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Network intervention analysis of anxiety-related outcomes and processes of acceptance and commitment therapy (ACT) for anxious cancer survivors

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ABSTRACT

Objective: Psychotherapies like Acceptance and Commitment Therapy (ACT) are thought to target multiple clinical outcomes by intervening on multiple mechanistic process variables. However, the standard mediation approach does not readily model the potentially complex associations among multiple processes and outcomes. The current study is one of the first to apply network intervention analysis to examine the putative change processes of a psychotherapy.

Methods: Using data from a randomized trial of ACT versus minimally-enhanced usual care for anxious cancer survivors, we computed pre-to post-intervention (n = 113) residualized change scores on anxiety-related outcomes (general anxiety symptoms, cancer-related trauma symptoms, and fear of cancer recurrence) and putative processes of the intervention (experiential avoidance, self-compassion, and emotional approach coping). We estimated a network model with intervention condition and residualized change scores as nodes.

Results: Contrary to the expectation that intervention effects would pass indirectly to outcomes via processes, network analysis indicated that two anxiety-related outcomes of the trial may have acted as primary *mechanisms* of the intervention on other outcome and process variables.

Conclusions: Network intervention analysis facilitated flexible evaluation of ACT's change processes, and offers a new way to test whether change occurs as theorized in psychotherapies.

Clinical psychological science has long focused on the question of which psychological *processes*[1] are targeted by which therapies to produce clinical improvement (Kazdin, 2007). This question has taken on an increasing level of interest and importance as methods have advanced for gathering and analyzing multivariate longitudinal datasets relevant to psychotherapy (e.g., Hofmann et al., 2020; Piccirillo & Rodebaugh, 2019), and as evidence-based therapies have increasingly been adapted from narrower, diagnosis-specific protocols to transdiagnostic, modular and highly flexible interventions. Accordingly, such transdiagnostic interventions, which include acceptance and commitment therapy (ACT; S. C. Hayes et al., 2012) and transdiagnostic forms of cognitive behavioral therapy (e.g., Barlow, 2011), are thought to target multiple processes and thereby to influence numerous clinical outcomes (Gloster et al., 2020; Talkovsky & Norton, 2018). A common refrain (e.g., Hofmann et al., 2020) during the current period of evidence-based practice is that in order to tailor interventions for new groups, and even to specific individuals, we must better understand how evidence-based psychotherapies influence different processes, and how those processes influence clinical outcomes of interest. To this end, the current study innovatively applies network intervention analysis (Blanken et al., 2019), a recently developed approach to examining the direct and indirect effects of a intervention, toward estimating the relationship of intervention processes and outcomes in the context of an ACT trial for anxious cancer survivors.

Paralleling the broader psychotherapy literature, studies to date that examine processes of ACT have mostly used standard mediation

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[1] We use the term 'processes' here following the precedent of Hayes, Hofmann, and their colleagues (2019), who defined therapeutic processes as "the underlying change mechanisms that lead to the attainment of a desirable treatment goal." In their work to date on this topic (e.g., S. C. Hayes & Hofmann, 2018; Hofmann et al., 2020), therapeutic processes are differentiated from psychopathology dimensions and symptoms.

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analysis, which estimates a relatively simple causal chain from the intervention condition assignment to one or a few mediating process variables to a single outcome variable (e.g., A. F. Hayes, 2018). Similar to meta-analytic findings examining theorized mediators of cognitive behavioral therapy (Parsons, 2021) and mindfulness-based psychotherapeutic interventions (Johannsen et al., 2022) that found relatively small mediating effects of theorized processes, Stockton and colleagues' (2019) systematic review examining the evidence for core theorized ACT processes as mediators in ACT trials yielded mixed results. This lack of strong, consistent evidence for theorized processes as actual mediators may be due at least in part[2] to greater complexity of the interrelationships of processes and outcomes than is captured in current standard mediation approaches or theories of how psychotherapies work (Hofmann et al., 2020). Given the modest size and mixed results of existing psychotherapy mediation findings, a more exploratory mode of research is likely needed to generate new hypotheses (Munafò et al., 2017) regarding the mechanistic pathways that underlie the effects of psychotherapy.

Standard mediation analysis has notable limitations in its application as an exploratory tool for investigating psychotherapy processes. The standard mediation approach typically accommodates only one or a few (A. F. Hayes, 2018) putative mechanistic variables, and typically only one outcome variable, despite that many contemporary evidence-based psychotherapies target multiple processes and are directed at multiple outcomes. Process variables may even have mechanistic effects on other process variables (Hanley et al., 2021) and outcome variables may operate as processes on other outcomes (e.g., Starr & Davila, 2012). Yet standard mediation studies typically do not analyze all associations among process and outcome variables; thus, the unique effect of an intervention on associated processes or outcomes may be masked or incomplete, and the presence of mechanistic relationships among multiple processes or among multiple outcomes cannot be assessed. Omitting such paths may be sensible in confirmatory research, but it stymies exploratory analyses.

Network intervention analysis, specifically using mixed graphical models (Haslbeck & Waldorp, 2020) to estimate the network, addresses these limitations of the standard mediation approach. First, in contrast to the standard mediation approach, the network approach can readily accommodate numerous putative processes and clinical outcome variables in a single model, and makes no *a priori* assumptions about which specific variables should have mechanistic effects on which others. Second, and relatedly, the network structure estimates the relationships among *all* variables in the network, and yields estimates of the unique effects of each variable in the network. Thus, the network intervention approach may yield useful information about the *unique* direct effects of an intervention on a specific variable, accounting for all other effects of the intervention and among other measured variables.[3]

For these reasons, network intervention analysis provides a potentially promising alternative strategy to examining treatment processes of psychotherapy. It has typically been used to examine the direct and indirect effects of randomization to a psychotherapy intervention condition versus a control condition on symptoms of depression or other clinical presentations (e.g., Bernstein et al., 2021; Blanken et al., 2021; Boschloo et al., 2019). These past studies have not, however, included process variables as part of their networks. Building toward the approach to examining therapeutic processes in networks, Curtiss et al. (2021) used network analysis to evaluate the putative process variables of two psychotherapy treatments. However, they did not include treatment condition in the network. To examine the direct and indirect effects of treatment, the treatment assignment variable must be included in the network. Lancee et al. (2022) examined the effect of treatment condition on processes of CBT for insomnia, but did not examine the relationships between and among processes and outcomes to comprehensively assess which variables were mechanistic.

Building upon the literature to date, the current study examines both the effects of intervention condition on change in process and outcome variables and the relationships among and between process and outcome variables. Analyzing this combination of effects enables the evaluation of which variables serve as processes. Following this logic, the current study examined network intervention effects in the context of the Valued Living trial (Arch et al., 2019, 2021), a randomized controlled trial of ACT versus minimally enhanced usual care for anxious cancer survivors.

To characterize the processes of ACT's effects in that trial, Fishbein et al. (2022) analyzed multiple potential processes of the Valued Living trial's intervention effects on three anxiety-related outcome variables. Consistent with common practice in the statistical (e.g., A. F. Hayes, 2018) and empirical (e.g., Stockton et al., 2019) literatures, they pre-specified mediators and outcome variables, and estimated unique *a*, *b* and *c'* paths in single mediation models of mediator and outcome variables pairs. They found that in the Pre-to Post-intervention interval, ACT participants improved significantly more on self-compassion and emotional approach coping (EAC), and found that improvement on those two processes significantly or marginally mediated ACT's effects on cancer-related trauma symptoms, fear of cancer recurrence, and general anxiety symptoms. However, ACT did not lead to significantly greater improvement on cancer-related experiential avoidance.

The main purpose of the present study was to compare network analysis results to the known findings of the standard mediation analysis (Fishbein et al., 2022), and specifically, to examine whether those analytic approaches indicated the same pattern of relationships among intervention processes and outcomes. The current exploratory analysis thus investigated whether the same indirect intervention effects of self-compassion and EAC on anxiety-related outcomes observed in the standard mediation analysis would emerge in the pre-to post-treatment network. It also evaluated whether there would be evidence for the indirect effects of assignment to ACT on process variables via other process variables, on outcome variables via other outcome variables, or even on process variables via outcome variables.

1. Methods

1.1. Original trial design

This study analyzed data from the Valued Living trial (Arch et al., 2019, 2021), wherein anxious cancer survivors were randomized (1:1 allocation) either to a 7-week ACT-based group intervention (one 2-hr session per week) or to usual care minimally enhanced by provision of a sheet of community mental health and supportive care resources and encouragement to reach out to their oncology social worker as needed (i.e., minimally enhanced usual care; MEUC). In order to test the intervention within a typical practice setting where anxious cancer survivors would be likely to receive supportive interventions (Petrelli, 2010), the study was carried out within a community oncology practice network. The ACT groups were facilitated by onsite community oncology social workers who received 3 days of in-person training on the ACT-based treatment manual plus four 1-h phone trainings; only one social worker had a previous background in ACT. Readers are directed to Arch et al. (2021) for further details of the full trial sample, study conditions,

[2] Psychometric issues with widely-used ACT process variable measures (Reilly et al., 2019; Tyndall et al., 2019) and nonalignment of modeled time lags with the actual time course of causal pathways between processes and outcomes (e.g., Hofmann et al., 2020) likely are also important factors driving the findings to date.

[3] The standard mediation approach could, in theory, be extended to accommodate numerous process and outcome variables, and to model associations between many (or even all) variables in the model. Yet such an approach is rarely if ever taken in the empirical literature. Network intervention analysis is designed to model many associations between related variables, as described in detail in the *Methods*.

and outcomes. The trial was approved by the Institutional Review Board of the University of Colorado Boulder and was pre-registered on clinicaltrials.gov (NCT02550925).

In the current study, we focus on data from pre-intervention baseline (Pre), post-intervention (Post), and the final follow-up (FU) timepoint, assessed 8 months after Pre. All measures were administered at all timepoints and were assessed online in Qualtrics (Provo, UT).

1.2. Participant eligibility criteria

Eligibility criteria for the Valued Living trial were as follows: 1) completed primary treatment for cancer between 1.5 and 24 months before enrollment; 2) screened positive for moderate to high cancer-related anxiety (scored ≥5 on a 0–10 scale measuring current anxiety about cancer or survivorship [Arch & Mitchell, 2016]) and for general anxiety or depression symptoms (scored ≥3 on the Generalized Anxiety Questionnaire-2 [Plummer et al., 2016] or Patient Healthcare Questionnaire-2 [Löwe et al., 2005]); 3) had no evidence of current disease for solid tumor cancers, or an asymptomatic or remitted hematologic malignancy; 4) proficient in English; and 5) had not started a new antidepressant or anxiolytic medication within two months of enrollment.

1.3. Current study participants

The method to estimate network models used here requires complete data; we therefore only used a participant's data in a network if they had valid responses on all current study measures at both timepoints reflected within that network. Thus, though the total trial enrollment was $N = 134$, only participants with complete Pre and Post data were included in the Pre-Post intervention network ($n = 113$; see Table 1). They were on average 56.49 ($SD = 10.73$) years old upon enrolling in the trial, majority white, non-Latinx (87.39%) and female (89.38%). At enrollment, they reported a median annual income of $61,000–80,000 USD and a median educational attainment of a Bachelor's degree. Slightly over half of these participants (59.82%) were diagnosed with breast cancer. Further demographic details are provided by Arch et al. (2021). ACT and MEUC participants did not differ on demographic variables, $ps \geq .687$. However, ACT participants reported slightly more elevated levels of cancer-related trauma symptoms and cancer-related experiential avoidance prior to beginning the intervention ($ps \leq .033$).

Table 1
Pre-Post Network Sample Baseline Characteristics.

Category	MEUC	ACT	*p*
N	58	55	
Age– *M (SD)*	56.14 (11.52)	56.85 (9.92)	.724
Female - % (*N*)	91.38 (53)	87.27 (48)	.687
White, Non-Latinx Race/Ethnicity - % (*N*)	85.96 (49)	88.89 (48)	.859
At least $61,000 USD Annual Income - % (*N*)	55.17 (32)	52.73 (29)	.943
At Least Bachelor's Degree - % (*N*)	79.31 (46)	67.27 (37)	.217
Initial diagnosis Stage 0-I - % (*N*)	62.07 (36)	60.00 (33)	.974
Breast Cancer (vs other cancer type) - % (*N*)	64.91 (37)	54.55 (30)	.354
Scores at pre-intervention			
HADS – *M (SD)*	9.74 (3.07)	10.58 (3.23)	.169
CARS– *M (SD)*	3.92 (1.27)	4.32 (0.99)	.068
IES-R– *M (SD)*	1.41 (0.57)	1.63 (0.54)	.033
AAQc – *M (SD)*	45.74 (13.57)	51.84 (9.57)	.007
SCS – *M (SD)*	3.11 (0.72)	2.97 (0.67)	.292
EAC – *M (SD)*	2.55 (0.77)	2.33 (0.59)	.081

Note. We compared conditions using *t*-tests for continuous variables and χ^2 tests for dichotomous variables. The fourth column presents *p* values associated with these tests.
AAQc = Acceptance and Action Questionnaire-Cancer; CARS = Concerns About Recurrence Scale; EAC = Emotional Approach Coping scale; IESR = Impact of Events Scale-Revised; HADS = Hospital Anxiety and Depression Scale – Anxiety subscale; SCS = Self-Compassion Scale Short Form.

1.4. Measures

Information regarding the full set of variables assessed in the Valued Living trial is provided by Arch et al. (2019, 2021). By design, the current study parallels the standard mediation analysis of the Valued Living trial (Fishbein et al., 2022) in that it examines three putative processes of the ACT intervention and three anxiety-related outcomes that were administered at each trial timepoint. Each variable's conditional means by timepoint are provided in Supplemental Figure A1 (see Appendix A).

As outcome variables, the current study examined anxiety symptoms using the Hospital Anxiety and Depression Scale – Anxiety subscale (HADS-A, current study pre-intervention ω_{Total} reliability estimate = 0.82; Zigmond & Snaith, 1983), cancer-related trauma symptoms using an adapted version of the Impact of Events Scale-Revised (IES-R; $\omega_{Total} = 0.85$; Weiss & Marmar, 1997), and fear of cancer recurrence using the Concerns About Recurrence Scale–Overall score (CARS; $\omega_{Total} = 0.85$; Vickberg, 2003). Lower scores on these measures indicate lower anxiety/fear. In the Valued Living trial, the ACT condition showed greater improvement from Pre to Post (Fishbein et al., 2022) and from Pre to FU (Arch et al., 2021) on trauma symptoms and fear of recurrence. However, the conditions did not differ in change on HADS-A anxiety symptoms from Pre-to Post-intervention, and the ACT condition showed only marginally greater improvement than MEUC on anxiety symptoms from Pre-intervention to the 8-month follow-up timepoint.

The three process variables from the trial that were analyzed presently are: cancer-related experiential avoidance using the Cancer Acceptance and Action Questionnaire (AAQc, $\omega_{Total} = .83$; Arch & Mitchell, 2016), self-compassion using the Self-Compassion Scale Short Form (SCS, $\omega_{Total} = 0.87$; Raes et al., 2011), and EAC using the EAC scale ($\omega_{Total} = 0.91$; Stanton et al., 2000).

We assessed these specific variables because they were each conceptualized as processes of the intervention in the Valued Living trial. Experiential avoidance is a core process targeted by ACT (S. C. Hayes et al., 2012), and the AAQc specifically measures avoidance of thoughts and feelings about cancer and its consequences. Self-compassion is a process that is closely tied to the flexible self-perspective taking dimension of ACT's theoretical model (Neff & Tirch, 2013), and the common humanity and self-kindness elements of self-compassion were specifically targeted by the Valued Living trial intervention. Lower self-compassion is associated with higher anxiety in cancer patients (Hughes et al., 2021), thus highlighting it as a potentially important process in the current study sample. EAC is a process that consists of actively acknowledging, processing, and expressing emotions about a situation as a means of responding effectively to it. Thus, EAC is broadly consistent with ACT, but is also likely consistent with other EBPs and nonspecific, supportive therapies that promote exploring and discussing emotions. Moreover, greater EAC usage is associated with higher self-reported psychological well-being in breast cancer survivors (Stanton, Danoff-Burg et al., 2000).

The standard mediation analyses of the Valued Living trial (Fishbein et al., 2022) also assessed values-consistent behavior (measured with two separate instruments) and non-cancer-specific experiential avoidance as putative of the intervention. However, since there was considerable missing data on two of these measures, and because the third was not associated with the anxiety-related outcomes in the mediation models, we omitted them from the current study analyses.

Lower scores on the AAQc, and higher scores on the SCS and EAC measures, indicate improvement expected with ACT. As shown by Fishbein et al. (2022), in standard mediation analyses of the Valued Living trial, improvement in self-compassion and EAC both improved more from Pre to Post in the ACT condition, and both partially mediated

the effect of ACT on Pre-Post improvement in cancer-related trauma symptoms and fear of cancer recurrence. Contrary to expectations (and further detailed in the Discussion below), cancer-related experiential avoidance did not improve more in the ACT condition and was thus not a mediator.

1.5. Analytic approach

The present study used network intervention analysis (Blanken et al., 2019). In contrast to previous network intervention analysis studies, this study is one of the first to apply a network intervention analysis to a combination of process and outcome variables and to examine both intervention effects and effects between and among process and outcome variables. Networks were estimated as mixed graphical models using the 'mgm' R package (version 1.2–12; Haslbeck & Waldorp, 2020). R syntax for the current study analyses is available at https://osf.io/ae9xz/.

1.6. Estimation procedure

1.6.1. Network intervention analysis

To examine network intervention effects, we used Mixed Graphical Models (MGMs; see Fig. 1). MGMs estimate the unique associations (*edges*) between and among continuous and categorical variables (*nodes*) in a network, using an L1-regularized ("lasso") nodewise regression approach as implemented in the 'mgm' R package (Haslbeck & Waldorp, 2020). Lasso regularization performs data-driven selection of edges in the network by shrinking all parameter estimates toward zero and setting small estimates exactly to zero. By virtue of this selection process, lasso regularization yields a relatively 'sparse' network comprised just of the strongest edges observed in the sample. Weaker edges that may arise due to spurious associations between variables are thereby eliminated (Epskamp & Fried, 2018), thus reducing the rate of false positives. This provides a more parsimonious (and thus potentially more easily interpretable; James et al., 2021) network structure.[4]

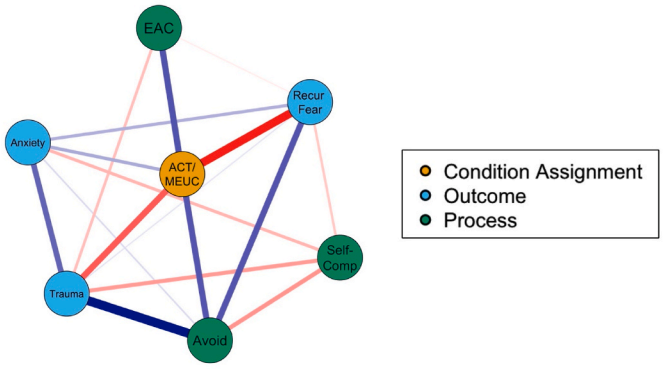

Fig. 1. *Pre-Post Intervention Network*

Note. Blue edges between nodes reflect positive associations (i.e., higher values on one variable are associated with higher values on the other), whereas red edges between nodes reflect negative associations (i.e., higher values on one variable are associated with *lower* values on the other). Thicker edges reflect larger absolute values of edge estimates computed from the study sample. Intervention condition (labeled ACT/MEUC) is coded as 0 = MEUC, 1 = ACT; thus, edges between the condition node and other nodes reflect the effect of assignment to ACT relative to MEUC. The general anxiety symptom, cancer-related trauma symptom, fear of cancer recurrence, and experiential avoidance variables are scored such that lower scores indicate improvement, whereas higher scores indicate improvement on the self-compassion and emotional approach coping variables. Edges between all nodes were estimated, but only nonzero-magnitude edges are shown. Thicker edge weights and more saturated colors denote higher magnitudes of associations. The network node layout was generated using the Fruchterman-Reingold algorithm. Numeric values associated with each edge are provided in Table 2. Anxiety = General anxiety symptoms; Avoid = Experiential avoidance; EAC = Emotional approach coping; Recur Fear = Fear of cancer recurrence; Self-Comp = Self-compassion; Trauma = Cancer-related trauma symptoms. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

In an MGM, the associations between pairs of continuous variables can be interpreted similarly to partial correlations. Partial correlations reflect the unique linear association between two variables, after accounting for all other variables in the model. Edges connecting the intervention condition node and a measured variable node reflect the difference between the two conditions in standardized units ($M = 0$, $SD = 1$) of the measured variable. In this sense, they may be interpreted as effect sizes (adjusted for relations among all variables in the model). Edges connecting two measured variables can be interpreted as standardized regression weights, or in other words, the expected effect of a one unit difference in one variable on the other when both variables are standardized and when keeping all other variables constant.

The mediation analyses previously conducted on the Valued Living trial data (Fishbein et al., 2022) used full ANCOVA-equivalent structural equation models (see Valente & MacKinnon, 2017). However, the ANCOVA approach was not feasible for the current network analysis given that it would require adding each variable twice (i.e., once for each measurement occasion) to each network, which would drastically reduce statistical sensitivity given the study's sample size. We therefore proceeded to compute change scores using residualized change scores, an approach that maintains some of the statistical advantages of ANCOVA modeling over simpler difference score models (Valente et al., 2021; Valente & MacKinnon, 2017). We obtained residualized Pre-Post change scores (henceforth, Pre-Post scores) by separately regressing each variable's values at Post on its values at Pre, and then storing the residuals of those regression equations.

As described above, given the manner of scoring each measure, negative (<0) change scores indicate greater within-person improvement relative to the average person in the sample on the anxiety symptom (HADS-A), cancer-related trauma symptom (IES-R), fear of cancer recurrence (CARS), and cancer-related experiential avoidance (AAQc) measures used in the present study, whereas positive (>0) change scores indicate greater within-person improvement relative to the average person in the sample on self-compassion (SCS) and EAC measures. The six Pre-Post score variables and a condition assignment variable (0 = MEUC, 1 = ACT) were entered into a MGM to examine Pre-Post network intervention effects (Fig. 1).

The Pre-Post intervention network described above was the main network of interest in the current study. However, because the main outcomes analyses of the Valued Living trial (Arch et al., 2021) examined change on outcomes from Pre to FU, we repeated the above analytic steps with Pre-FU scores ($n = 107$). For brevity, the results of the Pre-FU network intervention model are presented in Appendix A.

1.6.2. Bootstrapping to obtain inclusion percentage

To further evaluate to what extent the sample-derived estimate of each edge generalizes to the population of interest, we fit MGMs on 5000 nonparametric bootstrapped samples. We examined the percentage of bootstrap samples in which an edge was nonzero and in the same direction as the sample estimate (*i.e.,* the *inclusion percentage*), with a higher percentage indicating that the strength of an edge was more robust to differences in sample composition. When interpreting the network structure in Results below, we focused on nonzero edges with

[4] The tuning parameter that determines the cutoff of edge magnitudes that will be set to zero is determined by the model-fitting algorithm. Typically, the algorithm examines a range of tuning parameters and selects the one that optimizes overall fit according to cross-validation or an information criterion statistic. In the present study, cross-validation was used to determine the optimal overall fit, as per Friedman et al. (2010).

an inclusion percentage of at least 60%.[5] We also computed 95% quantiles of the numerical estimate for each edge. Due to small values being regularized to zero in the lasso procedure, these quantiles should not be used for null-hypothesis significance testing (Williams, 2021).

1.6.3. Predictability of nodes

To further characterize the observed network effects, we computed the *predictability* of each measured variable node in the network by computing the total variance explained (R^2) in scores for a given measured variable by its associations with other network nodes (Haslbeck & Waldorp, 2018). Higher R^2 values for a given node indicate that more of its variance is accounted for by relationships with other nodes.

1.6.4. Moderated Network Models

In a final network modeling step, we fit Moderated Network Models (Haslbeck et al., 2021; see Supplemental Figure B1), wherein not only the means of measured variables, but also the edges in the network can be a function of condition assignment. This modeling step allows for examination of whether conditions may have differed in overall network structure. The ACT and MEUC groups' unique models were identical in the Pre-Post interval and very similar in the Pre-FU interval. For brevity, we report the details of these models in Appendix B.

1.6.5. Replication of standard mediation analyses

We sought to confirm that the Pre-Post mediation findings from the full Valued Living trial sample ($N = 134$; Fishbein et al., 2022) held in the current Pre-Post analytic sample of $n = 113$. Because we computed residualized change scores for the network models in the current study, we likewise computed the standard mediation analyses using residualized change scores (Valente & MacKinnon, 2017). In these models, mediator Pre-Post residualized change scores were regressed on intervention condition (*a* path) and outcome Pre-Post residualized change scores were regressed on mediator Pre-Post residualized change scores (*b* path) and trial condition (*c'* path). We estimated mediation path models with each process variable mediating each outcome variable, totaling nine unique models, and computed standard errors of the indirect effect (*ab*) over 10,000 nonparametric bootstrapped samples. The results of these models are described below, and parameter estimates are provided in Supplemental Table C1.

Additionally, to ensure the residualized change score mediation models yielded the same overall pattern of results as the parallel ANCOVA models, we replicated the ANCOVA-equivalent mediation models in the current Pre-Post analytic sample (see Supplemental Table C2). The results of these models were consistent overall with the residualized change score models; we thus focus on interpretation of the residualized change score models in the Results and Discussion below.

2. Results

2.1. Pre-Post intervention network

2.1.1. Intervention effects

The final Pre-Post network is displayed in Fig. 1, and intervention effects are shown as edges connected to the ACT/MEUC node. Assignment to the ACT intervention was associated with more positive change scores in EAC (indicating ACT participants improved more relative to MEUC; edge present in 95% of models across bootstrap samples; Table 2), fear of cancer recurrence (98% inclusion) and cancer-related trauma symptoms (94% inclusion). However, ACT was associated with more *positive* change scores in cancer-related experiential avoidance (93% inclusion) and anxiety symptoms (70% inclusion), indicating that ACT improved less than MEUC (see also Supplemental Figure A1).

2.1.2. Associations among process variables

The associations among process variables are displayed as edges in Fig. 1 connecting process variable nodes. More negative experiential avoidance change scores (indicating *less* experiential avoidance at Post relative to Pre) were associated with more positive self-compassion change scores (93% inclusion; Table 2). EAC was not associated with other process variables.

2.1.3. Associations among anxiety outcomes

The associations among anxiety outcomes are displayed as edges in

Table 2
Sample and Bootstrapped Pre-Post Network Parameter Estimates.

Edge Definition		Pre to Post Network Estimate		
Variable 1	Variable 2	Sample Estimate	Bootstrap Mean [95% Quantile]	Inclusion %
Intervention Effects				
Intervention Condition	HADS	0.14	0.16 [0.00, 0.42]	70
Intervention Condition	IESR	−0.29	−0.28 [-0.54, 0.00]	94
Intervention Condition	CARS	−0.39	−0.38 [-0.63, −0.13]	98
Intervention Condition	SCS[a]	0.00	0.04 [-0.17, 0.28]	35
Intervention Condition	EAC[a]	0.29	0.30 [0.00, 0.54]	95
Intervention Condition	AAQc	0.28	0.28 [0.00, 0.52]	93
Process Variable Associations				
SCS[†]	EAC[a]	0.00	0.05 [0.00, 0.19]	47
SCS[†]	AAQc	−0.19	−0.19 [-0.35, 0.00]	93
EAC[†]	AAQc	0.00	−0.04 [-0.18, 0.00]	42
Outcome Variable Associations				
HADS	IESR	0.26	0.25 [0.06, 0.41]	98
HADS	CARS	0.13	0.12 [0.00, 0.26]	78
IESR	CARS	0.04	0.07 [0.00, 0.24]	51
Process-Outcome Associations				
HADS	SCS[a]	−0.13	−0.13 [-0.27, 0.00]	85
HADS	EAC[a]	0.00	−0.01 [-0.15, 0.14]	25
HADS	AAQc	0.06	0.09 [0.00, 0.27]	65
IESR	SCS[a]	−0.18	−0.16 [-0.3, 0.00]	91
IESR	EAC[a]	−0.12	−0.09 [-0.23, 0.00]	73
IESR	AAQc	0.44	0.42 [0.26, 0.58]	100
CARS	SCS[a]	−0.10	−0.08 [-0.23, 0.00]	65
CARS	EAC[a]	−0.03	−0.06 [-0.21, 0.00]	51
CARS	AAQc	0.29	0.27 [0.12, 0.41]	99

Note. Estimates are derived from a mixed graphical model containing nodes for intervention condition (coded 0 = MEUC; 1 = ACT) and Pre-Post change scores on six variables.

The HADS, IES-R, CARS, and AAQc (i.e., all measures except those denoted with [†]) are scored such that lower scores indicate improvement. 5000 nonparametric bootstraps were estimated to obtain the bootstrapped mean and 95% quantiles for each edge value. Inclusion % was computed as the number of nonparametric bootstraps out of 5000 in which the edge was nonzero and in the same direction as the sample estimate and bootstrap mean; higher inclusion % indicates that the edge was present in more bootstrapped models, and thus was more robust to sample composition.

AAQc = Acceptance and Action Questionnaire-Cancer; CARS = Concerns About Recurrence Scale; EAC = Emotional Approach Coping scale; IESR = Impact of Events Scale-Revised; HADS = Hospital Anxiety and Depression Scale – Anxiety subscale; SCS = Self-Compassion Scale Short Form.

[a] indicates variables (EAC and SCS) wherein higher scores indicate improvement.

[5] There is no standard inclusion percentage value used in the network literature to establish which network edges should be interpreted. We chose 60% as a cutoff that would ensure all interpreted network edges were reasonably robust to sample composition, but that would not be so conservative as to discount potentially important but weaker effects in this exploratory analysis. When the sample edge estimate was zero, we calculated inclusion percentage as the number of bootstrapped samples in which the edge estimate matched the direction of the mean bootstrap estimate.

Fig. 1 connecting anxiety outcome nodes. Reduction in anxiety symptoms was associated with reduction in trauma symptoms (98% inclusion; Table 2) and fear of cancer recurrence (78% inclusion) over the Pre-Post interval.

2.1.4. Process-outcome associations

The associations between process and outcome variables are displayed as edges in Fig. 1 connecting process variable and anxiety outcome nodes. Change in self-compassion was negatively associated with change in anxiety symptoms (85% inclusion), trauma symptoms (91%), and fear of cancer recurrence (65% inclusion). Thus, the network effects suggest that greater Pre-Post improvement in self-compassion was associated with greater Pre-Post improvement on all three anxiety-related outcomes. Change in experiential avoidance was positively associated with change in trauma symptoms (100% inclusion; Table 2), fear of recurrence (99% inclusion), and anxiety symptoms (65% inclusion); thus, as was the case with self-compassion, greater improvement in experiential avoidance was associated with greater improvement in all three anxiety-related outcomes. By contrast, change in EAC was negatively associated with change in trauma symptoms (73% inclusion), but not anxiety symptoms or fear of recurrence. Thus, improvement in self-compassion was only associated with improvement in trauma symptoms.

2.1.5. Node predictability

Predictability was highest for trauma ($R^2 = 0.58$), indicating that over half of the variance in participants' change in trauma symptoms was explained by change in other variables within the network, including Condition. The nodes with the next highest predictabilities were experiential avoidance ($R^2 = 0.53$), anxiety symptoms ($R^2 = 0.36$) and fear of cancer recurrence ($R^2 = 0.34$). The lowest variance explained was for self-compassion ($R^2 = 0.29$) and EAC ($R^2 = 0.27$).

2.2. Standard mediation analyses

2.2.1. Residualized change score models

In the current Pre-Post analytic sample, ACT participants improved significantly more on EAC, but not experiential avoidance or self-compassion, relative to MEUC (*a* paths; Supplemental Table C1). Associations between process and outcome variables were significant and in the expected direction (*b* paths), with the exception of a marginally significant ($p = .050$) negative effect between EAC and general anxiety symptoms. EAC was a significant partial mediator of cancer-related trauma symptoms (*ab*; p = .034) and a marginal partial mediator of fear of cancer recurrence ($p = .083$) and general anxiety symptoms ($p = .070$); however, neither experiential avoidance nor self-compassion showed mediating effects.

2.2.2. ANCOVA-equivalent models

ANCOVA-equivalent standard mediation models suggested a trend toward significantly more improvement on self-compassion in ACT participants (Supplemental Table C2 *a* paths; *ps* = .054-.107) but, as with the residualized change score models, those effects were not significant. Self-compassion approached but did not reach full significance as a mediator of trauma symptoms (*ab* $p = .070$). The pattern of observed effects was otherwise the same as in the residualized change score models described above.

3. Discussion

The present study examined network intervention effects in a randomized controlled trial of ACT versus minimally-enhanced usual care for anxious cancer survivors with a focus on anxiety-related outcomes and ACT-relevant process variables. The network computed over the Pre-Post interval suggested that two anxiety-related outcomes carried indirect salutary effects of the intervention onto two putative processes (self-compassion and experiential avoidance) and the third anxiety-related outcome (general anxiety symptoms). Critically, the standard mediation findings obtained with the same trial dataset and variables (Fishbein et al., 2022) did not replicate in the network analysis. This study, which is one of the first to examine both putative process variables and outcome variables using network intervention analysis, thus highlights the potential utility of the network intervention approach to examine mechanisms of multi-component psychotherapies in an exploratory manner. We note, however, that the present study is limited to capturing contemporaneous change between measured variables and thus cannot speak directly to causality of mechanisms.

3.1. Findings from putative process variables

The Pre-Post network indicated that ACT participants improved less on cancer-related experiential avoidance than MEUC (see Pre-Post network in Fig. 1 and longitudinal change in Supplemental Figure A1). This finding is contrary to what would be expected in an ACT-based intervention (S. C. Hayes et al., 2012). Experiential avoidance is a core theoretical process targeted by ACT and is the most widely-supported mediator of ACT across trials (Stockton et al., 2019). Thus, the finding in the present study that experiential avoidance was not directly targeted by ACT is surprising. However, that finding is consistent with the standard mediation analysis findings for these data that showed no mediating effect of cancer-related experiential avoidance on anxiety outcomes (Fishbein et al., 2022). The current network analyses suggest that, as with self-compassion (see below), improvement in cancer-related experiential avoidance was associated with improvement over the same time period in cancer-related trauma symptoms and fear of cancer recurrence. This finding suggests the possibility of a mechanistic pathway of outcome variables passing the effects of the ACT intervention to a putative process variable.

Findings from standard mediation analyses regarding emotional approach coping as a mechanism of the intervention (Fishbein et al., 2022) largely replicated in the Pre-Post network. However, findings regarding self-compassion differed between the network and standard mediation models. Whereas the standard mediation analysis (Fishbein et al., 2022) indicated that self-compassion was a significant or marginal partial mediator of ACT's effects on all three cancer-related trauma symptoms, the current network analysis indicated the opposite: ACT was associated with greater improvement in self-compassion via its direct effects on cancer-related trauma symptoms and fear of cancer recurrence. Thus, the current network analysis findings suggest that two anxiety-related outcomes passed an indirect effect of the ACT intervention onto self-compassion. A potential implication of this finding, worthy of further investigation, is that improvement in anxiety-related outcomes served as a mechanism of the intervention's effect on self-compassion. We note, however, that the current study potentially lacked power to detect a smaller but present meaningful direct effect of the intervention on self-compassion, in addition to the indirect effects of the intervention on self-compassion described above.

3.2. Findings from anxiety-related outcomes

Assignment to ACT was directly associated with greater improvement in cancer-related trauma symptoms and fear of cancer recurrence but *less improvement* in general anxiety symptoms. This finding was surprising given that ACT showed marginally greater improvement in latent curve models in the full trial sample (Arch et al., 2021) and because it is contrary to theoretical expectations that ACT would lead to greater improvements in all three anxiety-related outcomes; it is not obvious why general anxiety symptoms showed less improvement with ACT. However, ACT was indirectly associated with improvement in general anxiety symptoms via its direct effects on cancer-related trauma symptoms and fear of cancer recurrence. The network findings thus suggest that cancer-related trauma symptoms and fear of cancer

recurrence may have served as mechanisms of the ACT intervention on general anxiety symptoms. This finding highlights the importance of modeling associations among outcome variables, and thereby identifying the *unique* intervention effects on each outcome. It also raises an intriguing hypothesis that some clinical outcomes may serve as mechanisms of change on other outcomes – in the case of the present study, that addressing cancer-specific forms of anxiety with ACT appears to have reduced broader anxiety symptoms.

3.3. Network predictability

Network model predictability, the variance explained across the network by each node, was highest for cancer-related trauma symptoms and experiential avoidance; more than 50% of the variance in Pre-Post change scores on these variables was accounted for by the other variables in the network. The lowest estimates of predictability were for self-compassion and emotion approach coping in the Pre-Post network. Future network intervention analyses, especially those with higher sample sizes, may benefit from the inclusion of other symptom-based outcomes, like depression symptom scores, or from examining additional therapeutic processes, in order to increase the variance explained for these nodes in the network.

3.4. Considerations and implications

Two important considerations in interpreting the current findings relative to the standard mediation analyses (Fishbein et al., 2022) are that the latter used a larger sample of ($N = 134$ vs. $n = 113$ currently) and estimated full ANCOVA-equivalent mediation models (vs. residualized change score models; Valente & MacKinnon, 2017). As a check, we therefore fit standard mediation models using residualized change score (Supplemental Table C1) and the ANCOVA-equivalent approaches (Supplemental Table C2) using only data from $n = 113$ participants who were included in the Pre-Post network. In contrast to the full study sample analyses (Fishbein et al., 2022), self-compassion intervention and mediation effects were nonsignificant in the standard mediation analyses conducted with the current $n = 113$ sample. However, the full study sample pattern of results observed for cancer-related experiential avoidance and emotional approach coping was maintained in the current subsample. Thus, with the exception of network findings for self-compassion, the current findings are unlikely to have been due to use of a subsample.

If replicated, the current set of findings suggests that a fruitful approach to treatment may be to directly target core anxiety symptoms and emotional processing and expression. In anxiety treatment, directly targeting symptoms could involve extinction learning (Craske et al., 2014), for example. We stress, however, that further research is needed to replicate and extend the current findings before using them to inform treatment approaches.

3.5. Strengths, limitations, and future research directions

Study strengths include innovatively applying network intervention analysis to the simultaneous analysis of process and clinical outcome variables in a psychotherapy trial and direct comparing it to a standard mediation analysis conducted on the same dataset with the same variables. This comparison helped to demonstrate the utility of network intervention analysis. Finally, this study demonstrates how existing datasets from psychotherapy randomized trials might be analyzed with network intervention analysis, thus maximizing the knowledge gained from these typically resource-intensive trials.

This study also has limitations. First, though the study's per-condition sample size was comparable to several other network intervention analyses (Bernstein et al., 2021; Blanken et al., 2019; Lancee et al., 2022), a larger sample would yield more precise network estimates. The current study's sample size also precluded adding additional nodes to examine PTSD or general anxiety symptom-specific network effects, and precluded examining whether there were subgroups of intervention responders that would be best captured by different network structures. Second, though this study examined processes of the intervention with intra-individual change scores, consistent with typical practice in the mediation literature (e.g., Montoya & Hayes, 2017), it did not examine time-lagged relationships across variables and thus cannot yield insights about the temporal ordering of direct and indirect effects of the intervention. Third, despite randomization, individuals in the ACT group appeared to have higher baseline cancer-related trauma symptoms and experiential avoidance at pre-intervention (though they did not have higher scores on other measured variables). However, the finding that the two conditions had identical network structures in the Pre-Post interval (see Supplemental Figure B1) lends some confidence that dispositional differences between the two groups were limited. Finally, while this study used a 60% inclusion percentage cutoff to interpret network edges, we are unaware of previous formal studies that would inform whether this was an overly lax or conservative cutoff. Such studies, which could include simulations or applications in other datasets, would help to guide future network analytic research.

These results must be interpreted in light of how the intervention was delivered. The Valued Living trial was delivered by community clinicians most of whom had limited ACT experience and supervision, and was delivered in a group format over just seven sessions. This overall approach to the delivery of the intervention is both a strength of the study, because the study reflects how ACT may influence a network of process and outcomes in a 'real-world' context, and a limitation, because the study therefore may not reflect the network structure that would be obtained in a trial with all ACT-expert clinicians, weekly supervision, and individual intervention sessions. It is surprising that ACT did not yield greater improvement in experiential avoidance, a process core to the ACT model that has shown sensitivity to ACT in other trials (e.g., Stockton et al., 2019). We must therefore consider the possibility that, though the Valued Living trial clinicians were adherent to the content of the intervention manual (Arch et al., 2021), the length and group format of the intervention were insufficient to address experiential avoidance at the individual level.

Likewise, it is important to consider unique aspects of the study population and sample in interpreting the present findings. The current study sample was majority white and female, and were experiencing anxiety following treatment for a potentially lethal disease that could recur. Given this context, aspects of participants' anxiety may have been rational, more so than is typical in primary anxiety disorders. The network structure obtained in the current study may therefore not replicate in other anxious populations treated with ACT delivered in other formats and contexts.

Finally, simulation studies are needed to characterize the performance of network intervention analysis in identifying true change processes of an intervention. It would be especially helpful to characterize how sample size and process and outcome variable score distributions may influence estimation of the networks, as has been done with standard mediation (Fritz & MacKinnon, 2007). Additionally, it would be useful to compare the performance of standard mediation and network intervention models in the detection of mechanistic pathways.

4. Conclusions

The current study is one of the first to apply network intervention analysis to a set of process and clinical outcome variables from a psychotherapy trial. The network findings indicated that, in a randomized trial of ACT versus minimally-enhanced usual care for anxious cancer survivors (Arch et al., 2021), the direct effects of the ACT intervention were largely focused on two cancer-specific, anxiety-related outcomes (fear of cancer recurrence and cancer-related trauma symptoms), and on one general process variable (emotional approach coping), which in turn were associated with change in in general anxiety and other process

variables. These findings differ considerably from those of standard mediation analysis using the same data and variables (Fishbein et al., 2022). An intriguing possibility highlighted by this study is that variables considered to be 'outcomes' in a clinical trial in fact serve as processes of the intervention on other 'outcomes' and on other processes, possibilities that would be challenging to test efficiently in the standard mediation approach. Network intervention analysis thus offers a promising exploratory analytic approach for examining the core drivers of clinical improvement in psychotherapy and their manifestation in diverse clinical contexts.

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CRediT authorship contribution statement

Joel N. Fishbein: Conceptualization, Methodology, Software, Validation, Formal analysis, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Jonas Haslbeck:** Conceptualization, Methodology, Software, Validation, Formal analysis, Writing – review & editing. **Joanna J. Arch:** Conceptualization, Methodology, Investigation, Writing – review & editing, Supervision, Funding acquisition.

Declaration of competing interest

Mr. Fishbein and Dr. Haslbeck declare no conflicts of interest. Dr. Arch receives unrelated research funding from National Comprehensive Cancer Network, AstraZeneca, and the National Institutes of Health.

Data availability

Code available at https://osf.io/ae9xz/. Data not publicly available.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brat.2023.104266.

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