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Emotional approach coping among young adults with cancer: Relationships with psychological distress, posttraumatic growth, and resilience

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Abstract

Objective: Cancer, particularly, during young adulthood, can evoke difficult emotions, interfere with normative developmental activities, and challenge coping responses. Emotion-regulating coping efforts aimed at active emotional processing (EP) and emotional expression (EE) can be beneficial to cancer adjustment and perceptions of positive growth. However, it may be that EP and EE work differently to influence well-being. This study examines relationships of EP and EE with psychological distress, posttraumatic growth (PTG), and resilience. We expect that EP will be positively associated with PTG and resilience, whereas EE will be negatively associated with psychological distress.

Methods: Young adults with cancer ($M^{age} = 34.68$, N = 57) completed measures of emotional; approach coping (EP and EE), psychological distress (depressive symptoms, fear of cancer; recurrence [FCR]) and indicators of positive adjustment and growth (resilience and PTG).

Results: Greater use of EP was associated with higher resilience ($\beta = 0.48$, p = 0.003) and PTG ($\beta = 0.27$, p = 0.05), whereas greater use of EE was associated with lower resilience ($\beta = -0.33$, p = 0.04). The EE \times EP interaction was significant for FCR ($\beta = 0.29$, p = 0.04) such that low EE was associated with lower FCR in those with high EP. Interaction effects were not significant for depressive symptoms, resilience, or PTG.

Conclusions: Findings highlight differing relationships between EP and EE among young adults with cancer. Interventions aimed at increasing emotion-regulating coping strategies may prove useful in facilitating positive adjustment and growth, strengthening young adults' ability to cope with the diverse effects of disease, treatment, and survivorship.

KEYWORDS

depressive symptoms, emotional expression, emotional processing, fear of cancer recurrence, oncology, posttraumatic growth, resilience, young adult cancer

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1 | BACKGROUND

Young adults with cancer (aged 18-39) face many challenges resulting from cancer diagnosis and treatment. Disruptions to relational activities (e.g., marriage and family planning) and developmental milestones (e.g., educational/vocational attainment), alternations in social relationships, fear of cancer recurrence (FCR), and physical changes from cancer treatment contribute to the psychological burden of a cancer diagnosis during young adulthood and make this a distinct group requiring specialized care. Successful coping with the challenges and interruptions to daily life can foster positive changes and adjustment, including posttraumatic growth (PTG) and enhanced resilience.^{2,3} Coping efforts aimed at emotion regulation (e.g., processing and expressing emotions) have potential to impact indicators of both positive and negative adjustment to cancer. The aim of this study was to examine the relationship between specific emotional-regulating coping strategies of processing and expressing emotions and psychological distress (i.e., depressive symptoms and FCR), PTG, and resilience among young adults with cancer.

1.1 | Emotional approach coping

Emotional approach coping (EAC), which involves processing and expressing one's emotions in response to stressful experiences, has been proposed to play a critical role in adjustment to cancer.⁴ EAC calls upon functionalist theories of emotion,⁵ which suggest that processing and expressing emotions (e.g., fear and happiness) facilitates adjustment and underlies successful self-regulation.^{4,6,7} EAC further extends early emotion-focused coping research⁸ which was often confounded with negative emotions, distress, and avoidance.⁴

EAC involves two distinct yet related strategies: emotional processing (EP) and emotional expression (EE). EP involves an active attempt to acknowledge, explore, and understand one's emotions whereas⁴ whereas EE involves active verbal and/or nonverbal efforts to communicate or symbolize one's emotional experience. Commonly examined as a unitary construct averaging across EP and EE, these constructs are often only modestly, positively correlated. As such, research exists supporting differences in psychological distress and adjustment among chronic illness populations when EP and EE are examined separately. ^{4,6,9,10}

1.2 | Emotional processing and expression: adjustment to cancer

Emotional expression may influence adjustment by actively directing attention towards present concerns.⁴ Repeated EE may also serve to decrease attendance to negative emotions.^{4,11} Indeed, higher EE has been consistently associated with lower depressive symptoms and cancer-related intrusive thoughts among cancer survivors^{12,13} (e.g., FCR). While, to our knowledge, there are no studies of relationships between EE and FCR, EE in general is thought to influence

adjustment by putting feelings to words (i.e., affect labeling)^{14,15} Furthermore, expressing emotions to supportive others may release feelings about the possibility of death.¹⁶ This is an important relationship to more deeply understand as 65%–90% of young adult cancer survivors endorse FCR.¹⁵

Whereas the preponderance of research on emotional-regulatory coping predictors of cancer adjustment focuses on distress; investigations of emotional-regulatory coping predictors of positive adaptation and growth are needed to inform research targeted to helping young adults with cancer to thrive and bounce back (i.e., resilience) from cancer and gain increased appreciation for life (i.e., PTG). Emotional processing, which is often associated with items that pertain to a reflection on feelings 15,17 may facilitate meaning making by directing one's attention towards actively processing, acknowledging, and understanding emotions. This process may provide opportunities for young adults with cancer to return and exceed to prior levels of functioning, which is likely to elicit resilience and enhance PTG. 18

1.3 | The current study

While a sizeable body of literature characterizes coping strategies among young adults with cancer, ^{19,20} few have focused on emotion-regulating coping strategies aimed at actively processing and expressing emotions. ⁴ The need to understand EAC in young adults is paramount as young adults with cancer report greater psychological distress as well as greater positive growth than older survivors. ²¹ Younger age is also the most consistent predictor of increased FCR. ²² Moreover, painful negative emotions among young adults tend to persist across the cancer continuum. ²¹

Taken together, depressive symptoms, FCR, PTG, and resilience among young adults with cancer constitute the favorable and adverse psychological sequelae of a cancer diagnosis. Given that young adults with cancer often experience a long period of survivorship after diagnosis and treatment, EP and EE coping strategies that help foster positive psychological adjustment might be integral to facilitating long-term psychological well-being.

The purpose of this study was to examine the potential of coping through EP and EE on psychological distress (i.e., depressive symptoms and FCR) and positive aspects of well-being (i.e., PTG and resilience) among young adults with cancer. We hypothesized:

Hypothesis 1 Emotional processing will be positively associated with posttraumatic growth and resilience.

Hypothesis 2 Emotional expression will be negatively associated with depressive symptoms and fear of cancer recurrence.

Furthermore, given differences in distress and adjustment across EP and EE in prior literature, ^{4,6,9,10} we examined the moderating role of EP and EE on psychological distress and positive aspects of wellbeing. The specific hypotheses are as follows:

Hypothesis 3 Emotional processing(EP) will moderate the relationship between emotional expression(EE) and posttraumatic growth(PTG) and resilience, such that higher use of EP will be positively associated with PTG and resilience among those with relatively low EE.

Hypothesis 4 Emotional expression(EE) will moderate the relationship between emotional processing(EP) and depressive symptoms and FCR, such that higher use of EE will be negatively associated with depressive symptoms and fear of cancer recurrence among those with relatively low EP.

2 | **METHOD**

2.1 | Participants and procedures

Young adults with cancer who were diagnosed with cancer between the ages of 18-39 within the prior five years were recruited to take part in a broader study of cancer-related support communication.²³ Participants were recruited through social media posts (Facebook/ Twitter) via cancer-related social media organizations (Army of Women, GRYT Health, Lacuna Loft, and Young Survival Coalition) and directed to a link to complete the questionnaire. Participants were additionally recruited through the Pennsylvania State Cancer Registry where eligible participants were mailed a study information sheet and opted into receiving a survey link to the questionnaire. All participants completed the questionnaire online between December 2017 and March 2019, and were entered into a drawing to receive a gift card. Informed consent was obtained from all participants and procedures were approved by the appropriate Institutional Review Board (approval number: 2017-0807).

Demographic and medical characteristics are displayed in Table 1. Five participants were excluded from analyses due to incomplete data resulting in a final sample size of 57 young adults who ranged in age from 24-42 ($M_{\rm age} = 34.68$, SD = 4.89), were predominantly female (94.7%), White (93.0%), and diagnosed with breast cancer (71.9%), with average time since diagnosis at 2.5 years (M = 28.29 months, SD = 31.44).

2.2 Measures

2.2.1 | Emotional approach coping

EAC was measured using the EAC scales⁴ which consist of the 4-item EP ("I realize that my feelings are valid and important") and the 4-item EE ("I feel free to express my emotions") scales. Participants rated their agreement on a 4-point scale ranging from, (1) I don't do this at all to (4) I do this a lot. Cronbach's alpha was 0.87 for EP and 0.94 for EE.

TABLE 1 Study cample (N = 57)

Variable	N (%)	Range		
Age (M[SD])	34.68 (4.89)	24-42		
Female	54 (94.7%)			
Race/ethnicity				
White	53 (93.0%)			
Asian	2 (3.5%)			
Black/African American	1 (1.8%)			
Hispanic/Latino	1 (1.8%)			
Education				
High school degree	2 (3.5%)			
Some college/trade/business school	8 (14.0%)			
4-year college degree	23 (40.3%)			
Graduate degree	24 (42.1%)			
Employment status				
Employed	39 (68.4%)			
Student	3 (5.3%)			
Medical leave/disability/unemployed	15 (25.5%)			
Relationship status				
Single	11 (19.3%)			
Married/partnered	42 (73.7%)			
Divorced/widowed	4 (7.0%)			
Cancer type				
Breast	41 (71.9%)			
Other ^a	16 (28.1%)			
Cancer stage				
Early stage (0-III)	49 (86.0%)			
Stage IV	1 (1.8%)			
Not staged (e.g., brain cancer)	7 (12.2%)			
Treatment ^b				
Surgery	53 (93.0%)			
Chemotherapy	41 (71.9%)			
Hormone	37 (64.9%)			
Radiation	25 (43.9%)			
Treatment status				
Completed main treatment ^c	52 (91.2%)			
Months since diagnosis (M[SD])	28.29 (31.44)			

^aBrain/Hodgkin's/Cervical/Leukemia/Colon/Ovarian/Thyroid/Salivary gland/Testicular.

^b >1 treatment could be selected.

cincludes active hormonal therapy.

2.2.2 | Depressive symptoms

Depressive symptoms during the past week were measured by the 10- item version of the Center for Epidemiological Studies Depression Scale (CESD-10).²⁴ Participants rated their agreement with items on a 4-point scale, ranging from (0) *rarely or none of the time* to (3) *all of the time*. Sample items included, "I felt lonely" and "I felt happy". A total score of 10 is typically used as a cut off for identifying individuals at risk for clinical depression.²⁴ Scores were summed to a total score where higher scores reflected more depressive symptoms. Cronbach's alpha was 0.80.

2.2.3 | Fear of recurrence

FCR was measured using the 4-item adapted scale (for all cancer types) of the Concerns about Recurrence Scale.²⁵ Participants rated their agreement with items on a 5-point scale, ranging from (0) *not at all* to (4) *extremely*. A sample item included, "How often does the possibility that your cancer could recur upset you". A total score was calculated as the average of all items with higher scores indicating more resilience. Cronbach's alpha was 0.96.

2.2.4 | Resilience

Resilience was measured using the Brief Resilience Scale.²⁶ Participants rated their agreement with items on a 5-point scale, ranging from (1) *strongly disagree* to (5) *strongly agree*. A sample item included, "I tend to bounce back quickly after hard times". A total score was calculated as the average of all items with higher scores indicating more resilience. Cronbach's alpha was 0.85.

2.2.5 | Posttraumatic growth

PTG was measured using the 10-item Posttraumatic Growth Inventory (PTGI-SF).²⁷ Participants rated their agreement with items as a result of their cancer diagnosis on a 6-point scale ranging from, (0) *I did not experience this change* to (5) *I experienced this change* to *a very great degree*. A sample item included, "I changed my priorities about what is important in my life". A total score was calculated as the sum of all items with higher scores indicating more perceived PTG. Cronbach's alpha was 0.88.

2.3 | Data analytic plan

Descriptive statistics and zero-order correlations were conducted for key study variables. Associations between demographic (age, education, income, employment status [employed vs. not employed], and ethnicity), cancer-related variables (time since diagnosis, cancer type [breast vs. not], cancer stage, and treatment status), and history of a

depressive or anxiety disorder with dependent variables were examined as possible covariates. Significant associations were controlled for in relevant models.

Multiple linear regression was used to test study hypotheses. In each model, relevant covariates were entered in the first block, EP and EE were entered in the second block, and the interaction term (EP \times EE/EE \times EP) was included in the third block. To avoid multicollinearity, variables were centered around the mean, and interaction terms were analyzed in accordance with methods outlined by Aiken & West. 28 To interpret significant interaction terms, simple slopes analyses were conducted with values at one standard deviation above and below the mean of EP/EE using the PROCESS macro 29 in SPSS. Adjustments for multiple comparisons were not made.

2.3.1 | Power analysis

Power analyses were conducted using G*Power 3.1. An a priori power analysis, with n=52 as the smallest possible sample size at 80% power to detect moderate to large effects given an alpha of 0.05, suggested that we were adequately powered given our sample size. Furthermore, a post-hoc power analysis was conducted to determine whether the final sample size (N=57) obtained in this study was sufficient to detect an effect. With an effect size of 0.15, a sample size of 57 and a significance criterion of 0.5, the statistical power was adequate (>80%).

3 | RESULTS

3.1 | Descriptive statistics and identification of covariates

Descriptive statistics and correlations are presented in Table 2. On average young adults reported moderately engaging in EP (M=2.70, SD = 0.75) and EE (M=2.47, SD = 0.87). They reported thinking about FCR a moderate amount (M=3.73, SD = 1.53), and experienced high levels of PTG (M=27.51, SD = 10.18) and resilience (M=3.43, SD = 0.71). Over half of the sample (n=32; 56.3%) met the CESD-10 cutoff of \geq 10 (M=11.16, SD = 5.44) indicative of clinical depression.

3.2 | Hypothesis testing

Hypothesis 1: *Emotional processing*. Supporting the study hypothesis, greater levels of EP were significantly associated with higher levels of resilience ($\beta = 0.48$, p = 0.003) and PTG ($\beta = 0.27$, p = 0.05). See Table 3.

Hypothesis 2: Emotional expression. Contrary to what was hypothesized, greater levels of EE were only marginally associated with higher levels of FCR ($\beta=0.31, p=0.06$) and were not significantly associated with depressive symptoms. See Table 3.

TABLE 2 Descriptive statistics and correlations

Variable	М	SD	1	2	3	4	5	6
1. EP	2.70	0.75	-	0.56***	-0.13	-0.13	0.29*	0.42**
2. EE	2.47	0.87		-	-0.21	0.05	-0.02	0.38**
3. Depressive sx	11.16	5.44			-	0.26	-0.44**	0.04
4. FCR	3.73	1.53				-	-0.34*	0.02
5. Resilience	3.43	0.71					-	0.06
6. PTG	27.51	10.18						-

Abbreviations: EE, emotional expression; EP, emotional processing; FCR, fear of cancer recurrence; PTG, posttraumatic growth. p < 0.05, p < 0.01, p < 0.001.

Hypothesis 3: Emotional processing moderation. Contrary to hypotheses, there were no significant EP \times EE interactions for PTG and resilience.

Hypothesis 4: Emotional expression moderation. There was a significant EE \times EP interaction for FCR (β = 0.29, p = 0.04), which explained an additional 8% of the variance beyond the main effects (see Figure 1), however, in the opposite direction than hypothesized. Simple slope analyses revealed lower, and not higher, use of EE was associated with lower FCR among those engaging in high, and not low, EP ($\beta = -1.24$, p < 0.05). The slope was marginally significant for average levels ($\beta = -0.63$, p = 0.06) of EP and not significant at low levels of EP. There was no significant EE × EP interaction for depressive symptoms. See Table 3.

DISCUSSION

This study examined the relationship of EP and EE on psychological adjustment and positive outcomes among young adults with cancer. Coping through emotional-regulatory efforts may be an important tool for young adults with cancer; however, study findings suggest that EP and EE exert differential effects on psychological adjustment.

Contrary to hypotheses, EE was not associated with lower depressive symptoms and was marginally associated with higher, and not lower, FCR, potentially suggesting that the ability to express one's emotions might not uniformly aid in buffering negative emotions in the cancer context. Furthermore, use of EE was significantly associated with lower resilience. Given these patterns of findings, it is important to consider that the benefits of EE often do not occur in a vacuum and the social context surrounding EE plays an important role in facilitating adjustment.

Young adults with cancer often experience altered social relationships, feeling like their social networks lack understanding towards their cancer experience and find dealing with their cancer experience to be too difficult to handle. 30,31 Furthermore, young adults with cancer report receiving insufficient or constrained social support (e.g., pity and changing the subject). 30,31 It may be that a socially constraining environment is preventing young adults from successfully disclosing thoughts and feelings related to cancer. Future studies would benefit from extending current findings to

examine the influence of relevant social factors in the context of FF

Consistent with hypotheses, coping through EP was positively associated with resilience. This finding aligns with emotion regulation research suggesting that individuals faced with stressors can benefit from utilizing emotion regulation strategies aimed at processing and understanding one's emotions to maintain positive well-being and foster resilience.³² Given our finding of coping through EE being associated with lower resilience it may be that fostering resilience involves understanding emotions more deeply, rather than explicitly expressing emotions.

EP was also significantly positively associated with PTG, consistent with hypotheses. Indeed, PTG often involves a series of cognitive and emotional engagement. 14 EP that involves deliberate EP (e.g., reflection) is essential in the development of PTG, ¹⁴ especially when individuals try to make sense of a stressful event. Therefore, coping through EP may foster a deliberate focus on the meaning making after cancer³³ translating to increased feelings of PTG.

Our findings for EP being positively associated with resilience and PTG might also reflect a focus on the cancer experience as a transformative experience, a tangible change in relation to some sort of catalyst (e.g., changes experienced in postillness life),³⁴ that is fostered by an active attempt to acknowledge, explore, and understand one's emotions. Previous research among young adults with cancer has suggested that some young adults experience cancer as a positive transformative experience while others do not, often taking a fatalistic view of their cancer experience.³⁵ Drawing on current study findings fostering and encouraging EP may be one avenue to further understand how young adults restructure their cancer experience and themselves in positive ways.

The EE \times EP interaction was only significant for FCR. We had hypothesized that greater use of EE, in the context of low EP, would be associated with lower FCR; however, it was greater use of EP, in the context of low EE, that was associated with lower FCR. Several theorists^{36,37} have suggested that FCR comprises cognitions, beliefs, and emotions. It is plausible that young adults are more likely to actively process and try to understand thoughts related to FCR rather than communicate one's emotional experience surrounding FCR. This line of thinking aligns with previous research³⁸, which suggests that young adults do not want to burden their social

TABLE 3 EP/EE and psychological distress and adjustment

Variable	ΔR^2	В	SE	β
Depressive symptoms				
Block 1	0.18			
Income		-3.90	1.60	-0.30*
Hx depression		-0.55	1.34	-0.33*
Block 2	0.05			
EP		-0.31	1.12	-0.04
EE		-1.19	0.97	-0.19
Block 3	0.00			
$EE \times EP$		0.37	1.11	0.04
	F (5,56)) = 3.10*, a	adjusted R	$x^2 = 0.16$
Fear of cancer recurrence				
Block 1	0.04			
Time since diagnosis		-0.01	0.01	0.25 [†]
Block 2	0.04			
EP		-0.63	0.32	-0.31^{\dagger}
EE		0.54	0.28	0.31 [†]
Block 3	0.08			
$EE \times EP$		0.70	0.32	0.29*
	F (4,56)) = 2.46*, a	adjusted R	$t^2 = 0.16$
Resilience				
Block 1	0.13			
Employment		-0.37	0.20	-0.25
Hx depression		0.29	0.18	0.21^{\dagger}
Block 2	0.13			
EP		0.45	0.14	0.48*
EE		-0.27	0.13	-0.33*
Block 3	0.01			
$EP \times EE$		-0.10	0.14	-0.09
	F (5,56)) = 3.74**,	adjusted I	$R^2 = 0.20$
Posttraumatic growth				
Block 1	0.30			
Time since diagnosis		0.06	0.04	0.20^{\dagger}
Age		-0.38	0.24	-0.18
Ethnicity		-5.27	3.03	-0.20^{\dagger}
Hx anxiety		-5.50	2.32	-0.27*
Block 2	0.13			
EP		3.69	1.82	0.27*
EE		1.77	1.67	0.15
Block 3	0.01			
$EP \times EE$		1.47	1.86	0.09

TABLE 3 (Continued)

Variable	ΔR^2	В	SE	β		
	$F(7,56) = 5.35^{***}$, adjusted $R^2 = 0.35$					

Abbreviations: EE, emotional expression; EP, emotional processing. $^*p < 0.05, ^{**}p < 0.01, ^{**}p < 0.001, ^{\dagger}p < 0.10.$

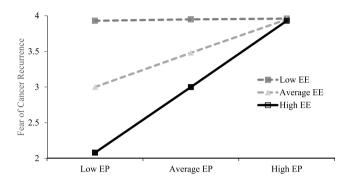


FIGURE 1 Interaction of EE and EP. Figure displays the interaction effect for fear of cancer recurrence. Analyses controlled for time since diagnosis. *Dashed lines* denote nonsignificant simple slopes; EE, emotional expression; EP, emotional processing

networks with their cancer experience. Future studies would benefit from considering the role that the social environment has in facilitating or hindering EE in the context of FCR.

It is also important to consider that young adults living increasingly in the digital age and future research would benefit from examining the role that online cancer support groups, cancer-related posts on social media, and blogging about one's cancer experience might play in facilitating EE and processing. Indeed, previous research has suggested that young adults frequently exchange support (i.e., emotional and informational), utilize coping strategies (i.e., humor and EE/venting), and often use metaphoric and euphemistic (i.e., lump and growth) language to describe their cancer and cancer experiences. ³⁹⁴⁰ These types of online talk, sharing personal feelings and experiences as well as journaling/blogging, can help shape EE and deepen EP which, given current study findings, may have implications for psychological distress and well-being.

4.1 | Study limitations

The present study is not without limitations. First, the data were cross-sectional in nature. Future studies should explore the potential for a dynamic relationship of coping through EP and EE on psychological adjustment, adaptation, and growth as it unfolds over time. All demographic and clinical data (including diagnosis) were self-reported. Moreover, the majority of participants were White, female and breast cancer sample, thus limiting generalizability. However, breast cancer is the leading site of new cancers diagnosed in older young adults (aged 30–39), which represents our sample mean, thus

accurately capturing this cohort. Furthermore, emotional regulation in the form of EP and EE are understudied in young adults with cancer, compared to the adult literature, which shows the benefit of EAC for psychological well-being, therefore laying the groundwork for future research to replicate these findings across a more heterogeneous young adult cancer population.

It should be noted that EP and EE were measured in regard to how young adults with cancer generally respond to emotions when experiencing a stressful situation. Future studies should explore the relationships of EP and EE when assessed using situational, cancerspecific stressors. It also may be true that some of our study findings may be explained by characteristics often generally present in young adulthood: optimism and a tendency to perceive that negative effects are rare. Last, majority of young adults were recruited through social media outlets which requires one to "like" or "follow" that specific cancer-related organization. It may be that those who are more inclined to follow these cancer-related organizations and access their supports experience benefits from EP and expression that may impact psychological distress and well-being. More work is needed to disentangle the role that social media might play in facilitating or impeding adjustment to disease among young adults with cancer.

4.2 | Clinical implications

Reinforcing the benefit of actively expressing and processing emotion by disclosing thoughts and feelings and dedicating time to understand what one is feeling is vital to positive adjustment to cancer. Providing psychoeducation to young adults with cancer about the benefit of expressing and processing emotions as well as education surrounding which coping strategy may be responsive to situational demands may promote greater psychological adjustment, positive adaptation, and growth after being diagnosed with cancer and throughout the cancer continuum.

An important implication of these findings for clinicians working with young adults with cancer is that EP and EE work differently to affect adjustment to disease in ways that imply that different emotional coping strategies may be differentially helpful and should be considered when evaluating and intervening on young adults coping. Specifically, tailoring coping interventions should capitalize on both EP and EE coping strategies to positively impact adjustment to disease. This might include a focus on expressing emotions, by putting feeling to words, and engaging in EP through affect labeling and cognitive reappraisal which serves to better acknowledge, explore and understand one's emotions.

5 | CONCLUSIONS

Actively processing and/or expressing one's emotional experiences can be considered a form of adaptive emotional regulation. Indeed, seminal conceptualizations of emotion regulation define this process as "the processes by which individuals influence which emotions they

have, when they have them, and how they experience and express these emotions". ³² In the context of coping, emotion regulation may serve a protective function in reducing psychological distress and facilitating positive adaptation and growth. However, emotion regulation strategies that promote active engagement with EP and expression may be underutilized among young adult cancer patients. Fostering EP and EE throughout the cancer trajectory has the potential to reduce stress and other negative psychological outcomes to promote adaptation and growth, subsequently improving the quality of life and well-being of young adults with cancer.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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