OXFORD

JNCI J Natl Cancer Inst (2017) 109(3): djw233

doi: 10.1093/jnci/djw233
First published online October 29, 2016
Article

ARTICLE

Linguistic Strategies for Improving Informed Consent in Clinical Trials Among Low Health Literacy Patients

Janice L. Krieger, Jordan M. Neil, Yulia A. Strekalova, Melanie A. Sarge

Affiliations of authors: STEM Translational Communication Center (JLK, JMN, YAS), Department of Advertising (JLK), and Division of Graduate Studies and Research (YAS), College of Journalism and Communications, University of Florida; Department of Advertising, College of Media and Communication, Texas Tech University (MAS), Gainesville, FL, Lubbock, TX.

Correspondence to: Janice L. Krieger, PhD, 2024 Weimer Hall University of Florida Gainesville, FL 32611, STEM Translational Communication Center, College of Journalism and Communications, University of Florida (e-mail: janicekrieger@ufl.edu).

Abstract

Background: Improving informed consent to participate in randomized clinical trials (RCTs) is a key challenge in cancer communication. The current study examines strategies for enhancing randomization comprehension among patients with diverse levels of health literacy and identifies cognitive and affective predictors of intentions to participate in cancer RCTs.
Methods: Using a post-test-only experimental design, cancer patients (n = 500) were randomly assigned to receive one of three message conditions for explaining randomization (ie, plain language condition, gambling metaphor, benign metaphor) or a control message. All statistical tests were two-sided.
Results: Health literacy was a statistically significant moderator of randomization comprehension ($P = .03$). Among participants with the lowest levels of health literacy, the benign metaphor resulted in greater comprehension of randomization as compared with plain language ($P = .04$) and control ($P = .004$) messages. Among participants with the highest levels of health literacy, the gambling metaphor resulted in greater randomization comprehension as compared with the benign metaphor ($P = .04$). A serial mediation model showed a statistically significant negative indirect effect of comprehension on behavioral intention through personal relevance of RCTs and anxiety associated with participation in RCTs ($P < .001$).
Conclusions: The effectiveness of metaphors for explaining randomization depends on health literacy, with a benign metaphor being particularly effective for patients at the lower end of the health literacy spectrum. The theoretical model demonstrates the cognitive and affective predictors of behavioral intention to participate in cancer RCTs and offers guidance on how future research should employ communication strategies to improve the informed consent processes.

Randomized clinical trials (RCTs) remain the gold standard in developing medical treatments for cancer and are essential for translating biomedical discoveries into evidence-based patient care (1). In the United States, the discovery of new treatments is often slow because of difficulties in recruiting patients to participate in RCTs (1). Less than 5% of cancer patients in the United States participate in RCTs, and those rates are lower for racial and ethnic minorities (2). As a result, approximately 75% of investigators do not meet their RCT recruitment goals (3).

A key barrier to patient participation in RCTs is how randomization to treatment condition is explained during the informed consent process (4–6). Randomization is a highly technical term for which there are no lay language synonyms; thus health care providers often struggle to adequately translate this concept for patients, especially those with low literacy (7). Comprehension of randomization is essential to informed consent; however, existing data are inconclusive as to how health literacy influences the efficacy of communication efforts in this context, and whether improved comprehension is positively or negatively related to behavioral intention to participate in RCTs (8,9).

Efforts to improve understanding of randomization in RCTs rely on one of two linguistic strategies: plain language and metaphors (10–12). The goal of plain language is to adapt complex

Received: May 31, 2016; **Revised:** August 10, 2016; **Accepted:** September 12, 2016

information so that it is easier to understand using techniques such as shorter sentences and nontechnical language (13). Research suggests that plain language is effective for increasing comprehension of cancer diagnoses and treatment options among patients with low health literacy (14). However, its effectiveness for improving comprehension of randomization in the context of RCTs is unclear (15).

Another common approach for explaining randomization is the use of metaphors. Metaphors can be an effective health communication tool because the process of comparing a familiar (eg, flipping a coin) and unfamiliar concept (ie, randomization) creates cognitive pathways wherein the similarity between the concepts becomes salient (ie, chance) (16). There is evidence that metaphors are superior to plain language for improving comprehension of randomization, but it is unclear whether this relationship varies according to health literacy (10,12). For example, research has shown that gambling metaphors (eg, toss of a coin) result in lower comprehension than metaphors that are more benign in nature (eg, pregnancy resulting in female vs male baby) when patients are unable to fully attend to randomization explanations (9). When cognitive resources are limited, such as when patients lack the knowledge or skills to process a statistical concept like randomization, metaphors may be particularly useful in clinical contexts. Thus, while metaphors may be useful across patient populations, metaphors in general, and benign metaphors in particular, should be most effective for patients with low health literacy.

Randomization comprehension is an important component of informed consent to participate in RCTs; however, there are other cognitive and affective responses to randomization messages that may influence patient intentions to participate in RCTs, including personal relevance. Personal relevance of health information increases patient engagement with health messages, as well as increases intention to participate in RCTs (17,18). Increasing patient comprehension of randomization may not correspond directly with increasing perceived relevance, particularly when the concept of chance is misaligned with a patient's personal goals and values for their cancer treatment (19,20).

There are also important affective processes associated with exposure to randomization information. Patients commonly make decisions about RCT participation while still coping with the negative emotions that accompanied their cancer diagnosis (21). For this reason, common vocabulary used during the RCT informed consent process may inadvertently increase patient anxiety. For example, explaining randomization as the flip of a coin can cause patients to perceive randomization negatively because they perceive that their cancer treatment is being treated like a "game" (8,9). As such, anxiety associated with explanations of randomization is expected to be an important predictor of intention to participate in RCTs (16,21–24).

The best predictor of a person's behavior is their reported intention to perform that behavior (25,26). Thus, patient intention to participate in RCTs is a valuable intermediary outcome for assessing how improving language in the context of patients with low health literacy can improve the informed consent process. Comprehension, personal relevance, and anxiety are commonly associated with intention to perform health behaviors (27–29); however, the importance of these constructs in the context of cancer RCTs has not been explored. Thus, the current study experimentally tests whether linguistic strategies differentially influence comprehension of randomization and examines whether personal relevance and anxiety mediate the influence of comprehension on intention to participate in RCTs.

Methods

Participant Recruitment

An online message design experiment approved by The Ohio State University Institutional Review Board was conducted with 606 participants recruited over a one-week period (May 7–14, 2014) via Qualtrics Panels, a proprietary opt-in online panel comprised of US residents. Eligible participants were age 18 years or older, able to read and write in English, had been diagnosed with cancer within the previous 24 months, and provided informed consent to participate. Participants who had previously participated in any type of cancer clinical trial as part of their treatment (n = 73) or who did not complete all dependent measures (n = 6) were removed from the data set prior to analysis.

Instrumentation

Stimuli

Participants were randomly assigned to one of four message conditions: control (n = 117), plain language (n = 128), gambling metaphor (n = 132), and benign metaphor (n = 123) (Supplementary Materials, available online). A plain language explanation of randomization served as a base message. The message utilizing a gambling metaphor included an additional 54 words comparing randomization to the chance a flipped coin would land on heads. The message utilizing a benign metaphor included an additional 55 words comparing randomization to the chance of a pregnancy resulting in a male or female child. This comparison was generated through formative research reported previously (9). The Flesch-Kincaid readability scores for each message were 8.0 (plain language), 8.7 (gambling metaphor), and 9.3 (benign metaphor).

Covariates

Study covariates (age, sex, education, race/ethnicity) were measured using instruments from the Health Information National Trends Survey (HINTS) (30). To enable comparison by race/ethnicity, dummy variables were created for the following groups: non-Hispanic white (coded as 0 for the referent), non-Hispanic black, and Hispanic (31,32). The remaining racial categories were limited in membership, which created disproportionate comparative groupings and were thus removed before analysis (n = 27). Perceived severity of cancer was measured using three items adapted from a previous study (eg, "Having cancer is/was a severe threat to my health") (33). Items were rated on a five-point Likert scale ranging from "strongly agree" to "strongly disagree" ($\alpha = .94$, mean = 4.10, SD = 1.07).

Health Literacy

Health literacy was measured using four items adapted from 2013 Health Information Trends Survey (HINTS) 4 Cycle 3 Methodology Report (34). The items assessed if patients felt they could easily find and interpret cancer information (eg, "The information you found was hard to understand"). Items were rated on a four-point Likert scale, with response categories ranging from "strongly agree" to "strongly disagree" ($\alpha = .86$, mean = 2.86, SD = .78).

Dependent Variables

Randomization comprehension was measured using three items adapted from the literature and modified based on field

ARTICLE

Table 1. Demographic characteristics of study participants (n = 500)

Characteristic	n (%)
Age, mean (SD), y	50.1 (17.1)
Sex, No. (%)	
Female	317 (63.4)
Male	183 (36.6)
Race/ethnicity, No. (%)	
Non-Hispanic white	415 (83.0)
Non-Hispanic black or African American	28 (5.6)
Hispanic or Latino	57 (11.4)
Education, No. (%)	
Associate degree and below	270 (54.0)
Four-year degree and above	230 (46.0)
Most commonly reported cancer diagnosis, No. (%)	
Breast	137 (27.4)
Melanoma	137 (27.4)
Prostate	59 (11.8)
Lung	41 (8.2)
Cervical/ovarian/uterine	36 (7.2)
Colorectal	27 (5.4)
Bladder	15 (3.0)

testing with cancer patients (35). The items were adapted to focus specifically on randomization and employ grammar and syntax familiar to US (as compared with UK) patients. The questions assessed the extent to which patients understood that treatment allocation was not associated with physician preference, patient preference, or patient health status (eg, "Randomization means that patients in a clinical study are allowed to choose treatment out of a list of options"). Items were reverse-coded and rated using a five-point Likert scale ranging from "strongly disagree" to "strongly agree" ($\alpha = .77$, mean = 3.65, SD = 1.07).

Personal relevance of clinical research was assessed using two items (36). Participants were asked how much attention they paid to clinical research and how relevant it was to them (eg, "Information about cancer clinical studies is personally relevant"). Items were rated on a five-point scale, with response categories ranging from "strongly disagree" to "strongly agree" ($\rho = .80$, mean = 3.63, SD = .90).

Anxiety was measured by asking participants to respond to the stem: "How would you feel if a doctor asked you to participate in a randomized clinical study?" Words reflecting positive and negative emotions were rated using a six-point scale ranging from "not at all" to "very much" (37). Anxiety was operationalized as the extent to which a participant reported feeling "tense" and "worried" ($\rho = .86$, mean = 3.47, SD = 1.51).

Behavioral intention to participate in a randomized clinical study was measured using three questions (38). The items assessed the extent to which cancer patients expressed interest in enrolling in a RCT in the future (eg, "If I was diagnosed with cancer again, I would want to participate in a randomized clinical study for my initial treatment"). Items were rated on a five-point scale, with response categories ranging from "strongly disagree" to "strongly agree" ($\alpha = .86$, mean = 3.01, SD = 1.05).

Statistical Analyses

Preliminary analyses were conducted to determine if randomization procedures were effective. Chi-square tests and analysis of variance (ANOVA) were used to verify there were no statistically significant differences among the treatment groups with regard to study covariates. A series of analyses were conducted to determine the effects of message condition on comprehension of randomization, as well as model how cognitive and affective variables influence behavioral intention to participate in RCTs. Analysis of covariance (ANCOVA) was used to determine the effect of the four message conditions (control, plain language, gambling metaphor, and benign metaphor) on comprehension of randomization in a RCT, using age, sex, education, race/ethnicity, and perceived severity of cancer as covariates. Pairwise comparisons were performed using a Sidak correction. Linear regression was used to examine the relationship between comprehension and behavioral intention, using age, sex, education, race/ethnicity, perceived severity of cancer, health literacy, and dummy codes for message conditions as covariates. Message conditions were included as covariates via comparison coding in the linear regression to account for their statistically significant influence on comprehension, as indicated in the ANCOVA results.

Version 2.15 of the SPSS PROCESS macro was used to test for simple moderation (ie, Model 1) with a multicategorical focal predictor and serial mediation (ie, Model 6) (39,40). In the simple moderation model, two analyses were run with message

Table 2. Randomization of participant covariates by message condition

	Message conditions				
Covariates	Control (n = 117)	Plain language (n = 128)	Gambling metaphor (n = 132)	Benign metaphor (n = 123)	P*
Age, mean (SD)	50.02 (17.54)	51.42 (16.20)	48.53 (16.56)	50.46 (18.31)	.59
Sex, No. (%)					.21
Male	40 (8.0)	48 (9.6)	57 (11.4)	38 (7.6)	
Female	77 (15.4)	80 (16.0)	75 (15.0)	85 (17.0)	
Race/ethnicity, No. (%)					.70
Non-Hispanic white	97 (19.4)	109 (21.8)	106 (21.2)	103 (20.6)	
Non-Hispanic African American	4 (0.8)	8 (1.6)	10 (2.0)	6 (1.2)	
Hispanic or Latino	16 (3.2)	11 (2.2)	16 (3.2)	14 (2.8)	
Education, No. (%)					.69
Associates degree or below	68 (13.6)	70 (14.0)	67 (13.4)	65 (13.0)	
Four-year degree and above	49 (9.8)	58 (11.6)	65 (13.0)	58 (11.6)	
Perceived severity, mean (SD)	4.16 (1.08)	3.91 (1.16)	4.18 (1.07)	4.16 (0.94)	.15
Health literacy, mean (SD)	2.87 (0.80)	2.83 (0.76)	2.80 (0.76)	2.95 (0.82)	.47

*Chi-square test for categorical variables; one-way analysis of variance test for continuous variables. All statistical tests were two-sided.

ARTICLE

Table 3. Unadjusted and adjusted means for comprehension in each message condition (n = 500)*

Message conditions	No.	Unadjusted mean (SD)	Adjusted mean (95% CI)†
Control	117	3.16 (0.94)	3.16 (2.98 to 3.34)
Plain language	128	3.77 (1.07)	3.74 (3.57 to 3.91)
Gambling metaphor	132	3.83 (1.08)	3.86 (3.69 to 4.03)
Benign metaphor	123	3.82 (1.07)	3.80 (3.63 to 3.98)

*One-way analysis of covariance. All statistical tests were two-sided. CI = confidence interval.
†Adjusted for the following covariates: age, sex, education, race/ethnicity, and perceived severity of cancer.

condition set as the focal predictor, health literacy as the moderator, and comprehension as the dependent variable. Age, sex, education, race/ethnicity, and perceived severity of cancer were included as covariates in both analyses. The first analysis implemented indicator coding to determine differences in comprehension between the control condition and each of the other conditions for varying levels of health literacy. The second analysis applied Helmert coding to identify differences in comprehension between the metaphorical conditions and the plain language condition for varying levels of health literacy. Helmert coding allows comparisons between levels of a nominal multicategorical variable (41).

In the serial mediation model, personal relevance and anxiety were tested as mediators operating in sequence to explain the indirect effect of comprehension on behavioral intention. Age, sex, education, race/ethnicity, perceived severity of cancer, health literacy, and message conditions were included as covariates. The message conditions were not included as focal predictors in the serial mediation analysis because of limitations of the software. Statistical mediation analysis with a multicategorical independent variable cannot be conducted with mediators in sequence (Model 6) (40). Given the documented influence of the message conditions and health literacy on comprehension, it is important to control for these effects when testing the proposed theoretical model. Bootstrapping was used to construct percentile-based, bias-corrected 95% confidence intervals (CIs) for specific and total indirect effects (39). All statistical tests were two-sided, and a P value of less than .05 was considered statistically significant.

Results

Participants

See Table 1 for a summary of participant demographic characteristics. The study had a final sample of 500 participants, comprised of 317 women and 183 men. Participants self-reported as non-Hispanic white (n = 415), non-Hispanic black or African American (n = 28), or Hispanic (n = 57), with an age range from 18 to 89 years (mean = 50.1 years, SD = 17.1 years). Table 2 reports the distribution of participant demographics and other study covariates by randomization condition.

Effects of Message Condition on Comprehension

The ANCOVA showed a statistically significant difference in comprehension of randomization among the message conditions ($F(3, 490) = 12.74$, $P < .001$, $\eta^2 = .077$). See Table 3 for the unadjusted (ie, original) and adjusted (for covariates) means and standard deviations/confidence intervals for comprehension in each condition. Pairwise mean comparisons are provided in-text below. Age ($P < .001$) and education ($P = .03$) were statistically significant covariates, while sex, race/ethnicity, and perceived severity of cancer were not. Comprehension was statistically significantly greater than control in both the gambling metaphor (mean difference = .70, $P < .001$, 95% CI = 0.37 to 1.04) and the benign metaphor conditions (mean difference = .64, $P < .001$, 95% CI = 0.30 to 0.98). Plain language was also associated with statistically significantly greater comprehension than control (mean difference = .58, $P < .001$, 95% CI = 0.24 to 0.92). However, there were no statistically significant differences in comprehension between the two metaphorical conditions (mean difference = .06, $P = 1.00$, 95% CI = -0.27 to 0.39), or when comparing the metaphorical conditions to the plain language condition (gambling mean

Table 4. Comparative effectiveness of message condition on comprehension at differing values of health literacy

Percentile	Health literacy value	Control				Plain language				Gambling metaphor			
			b	t	P*		b	t	P*		b	t	P*
10th	1.75	PL vs	.20	.90	.37								
		GM vs	.33	1.54	.12	GM vs	.14	.64	.52				
		BM vs	.66	2.94	.004	BM vs	.46	2.09	.04	BM vs	.32	1.49	.14
25th	2.25	PL vs	.37	2.33	.02								
		GM vs	.50	3.20	.002	GM vs	.13	.86	.39				
		BM vs	.66	3.98	<.001	BM vs	.28	1.77	.08	BM vs	.15	.95	.34
50th	3.00	PL vs	.63	4.88	<.001								
		GM vs	.76	5.90	<.001	GM vs	.13	1.00	.32				
		BM vs	.66	5.09	<.001	BM vs	.02	.17	.86	BM vs	-.10	-.83	.41
75th	3.50	PL vs	.81	4.85	<.001								
		GM vs	.93	5.61	<.001	GM vs	.12	.74	.46				
		BM vs	.66	4.12	<.001	BM vs	-.15	-.95	.34	BM vs	-.28	-1.73	.08
90th	4.00	PL vs	.98	4.31	<.001								
		GM vs	1.10	4.86	<.001	GM vs	.12	.52	.60				
		BM vs	.65	3.04	.003	BM vs	-.33	-1.50	.13	BM vs	-.45	-2.05	.04

*Simple moderation analysis conducted using PROCESS macro for SPSS. All statistical tests were two-sided. BM = benign metaphor condition; GM = gambling metaphor condition; PL = plain language condition.

ARTICLE

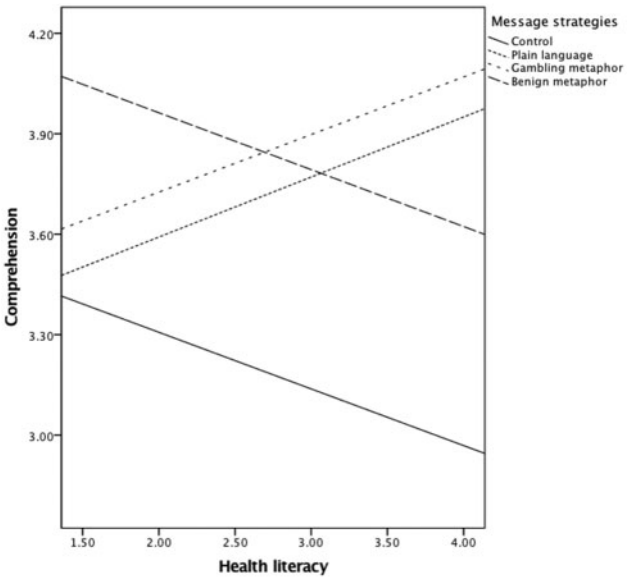

Figure 1. Comprehension of randomization for all message conditions at different levels of health literacy.

difference = .12, P = .90, 95% CI = -0.20 to 0.45; benign mean difference = .06, P = 1.00, 95% CI = -0.27 to 0.40).

Health Literacy as a Moderator of Message Condition and Comprehension

Table 4 presents the adjusted comparative effectiveness of the message conditions when probed at differing levels of health literacy. Figure 1 visually represents the results of the simple moderation analysis, showing the effect of message condition on comprehension at different levels of health literacy. Health literacy was a statistically significant moderator of randomization comprehension (P = .03), with message effectiveness dependent upon the level of patient health literacy. At the lowest level of health literacy (10th percentile, value = 1.75), only the benign metaphor resulted in statistically significantly greater comprehension of randomization when compared with the control condition (b = .66, t = 2.94, P = .004). At this level, the plain language (b = .20, t = 0.90, P = .37) and gambling metaphor conditions (b = .33, t = 1.54, P = .12) did not result in greater comprehension in comparison with the control. At higher levels of health literacy, all three message conditions resulted in statistically significantly greater comprehension in comparison with the control. When compared with the plain language condition, the benign metaphor resulted in statistically significantly greater comprehension at the lowest level of health literacy (b = .46, t = 2.09, P = .04). However, at the highest level of health literacy (90th percentile, value = 4.00), participants in the gambling metaphor condition had greater comprehension of randomization when compared with those in the benign metaphor condition (b = -.45, t = -2.05, P = .04).

Inverse Relationship Between Comprehension and Behavioral Intention

The linear regression (see Table 5) showed that comprehension had a statistically significant, inverse relationship with behavioral intention (β = -.29, $t(489)$ = -6.40, P < .001). Comprehension explained a statistically significant proportion of variance in behavioral intention ($F(11, 488)$ = 7.74, P < .001), uniquely accounting for 7.1% of the variability in behavioral intention beyond the control variables ($\Delta F(1, 488)$ = 40.96, P < .001).

Table 5. Regression of sociodemographic factors, message conditions, and randomization comprehension on behavioral intention

	Model 1		Model 2		Model 3	
Predictor variables	β	P*	β	P*	β	P*
Age	−.18	.001	−.18	.001	−.09	.06
Sex	−.02	.73	−.01	.76	−.003	.94
Education	−.07	.15	−.06	.15	−.04	.39
Health literacy	−.08	.10	−.08	.08	−.08	.07
Perceived severity	.05	.27	.05	.34	.04	.42
African American	.07	.12	.07	.14	.06	.18
Hispanic	−.02	.71	−.01	.76	−.03	.43
Plain language condition			−.10	.07	−.03	.59
Gambling metaphor condition			−.03	.60	.06	.30
Benign metaphor condition			−.05	.37	.03	.62
Comprehension					−.29	<.001
R^2	.70		.08		.15	
ΔR^2			.08	.33†	.07	<.001†
F	5.32	<.001	4.08	<.001	7.74	<.001

*Linear regression analyses. All statistical tests were two-sided. β = standardized beta coefficient; F = F statistic; R^2 = R square; ΔR^2 = R square change.
†P value of F for change in R^2.

Personal Relevance and Anxiety as Mediators of Comprehension and Behavioral Intention

Table 6 presents path coefficients, as well as indirect, direct, and total effects of the adjusted serial mediation analyses (see Figure 2 for visual representation). The inverse relationship between comprehension and behavioral intention was mediated by personal relevance and anxiety of participating in a RCT. Specifically, there was a statistically significant negative indirect effect of comprehension on behavioral intention through personal relevance and anxiety in serial ($a_1a_3b_2$ = -.003, 95% bias-corrected bootstrap CI [based on 10 000 samples] = -.01 to

Table 6. Path coefficients from serial mediation model illustrated in Figure 2*

Model pathways	B	P	Indirect effect (95% CI)
a_1	−.09	.03	
a_2	.09	.18	
a_3	−.17	.03	
b_1	.34	< .001	
b_2	−.19	< .001	
c'	−.29	< .001	
c	−.24	< .001	
a_1b_1			−.03 (-.06 to -.01)
a_2b_2			−.02 (-.04 to .01)
$a_1a_3b_2$			−.003 (-.01 to -.001)
Total			−.05 (-.09 to -.01)

*Serial mediation analysis conducted using PROCESS macro for SPSS. All statistical tests were two-sided. B = unstandardized beta coefficient; CI = bias-corrected bootstrap confidence interval.

ARTICLE

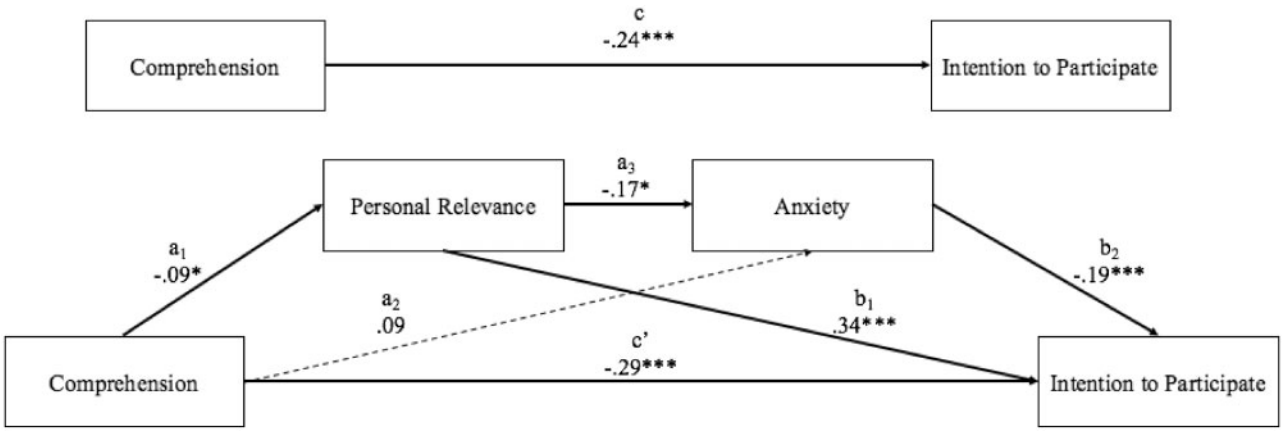

Figure 2. A serial mediation model showing the indirect effect of comprehension on behavioral intention to participate in randomized clinical trials through personal relevance and anxiety. The model demonstrates a statistically significant total indirect effect, and indirect effects via serial mediation. * $P < .05$; ** $P < .01$; *** $P < .001$. **Solid lines** represent statistically significant pathways. Serial mediation analysis conducted using PROCESS macro for SPSS. All statistical tests were two-sided.

-.001). Statistically significant negative associations exist between all variables in the proposed serial process. Increases in comprehension of randomization are associated with decreases in personal relevance of RCTs, which in turn increases anxiety of participating in a RCT. Further, anxiety is negatively related to intention to participate in a RCT; thus increases in anxiety due to decreases in personal relevance reduce behavioral intention.

Discussion

The current study demonstrates how different message strategies for explaining randomization influence cognitive and affective predictors of behavioral intention to participate in cancer RCTs. Several notable findings emerged from this study that can offer direction regarding how to improve comprehension of randomization during the informed consent process. Health literacy is an important predictor of how patients process and evaluate health information (42), and while existing literature suggests that plain language approaches may be beneficial for educating patients with low health literacy (13), our results show that a benign metaphor was the most effective strategy for enhancing randomization comprehension among patients with the lowest level of health literacy. However, patients with the highest levels of health literacy showed greater randomization comprehension when exposed to the gambling metaphor condition as compared with the benign metaphor condition. Taken together, these results show that metaphors can be more useful than plain language strategies for overcoming challenges associated with health literacy. Importantly, however, not all metaphors are equally effective across the health literacy spectrum, and messages should be customized to the needs of the patient.

Another noteworthy contribution of this study is that it demonstrates the cognitive and affective mechanisms that explain behavioral intention to participate in cancer RCTs. While previous research has identified the inverse relationship between comprehension of randomization and intention to participate in RCTs (16,21), the current model demonstrates that perceived relevance and anxiety are important mediators of this relationship. Specifically, improving comprehension of randomization reduces the perceived personal relevance of RCTs to a patient. This inverse relationship between comprehension and personal relevance likely reflects the discordance between patient misperceptions that medical treatment is tailored to their unique personal or medical characteristics and descriptions of randomized clinical studies in which patients are assigned to treatment without regard to individualized factors. This discordance inevitably reduces the personal relevance of clinical research, increases anxiety associated with RCTs, and decreases intention to participate in future RCTs. Subsequent research should explore the potential benefits of explaining to patients the extent to which treatment recommendations can be individually tailored in both standard and experimental treatment options (43). Further exploring the relationships between comprehension, personal relevance, and anxiety will be particularly important as personalized medicine studies continue to proliferate.

As with all research, this study has a few notable strengths and limitations. The strengths include using a large, national sample of patients who had received a cancer diagnosis within the past two years. Further, our confidence in the results is strengthened by the experimental design of the study and the careful construction of the stimuli. A potential limitation is that the stimuli used in the current study were not specific to a particular RCT and did not include specific information on the types of treatments being compared.

Funding

This study was supported by a grant from the National Cancer Institute (NCI) #U54 CA153604.

Notes

The NCI had no role in the design of the study; the collection, analysis, or interpretation of data; the writing of the manuscript; or the decision to submit the manuscript for publication.

References

1. Byrne MM, Tannenbaum SL, Glück S, Hurley J, Antoni M. Participation in cancer clinical trials: Why are patients not participating? *Med Decis Mak.* 2014; 34(1):116–126.

ARTICLE

2. Jimenez R, Zhang B, Joffe S, et al. Clinical trial participation among ethnic/racial minority and majority patients with advanced cancer: What factors most influence enrollment? *J Palliat Med*. 2013;16(3):256–262.
3. Institute of Medicine Forum on drug discovery, development, and translation. *Transforming clinical research in the United States: Challenges and opportunities: Workshop summary*. Washington, DC: National Academies Press; 2010. http://www.ncbi.nlm.nih.gov/books/NBK50892/. Accessed August 31, 2016.
4. Grand MM, O'Brien PC. Obstacles to participation in randomised cancer clinical trials: A systematic review of the literature. *J Med Imaging Radiat Oncol*. 2012;56(1):31–39.
5. Jenkins V, Fallowfield L. Reasons for accepting or declining to participate in randomized clinical trials for cancer therapy. *Br J Cancer*. 2000;82(11): 1783–1788.
6. Davis TC, Holcombe RF, Berkel HJ, Pramanik S, Divers SG. Informed consent for clinical trials: A comparative study of standard versus simplified forms. *J Natl Cancer Inst*. 1998;90(9):668–674.
7. Howard L, de Salis I, Tomlin Z, Thornicroft G, Donovan J. Why is recruitment to trials difficult? An investigation into recruitment difficulties in an RCT of supported employment in patients with severe mental illness. *Contemp Clin Trials*. 2009;30(1):40–46.
8. Krieger JL, Parrott RL, Nussbaum JF. Metaphor use and health literacy: A pilot study of strategies to explain randomization in cancer clinical trials. *J Health Commun*. 2011;16(1):3–16.
9. Krieger JL. Last resort or roll of the die? Exploring the role of metaphors in cancer clinical trials education among medically underserved populations. *J Health Commun*. 2014;19(10):1161–1177.
10. Galesic M, Garcia-Retamero R. Using analogies to communicate information about health risks. *Appl Cogn Psychol*. 2013;27(1):33–42.
11. Palmer-Wackerly AL, Krieger JL. Dancing around infertility: The use of metaphors in a complex medical situation. *Health Commun*. 2015;30(6):612–623.
12. Parrott R, Smith RA. Defining genes using "blueprint" versus "instruction" metaphors: Effects for genetic determinism, response efficacy, and perceived control. *Health Commun*. 2014;29(2):137–146.
13. Stableford S, Mettger W. Plain language: A strategic response to the health literacy challenge. *J Public Health Policy*. 2007;28(1):71–93.
14. Holmes-Rovner M, Stableford S, Fagerlin A, et al. Evidence-based patient choice: A prostate cancer decision aid in plain language. *BMC Med Inform Decis Mak*. 2005;5:16.
15. Davis TC, Williams MV, Marin E, Parker RM, Glass J. Health literacy and cancer communication. *CA Cancer J Clin*. 2002;52(3):134–149.
16. Jenkins V, Leach L, Fallowfield L, Nicholls K, Newsham A. Describing randomisation: Patients' and the public's preferences compared with clinicians' practice. *Br J Cancer*. 2002;87(8):854–858.
17. Anghelcev G, Sar S. The influence of pre-existing audience mood and message relevance on the effectiveness of health PSAs: Differential effects by message type. *Journal Mass Commun Q*. 2011;88(3):481–501.
18. Frew PM, Hou SI, Davis M, et al. The likelihood of participation in clinical trials can be measured: The Clinical Research Involvement Scales (CRIS). *J Clin Epidemiol*. 2010;63(10):1110–1117.
19. Celsi RL, Olson JC. The role of involvement in attention and comprehension processes. *J Consum Res*. 1988;15(2):210–224.
20. MacLeod C, Rutherford EM. Anxiety and the selective processing of emotional information: Mediating roles of awareness, trait and state variables, and personal relevance of stimulus materials. *Behav Res Ther*. 1992;30(5):479–491.
21. Jenkins V, Fallowfield L. Reasons for accepting or declining to participate in randomized clinical trials for cancer therapy. *Br J Cancer*. 2000;82(11):1783–1788.
22. Jenkins VA, Anderson JL, Fallowfield LJ. Communication and informed consent in phase 1 trials: A review of the literature from January 2005 to July 2009. *Support Care Cancer*. 2010;18(9):1115–1121.
23. Llewellyn-Thomas HA, McGreal MJ, Thiel EC, Fine S, Erlichman C. Patients' willingness to enter clinical trials: Measuring the association with perceived benefit and preference for decision participation. *Soc Sci Med*. 1991;32(1): 35–42.
24. Penman DT, Holland JC, Bahna GF, et al. Informed consent for investigational chemotherapy: Patients' and physicians' perceptions. *J Clin Oncol*. 1984;2(7): 849–855.
25. Ajzen I. Theories of cognitive self-regulation: The theory of planned behavior. *Organ Behav Hum Decis Process*. 1991;50(2):179–211.
26. Petty RE, Cacioppo JT. *Attitudes and persuasion: Classic and contemporary approaches*. Vol. xvii. Boulder, CO: Westview Press; 1996.
27. McCaffery K, Wardle J, Waller J. Knowledge, attitudes, and behavioral intentions in relation to the early detection of colorectal cancer in the United Kingdom. *Prev Med*. 2003;36(5):525–535.
28. Hu Y, Sundar SS. Effects of online health sources on credibility and behavioral intentions. *Commun Res*. 2009. http://crx.sagepub.com/content/early/2009/11/25/0093650209351512. Accessed August 31, 2016.
29. Schneider A, Andrade J, Tanja-Dijkstra K, White M, Moles DR. The psychological cycle behind dental appointment attendance: A cross-sectional study of experiences, anticipations, and behavioral intentions. *Community Dent Oral Epidemiol*. 2016;44(4):364–730.
30. Health Information National Trends Survey, Instruments. http://hints.cancer.gov/instrument.aspx. Accessed August 31, 2016.
31. Richardson A, Allen JA, Xiao H, Vallone D. Effects of race/ethnicity and socioeconomic status on health information-seeking, confidence, and trust. *J Health Care Poor Underserved*. 2012;23(4):1477–1493.
32. Lee T, Mathis A, Dutton M. An examination of early colorectal cancer screening guidelines for African Americans: Hints from the HINTS data. *J Health Disparities Res Pract*. 2016;31:9(1). http://digitalscholarship.unlv.edu/jhdrp/vol9/iss1/10. Accessed August 31, 2016.
33. Witte K. Predicting risk behaviors: Development and validation of a diagnostic scale. *J Health Commun*. 1996;1(4):317–42.
34. Health Information National Trends Survey 4 Cycle 3 Methodology Report. http://hints.cancer.gov/docs/Instruments/HINTS_4_Cycle_3_English_Annotated_508c_3_21_2014.pdf. Accessed August 31, 2016.
35. Curbow B, Fogarty LA, McDonnell K, Chill J, Scott LB. Can a brief video intervention improve breast cancer clinical trial knowledge and beliefs? *Soc Sci Med*. 2004;58(1):193–205.
36. Wells W, Leavitt C, Mcconville M. Reaction profile for TV commercials. *J Advert Res*. 1971;11(6):11–17.
37. Nabi RL. A cognitive-functional model for the effects of discrete negative emotions on information processing, attitude change, and recall. *Commun Theory*. 1999;9(3):292–320.
38. Krieger JL, Parrott RL, Nussbaum JF. Metaphor use and health literacy: A pilot study of strategies to explain randomization in cancer clinical trials. *J Health Commun*. 2010;16(1):3–16.
39. Hayes A. *An Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach*. New York: Guilford Press; 2013.
40. Hayes AF, Preacher KJ. Statistical mediation analysis with a multicategorical independent variable. *Br J Math Stat Psychol*. 2014;67(3):451–470.
41. Hayes A. Supplementary PROCESS documentation. http://afhayes.com/public/docaddendum.pdf. Accessed August 31, 2016.
42. Diviani N, van den Putte B, Giani S, van Weert JC. Low health literacy and evaluation of online health information: A systematic review of the literature. *J Med Internet Res*. 2015;17(5):e112.
43. Wade J, Donovan JL, Lane JA, Neal DE, Hamdy FC. It's not just what you say, it's also how you say it: Opening the "black box" of informed consent appointments in randomised controlled trials. *Soc Sci Med*. 2009;68(11): 2018–2028.