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Meaning in Life in Patients with Advanced Cancer: A Multinational Study

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Abstract

Background: Few studies have examined meaning in life, a novel existential outcome, in patients with advanced cancer across countries.

Objectives: We examined differences in meaning in life across 5 countries and identified factors associated with MIL.

Methods: This is a pre-planned secondary analysis of a prospective longitudinal multicenter observational study of patients with advanced cancer. Meaning in life was assessed using a validated scale which examined four domains of meaning: values, purpose, goals, and reflection. The total score ranged from 8 to 32, with a higher score indicating greater meaning in life.

Results: Among 728 patients, the median meaning in life score was 25/32 (interquartile range 23, 28). There was no significant difference in total meaning in life score among the 5 countries ($P=0.11$), though there were differences in domain sub-scores. In the univariate analysis, patients with higher intensity of physical symptoms by ESAS score (pain, fatigue, drowsiness, dyspnea,

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insomnia), depression, anxiety, spiritual pain, and financial distress had significantly lower meaning in life. However, patients with higher levels of education, who were married, and who had higher optimism had significantly higher meaning in life. In the multivariate analysis, higher total meaning in life scores were significantly associated with greater optimism (multivariate estimate = 0.33, $p < 0.001$), lower depression (-0.26 , < 0.001), spiritual pain (-0.19 , < 0.001) and financial distress (-0.16 , < 0.001).

Conclusion: Country of origin was not a determinant of meaning in life. However, meaning in life was significantly associated with optimism, depression, spiritual pain and financial distress, underscoring the multidimensional nature of this construct and potential opportunities for improvement in addressing meaning in life of patients with advanced cancer.

PRECIS:

This prospective study examined meaning in life and its correlates in 728 patients with advanced cancer from 5 countries, revealing that patients often considered themselves to have a moderate to high meaning in life score regardless of country or culture. Depression, spiritual pain, optimism, marital status, educational level, financial distress and physical symptoms, were significantly associated with meaning in life, underscoring the multidimensional nature of this construct and potential interventions to further enhance meaning in life.

Keywords

cultural diversity; financial support; neoplasms; psychological stress; palliative care; spirituality

INTRODUCTION

The quest for meaning in life is a defining human endeavor, and many have argued that finding meaning in life provides substantial resilience. Psychiatrist Victor Frankl argued that, “there is nothing in the world, I venture to say, that would so effectively help one to survive even the worst conditions as the knowledge that there is meaning in one’s life.”[1] As an existential concept, there are as many definitions of meaning as there are humans. However, a useful conceptualization is meaning as “a cognizance of order, coherence, and purpose in one’s existence, the pursuit and attainment of worthwhile goals, and an accompanying sense of fulfillment.”[2] Further quantifying these themes, Krause posited four domains of meaning in life: (1) values, which provide the basis for decision making, (2) purpose, a belief that one’s actions have a place in the larger order of things, (3) goals, creating expectations for the future, and (4) reflection, looking back at the past and reconciling what has occurred.[3]

Increasingly, investigators have worked toward measuring meaning in life, both qualitatively and quantitatively, and have recognized it as an important factor associated with health outcomes. A greater meaning in life was found to be associated with improved ability to adapt to stress,[4] lower odds of macroscopic cerebrovascular infarct,[5] decreased depression after traumatic events,[6] and decreased mortality in an elderly population.[7] Conversely, lower meaning in life has been associated with increased hopelessness, fatigue, and a wish for hastened death, especially in patients near the end of life.[8, 9]

Meaning in life has also become an area of focus in cancer research, seeking to understand how patients make sense of and cope with their cancer diagnosis and treatment. [4] A cancer diagnosis is often a touch-point for patients to reflect on their lives, motivating them to search for meaning in the midst of an adverse event.[3, 10, 11] A systematic review of meaning in cancer patients by Lee et al., found that the majority of studies were small, qualitative in nature, U.S.-based, with populations that are largely Caucasian, married, and female.[10] Moreover, there is a paucity of studies focused on patients with advanced cancer, who often have higher levels of existential distress.[10] A greater understanding of the determinants of meaning in life in patients with advanced cancer may allow clinicians to provide better goal-concordant care and to develop interventions aimed at enhancing this important aspect of patients' lives. In this multi-center study, we examined the meaning in life of patients with advanced cancer across 5 countries. We also examined patient characteristics associated with meaning in life.

METHODS:

Patient Population

This study is a pre-planned secondary analysis of a prospective longitudinal multicenter observational study of patients with advanced cancer seen at outpatient palliative care clinics.[13–15] All 5 participating tertiary care hospitals had access to comprehensive cancer treatments and palliative care. They included University of Texas MD Anderson Cancer Center in Houston, Texas; Barretos Cancer Hospital in Barretos, Brazil; Pontificia Universidad Catolica de Chile in Santiago, Chile; Tata Memorial Center in Mumbai, India; and King Hussein Cancer Center in Amman, Jordan. All centers had institutional review boards approve the study. All patients provided written informed consent.

Patients were enrolled from palliative care clinics during initial or follow-up consultations. Patients included in the study met the following criteria: (1) diagnosis of advanced cancer, defined as locally advanced, recurrent, or metastatic, (2) 18 years of age or older, (3) seen in the outpatient clinic at a participating center, and (4) scheduled to return to clinic 14–34 days after the first study visit for repeat of certain questionnaires. Patients with delirium as assessed by the Memorial Delirium Assessment Scale (>13/30) were excluded.[16]

Data Collection

The lead investigators from each site had an initial meeting in Houston to learn about study procedures and then met regularly via monthly teleconference to ensure longitudinal monitoring of data collection. Baseline patient characteristics including age, sex, race, marital status, educational level, and cancer diagnosis, were collected during the first study visit.

The Meaning in Life scale utilized at the first study visit was initially developed and validated by Krause in a population of older adults, and subsequently shortened to facilitate administration.[3, 6, 7, 17] The meaning in life scale consists of eight questions across four domains of meaning: values, purpose, goals, and reflection (Table 2). Each question is rated on a 4-point Likert scale ranging from “disagree strongly – 1” to “agree strongly – 4.” The

scores are then summed; a higher score indicates a higher level of meaning in life. Each domain has a sub-score between 2 and 8 with a total overall score range from 8 to 32. It has been utilized in multiple large studies as a means to quantify a patient's meaning in life and has good reliability estimates across the four components of meaning (0.86–0.93) and a reliability estimate for combined measures of meaning in life of 0.925.[3] The questionnaire was translated into the native languages of the respective countries and then back translated to ensure linguistic validity.

Edmonton Symptom Assessment System (ESAS) was administered to all patients at their first study visit and at their follow-up visit.[18] Patients rated the average intensity of ten common symptoms (pain, fatigue, drowsiness, nausea, lack of appetite, dyspnea, depression, anxiety, and sense of well-being) over the past 24 hours using a 0 to 10 scale with 0 meaning the symptom is absent, and 10 meaning the symptom is the worst imaginable. ESAS is a useful tool for tracking the response of patient's symptoms to palliative care interventions. An increase or decrease in 1 point on the scale has been shown to represent clinically important change in both improvement and worsening of symptoms.[14]

Additionally, patients were asked about spiritual pain, described as “pain that is deep in your soul (being) that is not physical” as well as financial distress. Patients ranked their level of spiritual and financial distress over the last month using a 0 to 10 numeric scale similar to the ESAS.[19, 20] Patients were also asked to rate their level of optimism over the past month using a 1–7 point numeric rating scale, where 1=very pessimistic and 7=very optimistic.[21] We used the CAGE questionnaire to assess the risk of alcoholism and Karnofsky performance status to assess overall function.[22, 23]

Statistical Analysis

The sample size was determined based on the primary aim of the original study, which was to determine the minimal clinically important difference for ESAS. We summarized the data with descriptive statistics, such as means, medians, and standard deviations. Univariate linear regression was used to evaluate the association between the total meaning in life score and each of the other variables. Kruskal-Wallis test was used to examine the difference in continuous variables among sites, while Chi-square or Fischer's exact test was used for the categorical variables. We examined the association between meaning in life scores and various variables with a P-value <0.05 in univariate analysis (i.e. demographics, symptom distress) using a multivariable linear model with backwards stepwise selection. Country was also included multivariable linear model as an adjustment given it was highly correlated with ethnicity, education, and stage of cancer. All computations were carried out in Statistical Analysis Software 9.4 (SAS Institute Inc., Cary, NC, USA). A P value of <0.05 was considered significant.

RESULTS

Demographics

Data was collected from December 8, 2011 through April 30, 2014. The demographics of our study population are reported in Table 1. US enrolled the largest number of patients

(n=300, 41%) followed by Jordan (n=182, 25%) and Brazil (n=131, 18%). The level of education differed significantly by country, with lowest level of education in India, and highest in the US. The majority of patients were married (70%), but this differed significantly by country. The most common cancer sites were gastrointestinal (22%), breast (18%), and respiratory (16%). The majority of patients had metastatic cancer (87%).

Meaning in Life Scores By Country

The median meaning in life score was 25/32 (interquartile range 23–28), with values, purpose, goals, and reflection sub-scores of 7 (6–8), 6 (5–7), 6 (6–7), and 6 (6–8) respectively (Table 2). The total meaning in life score was similar among the 5 countries (P=0.11); however, there were significant differences in sub-scores. For example, Jordan and the U.S reported higher values sub-scores; India had a lower purpose and goals sub-score but higher reflection sub-score compared to other countries (Table 2).

Predictors of Meaning in Life

In the univariate analysis (Table 3), patients with higher intensity of physical symptoms (i.e. pain, fatigue, drowsiness, dyspnea, insomnia), emotional distress (i.e. depression and anxiety), existential concerns (spiritual pain), and financial issues (financial distress, financial impact) had lower meaning in life. Patients with higher CAGE scores also had lower meaning in life. In contrast, being married, feeling optimistic, and having a higher level of education were associated with higher meaning in life. Other demographic variables such as age, sex, cancer site, and stage of cancer were not associated with meaning in life scores.

In the multivariate analysis, higher total meaning in life scores were significantly associated with greater optimism as well as lower depression, spiritual pain, and financial distress (Table 3). Country of origin was not a significant predictor of meaning in life.

DISCUSSION

Three major findings emerged from this study. First, the overall meaning in life score was generally high and did not differ significantly among patients with advanced cancer from different countries and cultures; however, we observed significant differences in individual sub-scores. Second, meaning in life was significantly associated with multiple factors, including psychological distress, spiritual concerns, patients' attitudes, and physical symptoms. Its association with psychosocial variables was particularly strong. Third, we identified financial distress as a novel predictor of lower meaning in life even after adjusting for many known variables. Together, these findings underscored the multidimensional nature of meaning in life and highlighted potential opportunities for interventions to improve meaning in life in patients living with advanced cancer.

The multinational nature of this study uniquely positioned us to investigate differences in meaning in life across cultures. We were intrigued by the finding that there was no significant difference in total meaning in life between the five countries, despite significant cultural, racial, and educational differences. This may point to meaning in life being a fundamental aspect of the human experience. Moreover, patients with advanced cancer may

exhibit a level of resilience that transcends culture—lower scores in one domain may be compensated by other higher scores in other domains to achieve a similar level of meaning in life. Our observation that total meaning in life scores did not differ amongst countries, but that there was a significant difference in certain domains has been reported by other investigators as well. For example, Tomás-Sábado et al., using a different, more qualitative meaning in life tool (SMiLE), elicited aspects of meaning in life in Spanish palliative care patients and then compared results with those of patients from Germany and Switzerland. [24] While all patients had similar levels of meaning in life, they found differences in how patients weighted the areas that contributed to their meaning in life.[24] Similarly, Kudla et al., compared palliative care patients in India and Germany and found that overall the meaning in life scores were similar but the domains that patients emphasized differed significantly.[25] Compared with groups of geriatric patients studied by Krause, the average meaning in life score of our patients was lower, 25 compared with 28 in his population. [7] The significance of this difference is not clear, as there is no established minimal clinically important difference for this tool. However, meaning in life in cancer patients versus the general population is an interesting area for future study.

We were impressed by the observation that meaning in life was associated with a large number of variables, ranging from physical symptoms and psychological distress to social status, spiritual concerns, and patients' attitudes. It is important to focus on the magnitude of association instead of statistical significance given the relatively large sample size. One important implication is that palliative care, as an inter-professional discipline that provides holistic care, is particularly well equipped to enhance meaning in life. As meaning in life becomes increasingly recognized as a clinical outcome of interest in its own right, we hypothesize that the diversity of palliative care interventions such as management of both psychological and physical symptoms, counseling, spiritual care, family conferences, and advanced care planning could have a positive impact on meaning in life. Our findings that psychosocial factors were particularly strongly associated with meaning in life fits with Park et al.'s recent systematic review that found that psychosocial interventions specifically targeting meaning and purpose are effective.[12] A loss of meaning in life can be viewed as a kind of existential distress, and is in fact an area in which psychologists have attempted to intervene. Breitbart, et al. piloted "Meaning Centered Psychotherapy" for patients near the end of life and found promising improvements in psychosocial outcomes including reduction in depression, hopelessness, and anxiety.[9] Another therapy focused on existential distress that was specifically developed for palliative care patients is "Dignity Therapy," a form of psychotherapy that allows patients to reflect on their lives and the things which they wish to transmit on to loved ones.[26–28] It has shown promise as a way of relieving existential distress in patients at the end of life, even in patients who have high levels of distress.[28] As more research focusing on psychosocial interventions to improve meaning in life are undertaken, our research may be helpful in disambiguating meaning from other related concepts.

A novel finding in our study is that financial distress was negatively correlated with meaning in life, independent of other known variables. As cancer treatment becomes more advanced, and thus more expensive, the financial toxicity of cancer therapy is increasingly being recognized and studied. A study from Zafar, et al. in 2013 found that patients spent a

median of \$456/month on cancer care related expenses, and 20% took less medication than prescribed to try to cut costs.[29] In 2016, Ramsey et al. reported that this financial toxicity taken to the extreme of bankruptcy was a risk factor for mortality; Fenn et al. found that patients who had financial problems related to their cancer had lower quality of life.[30, 31] Zafar hypothesized that this correlation could be related to loss of leisure activities, changes in habits due to financial stress, or due to changes in the quality of cancer care the patients receive.[29] Our findings add that financial distress is related to existential distress as shown by its association with lower meaning in life. Our findings, along with those of others, underscore the importance for clinicians to assess patients' financial distress and look for opportunities to intervene in this important aspect of care.

To our knowledge, this is the first study to quantitatively assess cancer patients' meaning in life with questions across four domains. However, we recognize that meaning in life is a complex and abstract concept that is challenging to define. Scales and questionnaires may not be able to capture the full experience of meaning. Additionally, this study of meaning in life was a secondary analysis, and thus our findings should be considered as hypothesis generating only. Because patients were only recruited from tertiary cancer care centers, our findings may not be generalizable in other settings. We also did not include some variables that may be determinants of meaning in life, such as hope, religion, performance status, social support, loneliness, and quality of life. Future studies are required to examine these aspects in further details.

Our study highlights the complex and multifaceted nature of meaning in life in patients with advanced cancer and points to the need for an interdisciplinary palliative care approach to treatment. These patients require treatment not only focused on alleviating psychological and physical symptoms, but also therapies aimed at addressing existential, spiritual, and financial distress. Future studies should consider assessing meaning in life as an outcome of interest in the clinical setting; it is easy to assess with an eight question tool, and may help clinicians recognize opportunities to intervene in patients' existential distress in an interdisciplinary way.

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Table 1.

Patient Characteristics

	Brazil (n=131)	Chile (n=71)	India (n=44)	Jordan (n=182)	U.S (n=300)	Total (n=728)
Age, mean (range)	58 (26–81)	60 (28–85)	51 (24–73)	55 (19–84)	58 (21–85)	57 (19–85)
Female, No. (%)	61 (46.6)	44 (62)	26 (59.1)	86(47.3)	144(48)	361(49.6)
Race, No. (%)						
Non-Hispanic White	0	0	0	0	229 (76.3)	229 (31.5)
Black	0	0	0	0	37 (12.3)	37 (5.1)
Hispanic	131 (100)	71 (100)	0	0	22 (7.3)	224 (30.8)
Asian	0	0	44 (100)	0	11 (3.7)	55 (7.6)
Jordanian	0	0	0	182 (100)	0	182 (25)
Other	0	0	0	0	1 (0.3)	1 (0.1)
Marital Status, No. (%)						
Single	16 (12.2)	16 (22.5)	2 (4.5)	19 (10.4)	45 (15.1)	98 (13.5)
Married	85 (64.9)	40 (56.3)	38 (86.4)	139 (76.4)	200 (67.1)	502 (69.1)
Divorced	30 (22.9)	15 (21.1)	4 (9.1)	24 (13.2)	53 (17.8)	126 (17.4)
Education, No. (%)						
Illiterate or high school or less	114 (87)	21 (29.6)	38 (86.3)	111 (61)	77 (25.7)	361 (49.6)
Some college up to bachelor's	16 (12.2)	47 (66.2)	5 (11.4)	58 (31.9)	173 (57.7)	299 (41.1)
Advanced degree	1 (0.8)	3 (4.2)	1 (2.3)	13 (7.1)	50 (16.7)	68 (9.3)
Cancer, No. (%)						
Breast	26 (19.8)	11 (15.5)	6 (13.6)	40 (22)	48 (16)	131 (18)
Gastrointestinal	25 (19.1)	26 (36.6)	7 (15.9)	31 (17)	68 (22.7)	157 (21.6)
Genitourinary	30 (22.9)	6 (8.5)	2 (4.5)	14 (7.7)	25 (8.3)	77 (10.6)
Gynecologic	16 (12.2)	6 (8.5)	15 (34.1)	7 (3.8)	20 (6.7)	64 (8.8)
Head and neck	5 (3.8)	0	7 (15.9)	18 (9.9)	40 (13.3)	70 (9.6)
Hematologic	4 (3.1)	8 (11.3)	1 (2.3)	10 (5.5)	8 (2.7)	31 (4.3)
Non-small cell lung	0	0	0	0	1 (0.3)	1 (0.1)
Other	10 (7.6)	6 (8.5)	3 (6.8)	25 (13.7)	39 (13)	83 (11.4)
Respiratory	15 (11.5)	8 (11.3)	3 (6.8)	37 (20.3)	51 (17)	114 (15.7)
Cancer Stage, No. (%)						
Advanced	0	0	0	8 (4.4)	8 (2.7)	16 (2.2)
Locally Advanced	23 (17.6)	8 (11.3)	6 (13.6)	9 (4.9)	34 (11.3)	80 (11)
Metastatic	108 (82.4)	63 (88.7)	38 (86.4)	165 (90.7)	258 (86)	632 (86.8)
CAGE positive, No. (%)	38 (29)	6 (8)	6 (14)	7 (4)	43 (14)	100 (14)
MDAS, mean (SD)	2.5 (1.5)	2.4 (1.9)	2.3 (1.1)	2.8 (2)	1.2 (1.3)	2 (1.7)
KPS baseline, mean (SD)	71 (13)	78 (13)	77 (6)	68 (14)	-- [†]	--
KPS follow-up, mean (SD)	70 (13)	75 (14)	74 (5)	66 (15)	69 (13)	69 (13)

[†]No KPS data collected from U.S. initial visit

Table 2.

Meaning in Life Levels by Country: sub-scores and total scores

Statement	<i>Median (Q1,Q3)</i>						P-value
	Brazil	Chile	India	Jordan	U.S	Total	
I have a system of values and beliefs that guides my daily activities. [†]	3 (3,4)	3 (3,4)	3 (3,4)	4 (3,4)	4 (3,4)	4 (3,4)	0.02
I have a philosophy of life that helps me understand who I am.	3 (3,4)	3 (3,3)	3 (2, 3.5)	3 (3,4)	3 (3,4)	3 (3,4)	<0.0001
Values Sub-score [‡]	6 (6,7)	6 (6,7)	6 (6,7)	7 (6,8)	7 (6,8)	7 (6,8)	0.003
I feel like I am living fully.	3 (3,4)	3 (2,4)	3 (2,4)	3 (2,4)	3 (2,3)	3 (2,3)	<0.0001
I feel I have found a really significant meaning in my life.	3 (3,4)	3 (3,4)	3 (2,3)	3 (3,4)	3 (3,4)	3 (3,4)	<0.0001
Purpose Sub-score	6 (6,7)	6 (5,7)	5 (4,7)	6 (5,7)	6 (5,7)	6 (5,7)	0.0001
In my life, I have clear goals and aims.	3 (3,4)	3 (3,4)	3 (2,3)	3 (3,4)	3 (3,4)	3 (3,4)	0.0004
I have a sense of direction and purpose in life.	3 (3,4)	3 (2,3)	2 (2,3)	3 (3,4)	3 (3,4)	3 (3,4)	<0.0001
Goals Sub-score	6 (6,7)	6 (5,7)	5 (4,6)	6 (6,8)	6 (6,7)	6 (6,7)	<0.0001
I feel good when I think of what I have done in the past.	3 (3,4)	4 (3,4)	4 (3,4)	3 (3,4)	3 (3,4)	3 (3,4)	<0.0001
I am at peace with my past.	3 (3,4)	3 (3,4)	4 (3,4)	3 (3,4)	3 (3,4)	3 (3,4)	0.02
Reflection Sub-score	6 (5,7)	7 (6,8)	8 (6,8)	6 (6,8)	6 (6,8)	6 (6,8)	<0.0001
Total Score [§]	25 (23,28)	25 (23,28)	26 (23,28)	24 (20.5, 27)	26 (23,29)	25 (23,28)	0.11

[†]Score per statement ranges 1–4[‡]Score per section ranges 2–8[§]Total score ranges 8–32

Table 3.

Factors associated with meaning in life scores

		Univariate Estimate (95%CI)	P-value	Multivariate Estimate (95%CI)	P-value
All sites					
Age		0.02 (−0.01, 0.04)	0.09		
Sex	Female vs Male	−0.01 (−0.56, 0.54)	0.97		
Marital status	Single vs Married	−1.41 (−2.22, −0.61)	<.001		
	Divorced vs Married	−0.76 (−1.49, −0.03)	0.04		
Country	Brazil vs US	−0.24 (−1.01, 0.53)	0.54	0.01 (−0.77, 0.78)	0.99
	Chile vs US	−0.23 (−1.20, 0.74)	0.64	0.03 (−0.85, 0.90)	0.96
	India vs US	−1.59 (−2.78, −0.41)	0.01	−0.45 (−1.62, 0.73)	0.46
	Jordan vs US	0.19 (−0.50, 0.88)	0.59	−0.06 (−0.78, 0.65)	0.87
Education level	Some college up to bachelors degree vs illiterate or high school or less	0.74 (0.17, 1.31)	0.006		
	Advanced degree vs illiterate or high school or less	1.29 (0.31, 2.26)			
Cancer class	Gastrointestinal vs Breast	−0.18 (−1.05, 0.69)	0.68		
	Genitourinary vs Breast	0.27 (−0.78, 1.32)	0.62		
	Gynecologic vs Breast	−0.15 (−1.26, 0.97)	0.80		
	Head and neck vs Breast	−1.01 (−2.1, −0.08)	0.07		
	Hematologic vs Breast	−0.23 (−1.69, 1.23)	0.76		
	Non-small cell lung vs Breast	−5.36 (−12.72, 1.99)	0.15		
	Other vs Breast	−0.29 (−1.32, 0.74)	0.58		
	Respiratory vs Breast	0.50 (−0.44, 1.43)	0.30		
Stage of cancer	Advanced vs Metastatic	−0.36 (−2.22, 1.51)	0.71		
	Locally advanced vs Metastatic	−0.68 (−1.55, 0.20)	0.13		
CAGE		−0.38 (−0.65, −0.12)	0.005		
Pain		−0.16 (−0.25, −0.07)	0.001		
Fatigue		−0.11 (−0.21, −0.02)	0.023		
Nausea		0.00 (−0.10, 0.10)	0.936		
Depression		−0.45 (−0.54, −0.36)	<.001	−0.26 (−0.35, −0.16)	<.001
Anxiety		−0.36 (−0.44, −0.27)	<.001		
Drowsiness		−0.15 (−0.24, −0.06)	0.002		
Appetite		−0.08 (−0.17, 0.02)	0.101		
Dyspnea		−0.14 (−0.23, −0.05)	0.004		
Sleep		−0.20 (−0.28, −0.11)	<.001		
Spiritual Pain		−0.41 (−0.50, −0.33)	<.001	−0.19 (−0.28, −0.09)	<.001
Financial Distress		−0.31 (−0.39, −0.23)	<.001		

	Univariate Estimate (95%CI)	P-value	Multivariate Estimate (95%CI)	P-value
Financial Impact	-0.34 (-0.42, -0.26)	<.001	-0.16 (-0.24, -0.08)	<.001
Optimism	0.46 (0.35, 0.58)	<.001	0.33 (0.20, 0.46)	<.001

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