21.2)	42 (25.5)
No/Retired	264 (75.6)	143 (77.7)	121 (73.3)
Missing	4 (1.1)	2 (1.1)	2 (1.2)
Nicotine use			
Yes	219 (62.8)	114 (62.0)	105 (63.6)
No	126 (36.1)	68 (37.0)	58 (35.2)
Missing	4 (1.1)	2 (1.1)	2 (1.2)
Alcohol use			
Yes	200 (57.3)	103 (56.0)	97 (58.8)
No	143 (41.0)	77 (41.8)	66 (40.0)
Missing	6 (1.7)	4 (2.2)	2 (1.2)
Time from diagnosis of primary tumor until start of study			
<1.5 mo	116 (33.2)	52 (28.3)	64 (38.8)
1.5–10.0 mo	114 (32.9)	66 (35.9)	48 (29.1)
>10.0 mo	116 (33.2)	65 (35.3)	51 (30.9)
Missing	3 (0.9)	1 (0.5)	2 (1.2)
Prior cancer-related treatment			
No	108 (30.9)	57 (31.0)	51 (30.9)
Yes, surgery	215 (61.6)	119 (64.7)	96 (58.2)
Yes, neoadjuvant systemic therapy	31 (8.9)	18 (9.8)	13 (7.9)
Yes, radiotherapy	42 (12.0)	18 (9.8)	24 (14.5)
Yes, chemoradiation	25 (7.2)	13 (7.1)	12 (7.3)
Yes, HIPEC	1 (0.3)	1 (0.5)	
Prior treatment for metastases			
No	270 (77.4)	132 (71.7)	138 (83.6)
Yes	76 (21.8)	51 (27.7)	25 (15.2)
(Neo)adjuvant systemic therapy	6 (1.7)	3 (1.6)	3 (1.8)
Radiotherapy	18 (5.2)	12 (6.5)	6 (3.6)
Surgery	57 (16.3)	36 (19.6)	21 (12.7)
Chemoradiation	2 (0.6)	2 (1.1)	—
HIPEC	13 (3.7)	12 (6.5)	1 (0.6)
RFA	12 (3.4)	10 (5.4)	2 (1.2)
Missing	3 (0.9)	1 (0.5)	2 (1.2)
Median number of organs with metastases	2	2	2
Metastases			
Liver	261 (74.8)	136 (73.9)	125 (75.8)
Lung	146 (41.8)	78 (42.4)	68 (41.2)
Lymph nodes	138 (39.5)	67 (36.4)	71 (43.0)
Peritoneal ^a	90 (25.9)	57 (31.0)	33 (20.0)

(continued on next page)

Abbreviations: CAPOX, capecitabine and oxaliplatin; CAU, care as usual; FOLFOX, leucovorin/5-fluorouracil/oxaliplatin; HADS, Hospital Anxiety and Depression Scale; HIPEC, hyperthermic intraperitoneal chemotherapy; MT, mutant type; PS, performance status; QLQ-C30, QoL of Cancer Patients questionnaire; QoL, quality of life; RFA, radiofrequency ablation; TES, targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care-oriented approach (S); WT, wild type.

eTable 3. Extended Baseline Patient Characteristics (cont.)

	Total Group (N=349) n (%)	TES Program (n=184) n (%)	CAU (n=165) n (%)
Median number of metastases	12	10	13
Distress			
Mean HADS score (SD)	9.52 (6.6)	8.8 (6.5)	10.3 (6.7)
Mean QoL (EORTC QLQ-C30) scores (SD)			
Physical functioning	74.4 (20.6)	76.0 (20.9)	72.6 (20.2)
Role functioning	64.3 (30.7)	68.3 (28.9)	59.8 (32.0)
Emotional functioning	77.1 (18.9)	78.3 (18.1)	75.9 (19.8)
Cognitive functioning	88.9 (15.4)	89.8 (14.2)	88.0 (16.5)
Social functioning	76.2 (25.8)	79.3 (23.8)	72.8 (27.5)
Global QoL	63.0 (21.8)	64.9 (22.0)	60.9 (21.3)

Abbreviations: CAPOX, capecitabine and oxaliplatin; CAU, care as usual; FOLFOX, leucovorin/5-fluorouracil/oxaliplatin; HADS, Hospital Anxiety and Depression Scale; HIPEC, hyperthermic intraperitoneal chemotherapy; MT, mutant type; PS, performance status; QLQ-C30, QoL of Cancer Patients questionnaire; QoL, quality of life; RFA, radiofrequency ablation; TES, targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care-oriented approach (S); WT, wild type.

eTable 4. Mean Observed Scores for Outcomes

	TES Program Mean (SD)	CAU Mean (SD)
Primary outcome		
Distress (HADS)		
T0	8.8 (6.5)	10.3 (6.7)
T1	8.7 (6.2)	10.2 (7.0)
T2	8.4 (6.6)	10.4 (7.6)
T3	8.0 (6.9)	9.9 (7.2)
T4	7.8 (6.0)	9.8 (7.3)
Secondary outcomes		
Physical functioning (EORTC QLQ-C30)		
T0	76.0 (20.9)	72.6 (20.2)
T2	75.3 (19.8)	67.1 (22.6)
T3	73.5 (21.9)	71.9 (21.3)
T4	76.7 (18.8)	71.9 (22.0)
Role functioning (EORTC QLQ-C30)		
T0	68.3 (28.9)	59.8 (32.0)
T2	64.9 (30.5)	55.6 (30.5)
T3	68.0 (29.6)	63.7 (28.4)
T4	71.5 (27.1)	65.3 (31.5)
Emotional functioning (EORTC QLQ-C30)		
T0	78.3 (18.1)	75.9 (19.8)
T2	81.8 (17.8)	79.3 (20.2)
T3	80.6 (20.7)	77.7 (20.8)
T4	83.8 (16.8)	80.2 (21.9)
Cognitive functioning (EORTC QLQ-C30)		
T0	89.8 (14.2)	88.0 (16.5)
T2	86.3 (17.6)	81.6 (21.7)
T3	86.9 (17.3)	81.3 (20.6)
T4	87.0 (17.3)	82.8 (18.3)
Social functioning (EORTC QLQ-C30)		
T0	79.3 (23.8)	72.8 (27.5)
T2	79.4 (22.4)	71.7 (28.0)
T3	79.1 (24.7)	74.2 (25.7)
T4	83.8 (21.0)	81.2 (24.4)

(continued)

Data are presented for patients that completed the questionnaires in the TES program arm at T0 (n=182), T1 (n=173), T2 (n=155), T3 (n=140), and T4 (n=110) and in the CAU arm at T0 (n=163), T1 (n=151), T2 (n=137), T3 (n=109), and T4 (n=87). Data are not corrected for clustering and baseline differences.

Abbreviations: CAU, care as usual; CSQ-8, Client Satisfaction Questionnaire-8; HADS, Hospital Anxiety and Depression Scale; QLQ-C30, QoL of Cancer Patients questionnaire; QoL, quality of life; T0, baseline; T1, shortly after the start of treatment; T2, 10 weeks after start of treatment; T3, 24 weeks after start of treatment; T4, 48 weeks after start of treatment; TES, targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care-oriented approach (S).

eTable 4. Mean Observed Scores for Outcomes (cont.)

	TES Program Mean (SD)	CAU Mean (SD)
Secondary outcomes (cont.)		
Global QoL (EORTC QLQ-C30)		
T0	64.9 (22.0)	60.9 (21.3)
T2	68.5 (21.5)	61.8 (22.6)
T3	68.1 (21.3)	66.7 (20.4)
T4	72.5 (16.8)	65.7 (22.3)
Patient satisfaction (CSQ-8)		
T2	25.5 (5.6)	25.0 (5.5)
T3	25.7 (6.0)	25.2 (5.3)
T4	26.2 (5.4)	25.0 (5.3)
Recognition of distress by clinicians, n (%)	79 (42.9%)	62 (37.6%)
Referral for distress by clinicians, n (%)	30 (16.3%)	20 (12.1%)

Data are presented for patients that completed the questionnaires in the TES program arm at T0 (n=182), T1 (n=173), T2 (n=155), T3 (n=140), and T4 (n=110) and in the CAU arm at T0 (n=163), T1 (n=151), T2 (n=137), T3 (n=109), and T4 (n=87). Data are not corrected for clustering and baseline differences.

Abbreviations: CAU, care as usual; CSQ-8, Client Satisfaction Questionnaire-8; HADS, Hospital Anxiety and Depression Scale; QLQ-C30, QoL of Cancer Patients questionnaire; QoL, quality of life; T0, baseline; T1, shortly after the start of treatment; T2, 10 weeks after start of treatment; T3, 24 weeks after start of treatment; T4, 48 weeks after start of treatment; TES, targeted selection (T), enhanced care (E), and referral to well-described effective interventions using a stepped care-oriented approach (S).

eAppendix 1. Review: Evaluation of Distress Screening on Psychological Well-Being

Objective

The objective of this review was to evaluate how screening programs for distress in patients with cancer affect psychological well-being.

Methods

Search Strategy

A PubMed search was performed for English-language studies published from inception up to February 20, 2018 using the terms “distress,” “screening,” “randomized trial,” and “cancer OR oncology”. Manual searches were performed on relevant systematic reviews.^{1–3}

Selection Criteria and Analyses of Eligible Studies

Eligible articles included English-language studies on patients with any type of cancer at any disease stage and with any treatment that reported original data. Randomized controlled trials (RCTs) were included that compared outcomes of psychosocial well-being between patients who did and did not undergo screening for distress. Studies were excluded if the control group also received screening (even in absence of subsequent discussion or treatment).

Data Collection and Analysis

We extracted data on design, setting and sample, screening and intervention, and effect on psychological well-being. Results of the trials were evaluated using the narrative synthesis approach.

Results

A total of 395 studies were retrieved. Of those, 330 studies were excluded after title review, and an additional 54 studies were excluded after abstract review; 11 studies were selected for full-text review, resulting in a total of 6 eligible randomized trials on the effect of screening for distress on psychological well-being.^{4–9} Among the 5 studies that were not included, 4 were excluded because the control group also received (minimal) screening,^{10–13} making it impossible to evaluate the effect of screening itself on psychological well-being, and 1 was excluded because it lacked an outcome measure of well-being.¹⁴

Screening and Intervention

eTable 1 provides an overview of the characteristics and outcomes of the included RCTs. Among the 6 studies, 5 screening tools for measuring distress were used: the Distress Thermometer and Problem List,^{5,6,9} the General Health Questionnaire (GHQ-12),⁷ the Screening Inventory of Psychosocial Problems (SIPP),⁴ and the Patient Health Questionnaire (PHQ-9) combined with the Generalized Anxiety Screener (GAS).⁸ A distress management plan was used in 4 of the studies^{5,7–9}; in 2 studies, no standardized plan was available on how to deal with the screening results.^{4,6}

Effect of Screening on Psychological Well-Being

None of the included studies showed a screening effect on primary well-being outcomes. In one study, however, screening and stepped care resulted in improved referral to psychosocial services.⁸ In Hollingworth et al,⁶ a subgroup analysis suggested that the Distress Thermometer/Problem List might be more effective in patients with better mood states at enrollment. In the trial by Braeken et al,⁴ post hoc analyses revealed a significant association between the intervention with early referral and improved quality of life and anxiety, suggesting that earlier referral might influence short-term quality of life and experienced anxiety in patients.

Conclusions

In this review, none of the 6 randomized trials evaluating distress screening found an effect on psychological well-being. Despite lack of supporting evidence, several clinical recommendations have been made for screening for psychological distress to be part of standard cancer care.^{15,16} In many of the included RCTs, researchers stated that future studies on screening programs should include distress as a patient outcome; use appropriate samples; include a detailed, theory-based distress management plan; offer staff training; and track staff and patient use of subsequent interventions.

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eAppendix 1. Review: Evaluation of Distress Screening on Psychological Well-Being (cont.)

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