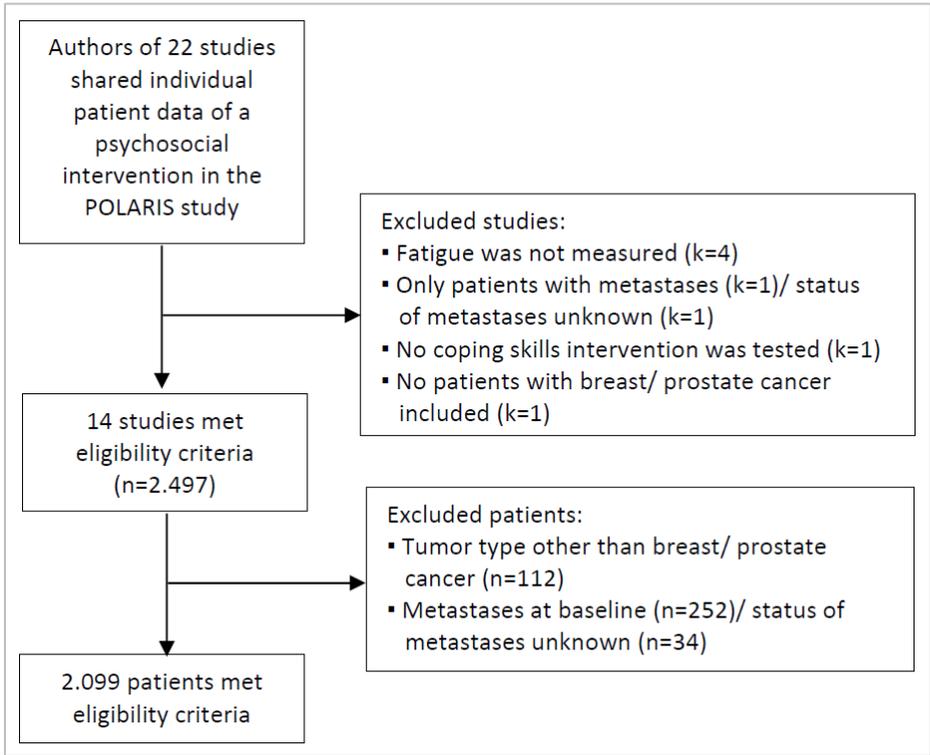


Figure 1. Flow-chart of included studies



Notes. k=number of studies; n=number of patients.

Table 1. Patient characteristics at baseline

	Patients with breast cancer		Patients with prostate cancer	
	Intervention (n=565)	Control (n=526)	Intervention (n=500)	Control (n=508)
<i>Sociodemographic characteristics</i>				
Age, mean (SD) years	52.7 (9.7)	53.3 (9.7)	62.2 (8.1)	61.9 (8.0)
Age in categories, n (%)				
<50 years	204 (36)	208 (40)	29 (6)	24 (5)
50-70 years	322 (57)	284 (54)	373 (75)	395 (78)
≥70 years	38 (7)	32 (6)	98 (20)	89 (18)
Unknown	1 (<1)	2 (<1)	-	-
Married/living with a partner, n (%)				
Yes	381 (67)	333 (63)	414 (83)	422 (83)
No	112 (20)	119 (23)	63 (13)	64 (13)
Unknown	72 (13)	74 (14)	23 (5)	22 (4)
Education level, n (%)				
Low/middle	210 (37)	227 (43)	229 (46)	227 (45)
High	138 (24)	135 (26)	247 (49)	259 (51)
Unknown	217 (38)	164 (31)	24 (5)	22 (4)
<i>Cancer treatment type</i>				
Surgery, n (%)				
Yes	561 (99)	526 (100)	229 (46)	266 (52)
No	4 (1)	-	259 (52)	237 (47)
Unknown	-	-	12 (2)	5 (1)
Radiotherapy, n (%)				
Yes	462 (82)	432 (82)	211 (42)	220 (43)
No	100 (18)	94 (18)	272 (54)	280 (55)
Unknown	3 (<1)	-	17 (3)	8 (2)
Chemotherapy, n (%)				
Yes	360 (64)	355 (68)	-	-
No	204 (36)	171 (33)	500 (100)	508 (100)
Unknown	1 (<1)	-	-	-
Hormone therapy, n (%)				
Yes	296 (52)	299 (57)	146 (29)	155 (31)
No	219 (40)	177 (34)	339 (68)	345 (68)
Unknown	50 (9)	50 (10)	15 (3)	8 (2)

Notes. Baseline characteristics did not differ significantly between the intervention and control group in (i) patients with breast and (ii) prostate cancer. Abbreviation: SD=Standard deviation.

Table 2. Potential moderators of the effect of psychosocial interventions on cancer-related fatigue on patient-level

	χ^2 [df], <i>p</i> -value
Patients with breast cancer	
<i>Socio-demographic characteristics</i>	
Age (continuous)	3.23 [1], 0.07
Age (<50 versus 50-70 versus \geq 70 years)	4.42 [2], 0.11
Having a partner (yes versus no)	0.35 [1], 0.55
Education level (low versus middle or high)	0.40 [1], 0.53
<i>Cancer treatment type</i>	
Surgery (yes versus no)	2.61 [1], 0.11
Radiotherapy (yes versus no)	0.64 [1], 0.42
Chemotherapy (yes versus no)	0.04 [1], 0.84
Hormone therapy (yes versus no)	0.02 [1], 0.89
<i>Baseline level of fatigue and other symptoms</i>	
Fatigue (continuous)	1.53 [1], 0.22
Clinically relevant fatigue (yes/no)	1.10 [1], 0.29
Depression (continuous)	0.01 [1], 0.94
Anxiety (continuous)	0.02 [1], 0.89
Pain (continuous)	2.48 [1], 0.12
Insomnia (continuous)	1.31 [1], 0.25
Patients with prostate cancer	
<i>Socio-demographic characteristics</i>	
Age (continuous)	0.01 [1], 0.91
Age (<50 versus 50-70 versus \geq 70 years)	0.78 [2], 0.68
Partner status (yes versus no)	3.44 [1], 0.06
Education level (low versus middle/high)	0.26 [1], 0.61
<i>Type of cancer treatment</i>	
Surgery (yes versus no)	0.21 [1], 0.65
Radiotherapy (yes versus no)	0.14 [1], 0.71
Hormone therapy (yes versus no)	0.19 [1], 0.66
<i>Baseline level of fatigue and other symptoms¹</i>	
Fatigue (continuous)	0.19 [1], 0.66
Clinically relevant fatigue (yes/no)	0.04 [1], 0.84
Pain (continuous)	0.19 [1], 0.66

Notes. Chi-square test with corresponding degrees of freedom (df) and *p*-values of the likelihood ratio test of the difference between models with and without interactions (χ^2) are presented. All analyses are controlled for the level of fatigue at baseline.

¹As data on the symptoms depression, anxiety, and insomnia were administered in only 7% of patients with prostate cancer, these variables were not tested as moderators in this patient sample. **p*<0.05.

Table 3. Intervention-related moderators of psychosocial interventions on fatigue in patients with breast cancer

	β (95% CI)	χ^2 [df], <i>p</i> -value
Type of intervention strategy		5.67 [1], 0.02*
Cognitive behavioral therapy	-0.27 (-0.40; -0.15)*	
Other	0.03 (-0.20; 0.25)	
Selection of patients with clinically relevant levels of fatigue		5.23 [1], 0.02*
Yes	-0.85 (-1.40; -0.30)*	
No	-0.17 (-0.28; -0.05)*	
Fatigue-specific intervention		4.62 [1], 0.03*
Yes	-0.48 (-0.79; -0.18)*	
No	-0.15 (-0.27; -0.03)*	
Timing (during versus post cancer treatment)		0.04 [1], 0.84
Intervention duration (<12 versus \geq 12 weeks)		1.32 [1], 0.25
Number of sessions (<6 versus \geq 6)		0.41 [1], 0.52
Professional guidance (yes versus no)		2.91 [1], 0.09
Leading profession (psychologist versus other)		2.45 [1], 0.12
Delivery mode (individual versus couple or group)		3.34 [1], 0.07
Type of delivery (face-to-face versus telephone)		0.76 [1], 0.38

Notes. The table presents regression coefficients (β) with 95% confidence intervals (CI) of the effect of psychosocial interventions stratified per intervention-related moderator subgroup, and chi-square tests (χ^2) with corresponding degrees of freedom (df) and *p*-values of the likelihood ratio test of the difference between models with and without interaction term. All analyses are based on study-level data and controlled for the level of fatigue at baseline. **p*<0.05.

APPENDIX

Table A1. Studies evaluating the effects of psychosocial interventions on fatigue (N=14)

Study	Country	Eligible patients ¹	Baseline fatigue screening ²	Fatigue instrument	Type control group	INTERVENTION CHARACTERISTICS							
						Fatigue-specific	Timing	Strategy	Duration, mean (SD)	Sessions, mean	Professional guidance	Delivery mode	Type of delivery
Patients with breast cancer													
Arving, 2007	SWE	143	No	QLQ-C30 fatigue	UC	No	During treatment	PST ^a	17 weeks	4	Nurse or psychologist	Individual	Face-to-face
Duijts, 2012	NL	212	No	SF-36 vitality	WL	No	Post treatment	CBT ^b	6 weeks	6	Psychologist and social workers	Group	Face-to-face
Gellaitry, 2010	UK	93	No	POMS fatigue	UC	No	Post treatment	EW ^c	<1 week	-	-	-	Self-guided
Gielissen, 2006	NL	30	Yes	CIS fatigue	WL	Yes	Post treatment	CBT ^b	26 weeks	13	Psychologist	Individual	Face-to-face
Graves, 2003	USA	32	No	POMS fatigue	WL	No	During + post treatment	SCT ^d	8 weeks	8	PhD candidate/trained intern	Group	Face-to-face
Heiney, 2003	USA	66	No	POMS fatigue	UC	No	Post treatment	CSI ^e	6 weeks	6	Group therapist	Group	Telephone
Mann, 2012	UK	96	No	SF-36 vitality	UC	No	Post treatment	CBT ^b	6 weeks	6	Psychologist	Group	Face-to-face
Northouse, 2005	USA	30	No	SF-36 vitality	UC	No	During + post treatment	DT ^f	12 weeks	5	Nurse	Couple	Face-to-face + telephone
Savard, 2005	CAN	57	No	MFI global fatigue	WL	No	Post treatment	CBT ^b	8 weeks	8	Psychologist	Group	Face-to-face
Vd Berg, 2015	NL	150	No	QLQ-C30 fatigue	UC	No	Post treatment	CBT ^b	16 weeks	-	-	-	Self-guided
Patients with prostate cancer													
Chambers, 2013	AUS	734	No	SF-36 vitality	UC	No	Pre + post treatment	CBT ^b	7 weeks	5	Nurse	Individual	Telephone

Table A1. Studies evaluating the effects of psychosocial interventions on fatigue (N=14)

Study	Country	Eligible patients ¹	Baseline fatigue screening ²	Fatigue instrument	Type control group	INTERVENTION CHARACTERISTICS							
						Fatigue-specific	Timing	Strategy	Duration, mean (SD)	Sessions, mean	Professional guidance	Delivery mode	Type of delivery
Northouse, 2007	USA	195	No	SF-36 vitality	UC	No	During + post treatment	DT ^f	17 weeks	5	Nurse	Couple	Face-to-face
Patients with breast (B) and prostate (P) cancer													
Goeden-dorp, 2010	NL	B: 70 P: 34	No	CIS fatigue	UC	Yes	During treatment	CBT ^b	30 (11.3) weeks	6	Psychologist	Individual	Face-to-face
Johansson, 2008	SWE	B: 112 P: 45	No	QLQ-C30 fatigue	UC	No	During treatment	CBT ^b	12 weeks	Median 3	Psychologist	Individual	Face-to-face

Notes. ¹Number of patients from each study that were eligible and included in the meta-analyses. ²Screening at baseline to select patients with fatigue.

Abbreviations: CIS fatigue=Checklist Individual Strength, subscale Fatigue Severity; Ftf=face-to-face therapy; MFI global fatigue=Multidimensional fatigue inventory, global fatigue score; POMS fatigue =Profile of Mood State fatigue subscale; QLQ-C30 fatigue=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 fatigue subscale; SF-36 vitality= Short Form-36 Item Health Survey vitality subscale; Tel=telephone; UC=usual care; WL=waiting list.

Intervention strategies: ^aProblem Solving Therapy: focuses on generating, applying, and evaluating solutions to identified problems. ^bCognitive Behavioral Therapy: focuses on recognizing and changing maladaptive thoughts and behaviors to reduce negative emotions and facilitate psychological adjustment. ^cDyadic Therapy: focuses on modifying problematic interactions within a relationship through conjoint sessions with partners. ^dExpressive Writing: individuals write about their thoughts and feelings related to a personally stressful or traumatic life experience.

^eCoping Skills Intervention: focuses on the acquisition of new cognitive skills aimed at cognitive or behavioral change. ^fSocial Cognitive Theory: experimental skill-building intervention based on the view that people learn by watching others.

Table A2. Baseline and post-intervention levels of fatigue

	Patients with breast cancer				Patients with prostate cancer			
	Intervention (n=584)		Control (n=547)		Intervention (n=500)		Control (n=508)	
	N	Mean (SD)/ %	N	Mean (SD)/ %	N	Mean (SD)/ %	N	Mean (SD)/ %
Fatigue								
SF-36 vitality subscale, range 0-100								
Baseline	164	48.7 (20.4)	160	46.7 (18.9)	460	45.3 (18.9)	465	44.3 (18.0)
Post-intervention	138	41.5 (20.1)	143	44.6 (19.4)	411	48.4 (19.7)	439	49.2 (19.9)
Clinically relevant level of fatigue (cut-off score ≤50)	85	52%	77	48%	201	44%	194	42%
QLQ-C30 fatigue subscale, range 0-100								
Baseline	161	30.9 (22.8)	126	33.5 (23.9)	22	30.3 (27.0)	17	21.6 (18.6)
Post-intervention	149	27.4 (22.6)	114	31.4 (22.6)	20	22.2 (21.6)	19	25.1 (20.2)
Clinically relevant fatigue (cut-off score ≥40)	49	30%	46	9%	5	22%	3	14%
POMS fatigue subscale, range 0-28								
Baseline	93	10.6 (7.0)	97	10.0 (7.5)	-	-	-	-
Post-intervention	79	9.5 (7.0)	85	9.2 (7.2)	-	-	-	-
CIS fatigue severity subscale, range 8-56								
Baseline	51	30.4 (15.6)	49	29.5 (15.3)	16	25.0 (15.1)	18	20.3 (11.0)
Post-intervention	50	23.5 (12.3)	45	30.4 (14.2)	16	17.7 (10.5)	18	22.7 (11.8)
Clinically relevant fatigue (cut-off score ≥35)	23	45%	19	39%	4	25%	3	17%
MFI general fatigue score, range 1-5								
Baseline	27	2.9 (0.7)	30	2.7 (0.6)	-	-	-	-
Post-intervention	23	2.5 (0.7)	27	2.5 (0.5)	-	-	-	-

Note. Higher scores indicate higher symptom levels.

Abbreviations: CIS fatigue=Checklist Individual Strength, subscale Fatigue Severity; MFI global fatigue=Multidimensional fatigue inventory, global fatigue score; POMS=Profile of Mood State; QLQ-C30 fatigue=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 fatigue subscale; SCL=Symptom Checklist; SF-36= Short Form-36 Item Health Survey.

Table A3. Baseline levels of depressive symptoms, anxiety, pain, and insomnia

	Patients with breast cancer				Patients with prostate cancer			
	Intervention (n=584)		Control (n=547)		Intervention (n=500)		Control (n=508)	
	N	Mean (SD)/ %	N	Mean (SD)/ %	N	Mean (SD)/ %	N	Mean (SD)/ %
Depressive symptoms								
HADS depression subscale, range 0-21	348	4.2 (3.7)	304	4.0 (3.4)	22	2.7 (2.4)	18	3.2 (3.2)
POMS depression subscale, range 0-60	93	7.3 (8.6)	98	6.4 (10.5)	-	-	-	-
BDI, range 0-63	15	14.8 (8.3)	13	10.2 (4.5)	-	-	-	-
WHQ depression subscale, range 0-1	47	0.4 (0.3)	46	0.5 (0.3)	-	-	-	-
SCL depression subscale, range 0-72	36	21.4 (5.2)	34	20.6 (4.1)	16	22.5 (6.8)	18	21.2 (6.1)
Anxiety								
HADS anxiety subscale, range 0-21	350	6.4 (4.3)	302	6.5 (4.5)	21	4.0 (3.2)	18	4.2 (4.1)
STAI state subscale, range 20-80	15	44.5 (13.1)	13	11.2 (3.1)	-	-	-	-
POMS anxiety subscale, range 0-36	92	8.3 (6.5)	98	6.3 (6.3)	-	-	-	-
WHQ anxiety subscale, range 0-1	47	0.3 (0.3)	46	0.5 (0.3)	-	-	-	-
SCL anxiety subscale, range 0-40	36	13.6 (3.2)	34	13.6 (4.0)	16	14.1 (3.7)	18	12.0 (2.5)
Pain								
QLQ-C30 pain subscale, range 0-100	254	24.5 (25.1)	208	22.9 (23.4)	38	21.1 (27.9)	36	17.1 (26.3)
SF-36 pain subscale, range 0-100	167	33.7 (27.0)	162	29.6 (24.9)	491	13.4 (19.9)	495	13.6 (20.2)
Insomnia								
QLQ-C30 insomnia subscale, range 0-100	255	36.5 (30.7)	208	36.3 (32.7)	38	22.8 (29.1)	36	14.8 (20.2)

Note. Higher scores indicate higher symptom levels.

Abbreviations: BDI=Beck Depression Inventory; HADS=Hospital Anxiety and Depression Scale; POMS=Profile of Mood State; QLQ-C30 =European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30; SCL=Symptom Checklist; SF-36= Short Form-36 Item Health Survey; STAI=State-Trait Anxiety Inventory; WHQ=Women’s Health Questionnaire.