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Associations between psychological symptoms and treatment outcomes of a massage therapy intervention: Secondary analyses of a randomized controlled trial

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ABSTRACT

Massage therapy (MT) may be more effective for certain subgroups of advanced cancer patients, but this is not well-studied. Psychological symptoms are one potential moderator of MT outcomes, as they occur frequently in MT patients. Therefore, we conducted a secondary analysis of data from a multi-site study which compared MT to simple touch in 380 adults with advanced cancer. We examined whether the presence of depression or baseline psychological symptom frequency moderated outcomes of change in pain, interference of pain, quality of life, 60-second heart and respiratory rates, and physical distress. We found significant main effects of depression and baseline psychological symptom frequency on changes in pain, 60-second heart and respiratory rates, quality of life, and physical distress for both MT and simple touch, but did not find differential responses between groups in moderator analyses. Results imply that psychological interventions could be targeted to patients with cancer who are receiving any type of touch therapy to improve outcomes.

1. Introduction

As the number of U.S. adults age 65 and older increases, so too will the prevalence of cancer and associated mortality. Along with pain and other symptoms, psychological symptoms are common in cancer patients, especially in advanced stages.[1–3] For example, the prevalence of depressive disorders in adults with advanced cancer has been estimated to be as high as 39 percent [4–8] and anxiety disorders as high as 29 percent.[5,6] These rates are higher than in the general population, with national survey data indicating that 6.7 percent of adults had a major depressive episode in the last year,[9] and that 18 percent had an anxiety disorder.[10] A range of treatments have been developed to address both psychological and physical symptoms in advanced cancer patients, with massage therapy (MT; an approach involving manual manipulation of soft tissue) gaining increasing attention.[11,12] MT is thought to address psychological and physical symptoms through several mechanisms, including the therapist's presence and communication, induction of a relaxation response, increased blood and lymphatic circulation and endorphin release, decreased inflammation, competition with pain signals, and reductions in anxiety, blood pressure, and heart rate.[11,13–18] MT has been found to be acceptable to advanced cancer patients,[19] and to be feasibly implemented both in home[19] and hospital settings.[11]

In addition to MT having an impact on psychological symptoms in advanced cancer patients, psychological symptoms could potentially act as a moderator of response to MT. Moderators specify for whom or under what conditions treatment is effective.[20] Identifying moderators is important for maximizing the benefits of evidence-based treatments like MT, as moderators can help inform clinicians about which clients may respond best to treatment and which clients might be better served by alternate treatments. Moderators can also help inform inclusion and exclusion criteria and choices for stratification in randomized controlled trials (RCTs), maximizing power.[20] Therefore, identifying whether psychological symptoms act as moderators of MT in advanced cancer patients could have significant research and clinical implications.

Research on psychological symptoms as moderators for outcomes of massage and related interventions is limited. Psychological symptoms have been identified as moderators for low back pain treatments in a meta-analysis, with those with higher depression and anxiety symptoms

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showing better treatment responses.[21] Depression has also been identified as a moderator of treatment for a self-management intervention for older adults with arthritis, with those with depression experiencing less improvement than those without depression.[22] Moderators of response to MT have also been examined for various conditions and populations, but none of the moderators considered (age of participants, gender of participants, level of practitioner training, and study setting) were significant.[17] To our knowledge, no studies have yet considered psychological symptoms as a moderator of treatment effect for MT in any population (including advanced cancer patients).

We begin to address this gap by conducting a secondary analysis of data from the "Reducing End-of-Life Symptoms with Touch (REST)" study, which compared MT to simple touch in 380 adults with advanced cancer [23] Published analyses of the REST study did not examine moderators of MT.[23–26] Though the REST study was published several years ago, to our knowledge it remains the only large-scale RCT to examine outcomes of massage therapy among advanced cancer patients, and therefore was ideal for answering questions about the role of psychological symptoms on MT outcomes in this population. The specific aims of project were:

1 To examine whether, across treatment groups in the REST study, baseline presence of depression or psychological symptom frequency are associated with primary and secondary study outcomes.
2 To test whether the presence of depression and baseline psychological symptom frequency moderate intervention effects.

We hypothesized that, in both treatment and control groups, the presence of depression and baseline psychological symptom frequency would be highly negatively associated with all outcome variables. We also hypothesized that the presence of depression and baseline psychological symptom frequency would moderate response to MT, with those with depression or more frequent psychological symptoms showing lower treatment effects.

2. Material and methods

The REST study was a prospective, two-group, randomized, single-blind clinical trial, conducted between November 2003 and October 2006 at fifteen U.S. hospice or palliative care clinical settings. To be eligible, participants had to be English-speaking, have a diagnosis of advanced cancer of any type (stage III or IV) with at least moderate pain in the week before enrollment (≥ 4 on a 0–10 scale), have a life expectancy of at least three weeks, and be able to consent. Exclusion criteria included receipt of professional massage within one month of enrollment, being on anticoagulant therapy, and having a known platelet count below 10,000. Initial sample size calculations were based on a review of previous studies with no treatment control group and are described in more detail in the original REST publication.[23]

Eligible participants provided written informed consent and were then randomized to either massage therapy (MT) or to a simple touch control group. The randomization sequence was generated by a SAS program that produced a randomized block design and was stratified by study site; more detail on randomization is provided in the original REST study publication.[23] Fig. 1 shows the study flow, following the Consolidated Standards of Reporting Trials (CONSORT) recommendations for randomized trials of nonpharmacologic treatment,[27] and is also described in the original REST study publication.[23] The control condition consisted of placement of both hands on different areas of the participants' body (e.g., lower back, base of neck, feet) for 3 min each. Both session types were 30 min long. The initial treatment session occurred within 48 h of baseline data collection, and participants received up to six sessions over two weeks, with at least 24 h between treatment sessions. The scheduling of remaining treatment sessions was determined by the treatment provider and the patient.

Assessments were conducted by face-to-face interviewer-administered questionnaires. Baseline assessments were conducted within 72 h of study enrollment. Measures were collected just before and after every treatment session by treatment providers who were not blinded to treatment assignment (immediate outcomes), as well as during 3 weekly visits over the 3–4 week period of participation (sustained outcomes). Final data collection occurred approximately one week after the final follow-up visits by blinded data collectors. More detail on the original study design and methodology can be found in the original REST study publication.[23]The Colorado Multiple Institutional Review Board and (as needed) site-specific institutional review boards reviewed and approved the original study. The current de-identified secondary analyses were reviewed by the City University of New York Institutional Review Board and determined to be exempt from further review.

2.1. Measures

The current analyses sought to examine the same outcome variables as in the original REST study analyses,[23] except that mood was not considered as an outcome (as it is likely to be highly correlated with baseline psychological symptoms).

Moderating variables: Moderators were selected *a priori* based on the analyses' research questions. Presence of depression was identified on the initial study screen based on interview or chart review, and baseline psychological symptom frequency was measured with the Memorial Symptom Assessment Psychological Symptom sub-scale (MSAS-PSYCH).[28] This measure includes items on the frequency of five psychological symptoms (worrying, feeling sad, feeling nervous, feeling irritable, difficulty concentrating) and provides a Psychological Symptom subscale score (the MSAS-PSYCH) based on these 5 items.

Primary outcomes (as in the original REST study) were immediate and sustained change in pain and interference of pain, as measured by the pain scale of the Memorial Pain Assessment Card (MPAC)[29] and the Brief Pain Inventory (BPI).[30,31]

Secondary outcomes (as in the original REST study) were 60-second heart and respiratory rates (immediate outcomes); quality of life (measured by the McGill Quality of Life Questionnaire (MQOL) and its subscales: physical symptoms, psychological symptoms, existential well-being, and support[32]) and physical distress (measured by the MSAS global and physical symptoms subscales)[28] (sustained outcomes).

We also utilized identical covariates to the original REST study analyses; covariates were initially selected based on the authors' clinical experience.[23] Covariates were: 1) demographics: age (in years; participant age > 90 was coded as 90 to maintain deidentification of data), and gender (male/female), 2) general health status: comorbid conditions (yes/no) and Karnofsky Performance Scale, 3) prior professional massage (yes/no), 4) expected benefit of massage (range1-not at all helpful to 5-very helpful), and 5) worst pain in prior week at study entry (measured via the BPI).

2.2. Analysis

We first generated descriptive statistics and frequency distributions for variables of interest overall and by treatment group. To minimize multiple comparisons associated with repeated assessments of immediate outcomes within treatment sessions, we followed the methodology used in the original REST study,[13] where a summary measure was constructed by taking the average of post-pre scores across all 6 treatment visits. All analyses were performed on the basis of the intention-to treat principle. Missing data was not imputed, since sensitivity analyses in the original REST study indicated no significant effect of missing data on study results, both in terms of the size of parameter estimates and standard errors. See Fig. 2 for variables analyzed.

To analyze Aim 1, we assessed associations between baseline presence of depression and psychological symptom frequency with both immediate and sustained outcomes using mixed-effects models with

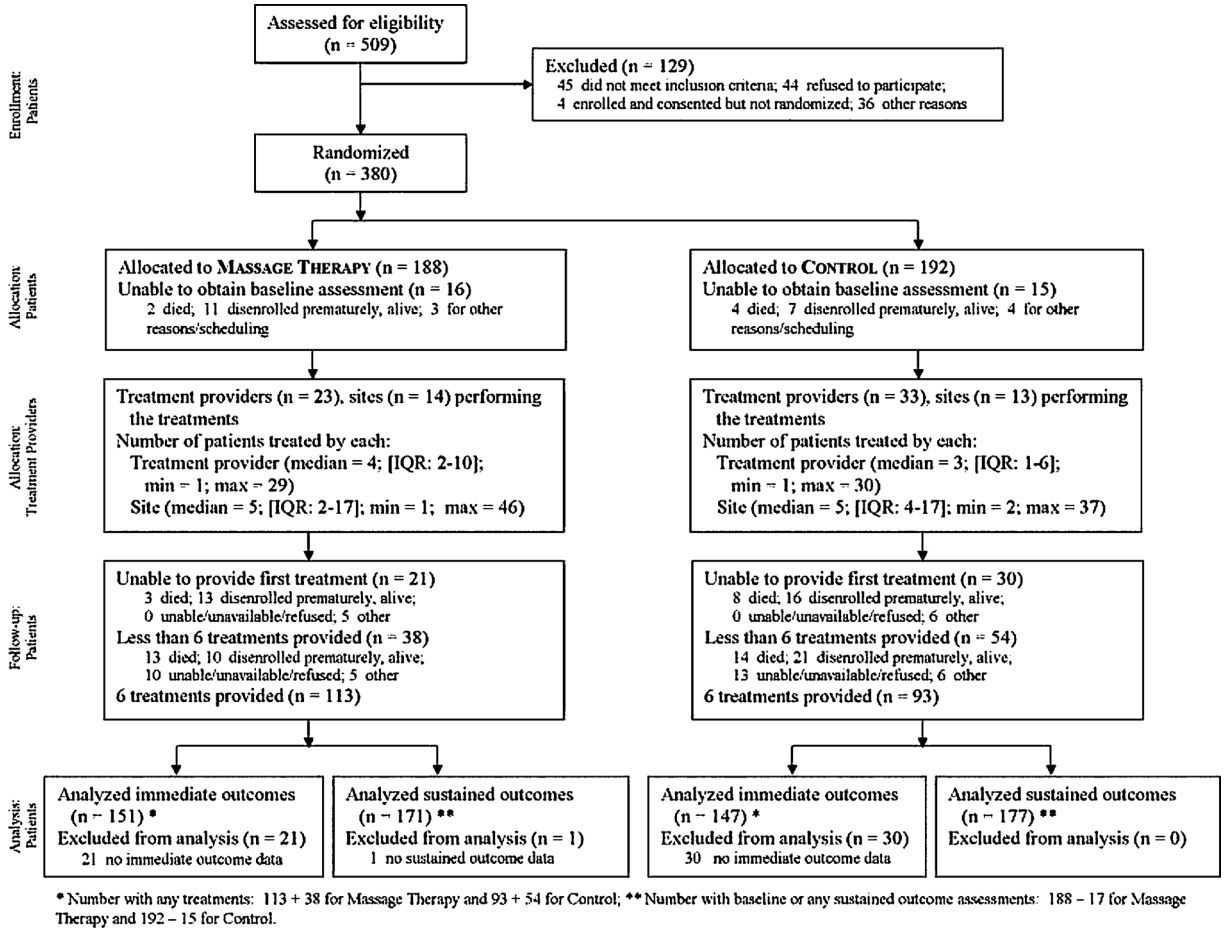

Fig. 1. Study Flow Diagram.

random intercepts and slopes. We ran separate models for all primary and secondary outcomes on the entire sample and by treatment group. Models included time (categorical indicator), treatment group (massage therapy vs. simple touch) and baseline depression or psychological symptoms frequency (MSAS-PSYCH) as main fixed effects.

To analyze Aim 2, we assessed each baseline psychological symptom measure as potential moderators of treatment effect on outcomes using mixed-effects models outlined above with an additional interaction term (time by treatment by baseline presence of depression or psychological symptom frequency). Effect sizes using Cohen's d[33] were calculated for sustained outcomes to assess the clinical significance of change from pre-treatment to last visit by baseline depression. A moderating effect was deemed present if the interaction was statistically significant and/or a substantial difference in effect size was observed.

All models were adjusted for key covariates used in the original REST outcome analysis[13]: demographics (age, gender), general health status (comorbid conditions, Karnofsky Performance Scale), prior professional massage, expected benefit, worst pain in prior week at study entry. Statistical significance was judged at a conservative level ($\alpha = 0.01$, two-sided) to adjust for multiple testing. Analyses were performed SAS 9.4 statistical software.

3. Results

We analyzed the same sample as in the original analyses. Participant characteristics are reported in Table 1. Randomization led to equivalency across groups.[23] Data on a total of 380 participants were analyzed, with 188 in the MT condition and 192 in the simple touch control group. At baseline, across treatment and control groups, 23.9% of the sample (n = 201) had depression, and average MSAS Psych score was 2.56 (SD = 0.79) (which is equivalent to symptoms being present and occurring occasionally to frequently)[28] (Table 1).

The original REST study demonstrated significant improvements in immediate and sustained pain, immediate mood, quality of life and physical distress in both treatment groups; MT was superior to simple

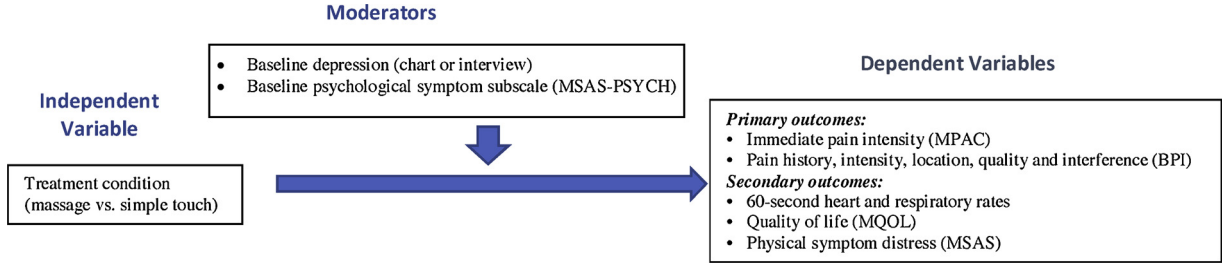

Fig. 2. Model of Moderation.

Table 1
Participant socio-demographics, clinical, and moderating variables (N = 380).

	Entire sample (N = 380)	Massage Therapy (MT) (n = 188)	Simple Touch (n = 192)
Sociodemographic variables			
Female gender, n (%)	232 (61.1)	120 (64)	112 (58)
White Race, n (%)		161 (86)	164 (85)
Education college or higher, n (%)	151 (39.7)	72 (38.3)	79 (41.1)
Married or committed relationship, n (%)	170 (44.7)	93 (49.5)	77 (40.1)
Age, years, M (SD)	64.8 (14.4)	65.3 (14.4)	64.2 (14.3)
Clinical variables			
Received prior professional massage therapy, n (%)	150 (39.5)	76 (40.4)	74 (38.5)
Perceived helpfulness of massage therapy (1-5 scale), M (SD)	3.9 (1.0)	4.0 (1.0)	3.9 (1.1)
Worst pain previous 24 hours (0-10 scale), M (SD)	6.6 (2.3)	6.7 (2.4)	6.4 (2.5)
Worst pain prior week (0-10 scale), M (SD)	7.7 (2.1)	8.0 (1.9)	7.6 (2.2)
Moderating variables			
Baseline Depression, n (%)	91 (23.9)	44 (23.4)	47 (24.5)
Baseline MSAS-PSYCH- Psychological symptom frequency, M (SD)	2.56 (0.79)	2.55 (0.81)	2.57 (0.78)

Table 2
Baseline presence of depression or psychological symptom frequency (MSAS-PSYCH) as predictors of treatment response.

	Overall			Massage Therapy (MT)			Simple Touch		
	Beta	95% CI	p-value	Beta	95% CI	p-value	Beta	95% CI	p-value
Primary Outcomes									
Pain MPAC Immediate									
Depression	−0.17	−0.56, 0.21	0.377	0.17	−0.44, 0.78	0.590	−0.47	−0.92, -0.02	0.042
MSAS-PSYCH	−0.23	−0.51, 0.05	0.106	−0.28	−0.68, 0.13	0.183	−0.14	−0.49, 0.22	0.438
Pain BPI Mean Sustained									
Depression	0.31	−0.04, 0.65	0.084	0.44	−0.02, 0.91	0.062	0.11	0.68, -0.40	0.617
MSAS-PSYC	0.57	0.40, 0.73	< 0.001	0.65	0.42, 0.89	< 0.001	0.52	0.30, 0.73	< 0.001
Pain BPI Worst Sustained									
Depression	0.25	−0.15, 0.65	0.223	0.51	0.00, 1.02	0.049	−0.04	−0.66, 0.57	0.888
MSAS-PSYCH	0.55	0.32, 0.78	< .0001	0.76	0.47, 1.04	< 0.001	0.33	−0.02, 0.67	0.064
Pain BPI Interference Sustained									
Depression	0.44	−0.96, 1.83	0.539	−0.02	−2.18, 2.14	0.986	0.74	−1.00, 2.48	0.399
MSAS-PSYCH	0.91	0.67, 1.15	< 0.001	1.09	0.74, 1.45	< 0.001	0.74	0.42, 1.05	< 0.001
Secondary Outcomes									
Heart Rate Immediate									
Depression	−0.17	−0.56, 0.21	0.377	0.17	−0.44, 0.78	0.590	−0.47	−0.92, 0.02	0.042
MSAS-PSYCH	−0.46	−1.27, 0.34	0.259	−0.28	−1.48, 0.81	0.565	−0.14	−0.49, 0.22	0.438
Respiratory Rate Immediate									
Depression	0.00	−0.61, 0.60	0.996	−0.10	−0.93, 0.73	0.810	0.06	−0.81, 0.94	0.988
MSAS-PSYCH	−0.27	−0.69, 0.25	0.361	−0.22	−1.48, 0.81	0.565	−0.32	−0.84, 0.20	0.227
Distress MSAS Global Sustained									
Depression	0.32	0.17, 0.47	< 0.001	0.43	0.22, 0.65	< 0.001	0.25	0.06, 0.44	0.012
MSAS-PSYCH	0.46	0.42, 0.51	< 0.001	0.48	0.42, 0.54	< 0.001	0.46	0.40, 0.52	< 0.001
Distress MSAS Physical Symptoms Sustained									
Depression	0.23	0.09, 0.37	0.001	0.28	0.08, 0.47	0.005	0.17	−0.02, 0.37	0.086
MSAS-PSYCH	0.19	0.13, 0.24	< 0.001	0.23	0.15, 0.31	< 0.001	0.16	0.08, 0.25	< 0.001
Quality of Life MQOL Overall Sustained									
Depression	−0.67	−1.18, -0.15	0.011	−0.70	−1.44, 0.04	0.065	−0.67	−1.37, 0.03	0.062
MSAS-PSYCH	−0.96	−1.22, -0.71	< 0.001	−1.21	−1.57, -0.84	< 0.001	−0.63	−0.97, -0.28	< 0.001
Quality of Life MQOL Physical Well-Being Sustained									
Depression	−0.60	−1.09, -0.11	0.018	−0.88	−1.62, -0.14	0.019	−0.35	−0.99, 0.29	0.280
MSAS-PSYCH	−0.53	−0.81, -0.25	< 0.001	−0.69	−1.10, -0.29	0.001	−0.36	−0.72, 0.00	0.049
Quality of Life MQOL Existential Sustained									
Depression	−0.47	−0.90, -0.04	0.033	−0.40	−0.99, 0.20	0.192	−0.64	−1.28, -0.01	0.046
MSAS-PSYCH	−0.56	−0.74, -0.38	< 0.001	−0.44	−0.69, -0.19	0.001	−0.58	−0.84, -0.33	< 0.001
Quality of Life MQOL Support Sustained									
Depression	−0.08	−0.47, 0.31	0.693	0.22	−0.33, 0.77	0.420	−0.28	−0.83, 0.28	0.324
MSAS-PSYCH	−0.32	−0.51, -0.12	0.002	−0.26	−0.54, 0.02	0.066	−0.39	−0.65, -0.13	0.004

Note. Estimates based on adjusted mixed-effects models with random intercepts and slopes and fixed effects of time, treatment group (massage therapy vs. simple touch) and baseline depression or psychological symptoms frequency (MSAS-PSYCH). Estimates for time and treatment groups are not shown.

touch with respect to immediate pain and mood.[13] We found that, across treatment groups, both the baseline presence of depression and psychological symptom frequency were associated with primary and secondary study outcomes. Specifically, higher baseline psychological symptom frequency was associated with smaller improvements than lower symptom frequency in sustained ($p < 0.001$) but not in immediate pain ($p > 0.01$) in both treatment groups. Participants with baseline depression also showed smaller improvements in pain outcomes than those without baseline depression, though the differences did not reach statistical significance (all $p > 0.01$). Finally, having baseline depression or higher baseline psychological symptom frequency were significantly associated with lower sustained physical

Table 3
Moderator analysis: p-values for significance of interaction term between baseline depression or psychological symptom frequency (MSAS-PSYCH) and treatment by time.

	Baseline			
	Depression		MSAS-PSYCH	
	F	p-value	F	p-value
Primary Outcomes				
Pain MPAC Immediate	0.44	0.722	0.96	0.413
Pain BPI Mean Sustained	0.57	0.782	1.32	0.237
Pain BPI Worst Sustained	0.81	0.579	1.01	0.426
Pain BPI Interference Sustained	1.28	0.255	0.44	0.879
Secondary Outcomes				
Heart Rate Immediate	0.97	0.406	0.43	0.731
Respiratory Rate Immediate	1.65	0.179	0.37	0.773
Distress MSAS Global Sustained	0.61	0.749	0.75	0.627
Distress MSAS Physical Symptoms Sustained	0.52	0.818	0.52	0.821
Quality of Life MQOL Overall Sustained	1.87	0.072	1.77	0.092
Quality of Life MQOL Physical Well-being Sustained	0.83	0.560	0.46	0.862
Quality of Life MQOL Existential Sustained	0.67	0.700	0.32	0.947
Quality of Life MQOL Support Sustained	1.21	0.295	0.42	0.887

Note. F is omnibus test for significance of the interaction term (time by treatment by baseline depression or psychological symptom frequency (MSAS-PSYCH)) from adjusted mixed-effects models. Immediate outcomes: numerator df = 3, sustained outcomes df = 7.

distress and quality of life than non-depression or lower baseline psychological symptom frequency (p range 0.065 - < 0.001). There was no association between baseline depression and baseline psychological symptom frequency with immediate heart rate or respiratory rate in either treatment group (all $p > 0.01$). (see Table 2).

The presence of depression and baseline psychological symptom frequency did not moderate intervention effects for any of the primary and secondary outcomes; no interaction terms were significant ($p > 0.01$, see Table 3). However, effect sizes show a pattern of slightly better sustained pain outcomes in both MT and simple touch among non-depressed patients, compared to those with baseline depression; these effects sizes were generally in the small to moderate range (Table 4). Improvement in physical distress and quality of life were slightly better among depressed patients receiving MT and non-depressed patients receiving simple touch.

4. Discussion

The current study identified a similar prevalence of depression as in other samples of advanced cancer patients.[5] The presence of depression and baseline psychological symptom frequency significantly predicted changes in pain, 60-second heart and respiratory rates; quality of life, and physical distress across treatment for both MT and simple touch. To our knowledge, this is the first study to identify this association in advanced cancer patients. This finding is also consistent with studies in other populations and for other conditions with associated pain, such as interventions on self-management in musculoskeletal pain or interventions for low back pain, which found that depression predicted outcome irrespective of intervention.[34,35]

Yet while depression has been found to act as a moderator for MT treatment for back pain [21] and in self-management interventions for musculoskeletal pain,[34] neither baseline depression nor psychological symptom frequency differentially predicted changes in pain, 60-second heart and respiratory rates, quality of life, and physical distress across treatment. That is, those with depression or higher psychological symptoms did not respond any more or less favorably to MT than to simple touch. This finding implies that future RCTs of MT in advanced cancer may not need to consider baseline psychological symptoms or the presence of depression in inclusion/exclusion criteria or stratification, though our results need to be replicated in other samples.

There are several possible reasons that both depression and frequent psychological symptoms were associated with poorer response to both MT and simple touch. First, psychological symptoms may mask advanced cancer patients' perceptions of improvements from treatment. Key symptoms of depression include sadness and hopelessness,[36] both of which can become a focus of treatment. Indeed, depression has been found to be associated with negative interpretations and appraisals of illness in patients with end-stage renal disease, which in turn affects emotional and behavioral responses.[37] These interpretations may either limit ability to respond to interventions, or limit patients' ability to communicate any improvements that they may be experiencing. In

Table 4
Moderator analysis: Mean change and within group effect sizes by baseline depression.

		Massage Therapy (MT)		Simple Touch	
		Depressed	Non-depressed	Depressed	Non-depressed
Primary Outcomes					
Pain BPI Mean Sustained	Mean change (baseline-last visit)	0.44	0.41	0.56	0.68
	Within group Cohen's d	0.21	0.31	0.25	0.56
Pain BPI Worst Sustained	Mean change (baseline-last visit)	0.90	0.97	0.76	0.84
	Within group Cohen's d	0.28	0.49	0.22	0.46
Pain BPI Interference Sustained	Mean change (baseline-last visit)	0.63	0.48	0.59	0.42
	Within group Cohen's d	0.23	0.28	0.20	0.27
Secondary Outcomes					
Distress MSAS Global Sustained	Mean change (baseline-last visit)	0.18	0.10	0.07	0.09
	Within group Cohen's d	0.22	0.20	0.09	0.18
Distress MSAS Physical Symptoms Sustained	Mean change (baseline-last visit)	0.21	0.06	0.04	0.10
	Within group Cohen's d	0.28	0.13	0.05	0.21
Quality of Life MQOL Overall Sustained	Mean change (baseline-last visit)	0.99	0.30	0.57	0.34
	Within group Cohen's d	0.33	0.16	0.18	0.20
Quality of Life MQOL Physical Well-being Sustained	Mean change (baseline-last visit)	0.65	0.28	0.26	0.46
	Within group Cohen's d	0.19	0.13	0.07	0.24
Quality of Life MQOL Existential Sustained	Mean change (baseline-last visit)	0.23	0.10	0.08	0.14
	Within group Cohen's d	0.13	0.08	0.04	0.14
Quality of Life MQOL Support Sustained	Mean change (baseline-last visit)	0.09	−0.14	0.24	−0.12
	Within group Cohen's d	0.05	−0.12	0.12	−0.12

Note: Mean change from baseline to last visit is estimated based on adjusted mixed-effects models with time by treatment by baseline depression interaction term. Within group Cohen's d is computed as the change in means from baseline to last visit divided by standard deviation of the change.

addition, psychological symptoms have been found to impact health and physiology, including appetite changes, platelet activation, increased inflammatory responses, functional decline, and sleep patterns.[38] It is possible that these physiological impacts may offset any benefits from massage therapy or simple touch. Additional reasons for the association between psychological symptoms and treatment outcomes could be identified in future work; qualitative research, which can provide in-depth exploration, could be particularly applicable.

One possible explanation for the lack of a moderating effect for both depression and psychological symptom frequency for MT, compared to simple touch, is that individuals with these symptoms have similar responses to both types of therapy. Another possible explanation is that these baseline psychological symptoms are not stable predictors of specific treatment outcomes in the context of changes in symptoms over time. Finally, neither treatment specifically addresses psychological symptoms; if one of the treatment types had done so, it is possible that a moderating effect might have occurred.

Results imply that advanced cancer patients with depression and/or frequent psychological symptoms who are receiving either MT or simple touch treatments could benefit from additional support. Though results only represent findings from a single, somewhat older, study, massage therapy is still a utilized intervention for cancer patients,[11,12] making findings applicable to cancer care today. Because symptoms appear to predict outcomes regardless of intervention type, it may be best to target psychological symptoms in early stages of cancer diagnosis, before symptoms progress. Brief treatments to specifically address psychological symptoms could be integrated or added onto MT treatment, or delivered prior to MT, to enhance treatment gains. A range of such evidence-based brief treatments exist, many of which have been applied to cancer patients. These include psychoeducation, cognitive behavioral therapy (CBT), problem solving therapy (PST), Behavioral Activation (BA) and acceptance and commitment therapy (ACT), and mindfulness-based treatments.[12,39–45] All of these treatments specifically address mood symptoms and are short-term and time-limited, enhancing their ease of implementation. However, given potential challenges around the duration, logistics, and implementation of these treatments in a population of advanced cancer patients, treatment may often need to be adapted. Adaptations that have been made include focusing on cancer-specific concerns and adjusting for and addressing limitations from fatigue and physical pain.[46] Treatments should also be individualized to each patient's needs.[12] For those with more severe depression symptoms, antidepressant medications may also be helpful, though interactions with chemotherapy or radiotherapy should be taken into account.[40]

4.1. Limitations

This study has several strengths, including random assignment and multiple follow-up assessments. There are some limitations, however. First, participants did not receive standardized measures of mental health disorders (e.g. PHQ-9 for depression, GAD-7 for anxiety). Therefore, we relied on chart data and brief self-report measures, which were part of longer scales, to assess psychological symptoms. We therefore cannot compare identified symptoms to these commonly used measures, and do not know whether the results from this study would be generalizable to results obtained by using alternative assessment interviews, such as clinical interviews. However, all measures used had pre-established validity and reliability. In addition, current assessment methods might have biased findings. Immediate outcome measures may also be biased, as they were obtained by treating therapists, who were not blinded to treatment assignment. Another limitation, due to the nature of the sample, was the fairly high participant drop-out due to death/disability, though we did account for this in analyses.

Moreover, the lack of a "usual care" control arm prevents examination of the differential impact of the simple touch control condition. Another limitation is the lack of follow-up data; we do not know whether the associations we found between psychological symptoms and outcomes persisted beyond the current follow-up. The lack of fidelity ratings for therapists is another limitation. As indicated earlier, however, all therapists were highly trained. Finally, the study was conducted in only 15 clinical settings, and only included those who were English speaking and had a life expectancy of three weeks or greater; results cannot be generalized to other samples.

5. Conclusions

Our findings support the importance of considering psychological symptoms when examining the efficacy of massage and related treatments in advanced cancer patients. This research adds to a small body of literature on moderators of treatment outcomes in cancer patients. Advanced cancer patients with psychological symptoms may require additional support in order to benefit from any type of touch therapy. Future work can attempt to replicate findings in other samples of cancer patients receiving massage therapy.

Declaration of Competing Interest

None.

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