Predicting Cancer Mortality: Developing a New Cancer Care Variable Using Mixed Methods and the Quasi-Statistical Approach

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Objective. To demonstrate the value of using a variable derived from qualitative analysis in subsequent quantitative analyses.

Data Sources/Study Setting. Mixed methods data were combined with 10-year mortality outcomes. Participants with cancer were recruited from services at a large teaching hospital, and mortality data were from the Social Security Death Index.

Study Design. An observational concurrent or convergent mixed methods design was used to collect demographics and structured ratings along with qualitative data from 909 cancer patients at baseline.

Data Collection/Extraction Methods. Coding rules for qualitative data were defined for open-ended responses from cancer participants speaking about their view of self, and a variable was numerically coded for each case. Mortality outcomes were matched to baseline data, including the view of self variable.

Principal Findings. Individuals with an improved view of self had a significantly lower mortality rate than those for whom it was worse or unchanged, even when adjusting for age, gender, and cancer stage.

Conclusions. Statistical analysis of qualitative data is feasible and can identify new predictors with health services' implications associated with cancer mortality. Future studies should consider the value of testing coded qualitative variables in relation with key health care outcomes.

Key Words. Cancer, mixed methods, prognosis, quasi-statistical, view of self

Decades after the 1971 National Cancer Act declared a "war on cancer" (National Cancer Institute 1971), cancer remains a major cause of death, with an estimated annual mortality rate of 173 per 100,000 in the United States (Howlader et al. 2009). Despite better detection and newer multimodal treatments, death rates for some cancers have not dropped appreciably or have

even risen (American Cancer Society 2012). Malignancies are not only a major cause of mortality, but they also entail a significant health burden, with an impact on patient quality of life and productivity (Ashing-Giwa, Lim, and Tang 2010; Broekx et al. 2011; Cohen et al. 2012; Hanly et al. 2012).

The principal way of determining prognosis in cancer patients is by staging. However, as an anatomical variable, cancer staging does not take into account overall functional status, which is influenced by comorbidities and other more subjective variables, such as affective, cognitive, and role functioning (Lehto et al. 2007). Although evidence is robust that there is a link between depression and health outcomes in cardiovascular disease (Diez-Quevedo et al. 2012; Machado-Vieira and Mallinger 2012), the relationship between psychological variables and outcomes in cancer patients remains unclear (Satin, Linden, and Phillips 2009). Emerging evidence indicates that optimistic or less pessimistic attitudes may predict cancer survival, although few studies have demonstrated this association (Schulz et al. 1996; Rasmussen, Scheier, and Greenhouse 2009; Novotny et al. 2010; Pinquart and Duberstein 2010).

Mixed methods research is one effective way of describing patients' subjective perceptions related with disease (Patton 2002; Creswell et al. 2011). Traditionally, however, qualitative research has been limited in its ability to provide prognostic information. Many mixed methods studies in health care settings use a sequential approach (Morse 2010) that does not concurrently gather the clinical and demographic variables needed to predict survival or other important outcomes when collecting qualitative data. In addition, requirements for thematic saturation—that is, the means of determining the adequacy of qualitative samples—can often be attained in relatively small groups of 10–30 participants (Sandelowski 1995; Kuzel 1999; Guest and Johnson 2006). Such sample sizes are typically too small to identify relevant correlations between health outcomes and qualitatively derived themes. In

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addition to an adequate sample size for statistical analysis of outcomes, the validation of prognostic factors using a mixed methods approach also obviously requires a longitudinal design to reach the relevant endpoints, such as completion of treatment, hospital discharge, or mortality.

One methodological approach has supported the application of qualitative research to the study of predictive associations. In the introduction to their 1992 edition of *Doing Qualitative Research*, Miller and Crabtree (1992) described a quasi-statistical approach to qualitative coding whereby texts (e.g., words, semantic units, themes) are divided into categories and examined statistically to "determine connections" among them. Inherent in this approach is the use of an empirical framework to examine the relationships between qualitative codes and, potentially, outcome measures or predefined endpoints. To promote the growth of mixed methods in clinical and health services research, we explored the use of this quasi-statistical approach as a way of attaining in-depth insights from participants (Fielding 2012) as well as robust predictive information.

We present an observational concurrent or convergent mixed methods' study that uses the quasi-statistical approach to explore a predictive model of cancer mortality. Drawing upon the cancer arm of the Patient Narrative Study with its large ($N = 909$) cohort, a mixed methods dataset and its decade long follow-up on outcomes, we examine ways that qualitatively derived categories can function as variables in statistical analyses to predict critical outcomes, such as mortality in the health care system. In this study, therefore, a category resulting from qualitative analysis is numerically coded and included in a model that assesses its relative contribution to the prediction of mortality in cancer patients, an example of integration through data transformation (see Fetters, Curry, and Creswell 2013).

METHODS

Study Sample

Patients treated in either the inpatient or outpatient settings at a large Midwestern teaching hospital were eligible for inclusion if they had a diagnosed malignancy, independent of disease stage or treatment. We excluded prisoners, patients unable to communicate verbally or to provide informed consent, and patients younger than 18 years of age. A trained interviewer obtained informed consent from each patient and asked them to engage in an extensive interview addressing psychosocial and health-related questions, and to com-

plete ratings on health status and psychosocial factors (see below). The patients also provided demographic information, including their age, gender, racial/ethnic identity, highest level of education, and employment and marital status. A physician extracted clinical data from the electronic medical record, including stage of cancer at the time of the interview. Date of death was abstracted from the Social Security Death Index. The protocol was approved by the Institutional Ethics Review Board of the University of Iowa in conformity with the ethical guidelines of the Declaration of Helsinki.

Semistructured Interview

Each enrolled participant was asked to engage in a semistructured interview with a trained assistant in an environment that ensured privacy. Patients were asked questions focusing on psychosocial dimensions of illness, including their attitudes toward illness and treatment. Each interview was recorded with a hand-held tape recorder and later transcribed verbatim. To ensure accuracy, randomly chosen transcriptions were compared with the original audiotapes. In the present study, we focused on the answers to a single question: "As you go through this experience, have you begun to think about yourself differently?"

Survey Instruments

After the interview, the patients were asked to complete demographic questions, the Hospital Anxiety Depression scale (HAD), and the Sickness Impact Profile (SIP). The HAD is a validated screening tool for the assessment of depressive and anxiety symptoms in emotional disturbances used within a hospital setting (Zigmond and Snaith 1983). HAD subscale scores for anxiety and depression are coded as low, moderate, or high according to standard cut points (Zigmond and Snaith 1983). The SIP is a well-validated health status survey, containing categories for social interaction, emotional balance, alertness, body care, ambulation, physical capacity to communicate, movement, and with subscales for psychosocial and physical status as well as a total score (Bergner et al. 1981).

Qualitative Coding

Twenty trained interviewers, each with over 1 year of experience in interviewing, participated in the codebook construction process. They read a random

selection of 50 interviews from a total of 150 and ranked the top 10 themes in terms of their overall frequency and importance. The principal investigator and two trained coders synthesized this list to create a main codebook, which included the central themes specific to each question.

For the "view of self" question, the first author and the two coders used an open, iterative approach to discover a pattern of patient responses without using preconceived coding categories. From this iterative process, we saw narrative patterns emerge that framed the answers in the classical sense of tragic, comic (e.g., happy ending), or that rejected a narrative of change all together. This pattern became consolidated in the final codes: (1) "improved," (2) "worse," or (3) "unchanged" view of self. For answers that combined improved, worse, and/or unchanged views of self, the coders selected the category that best captured the overall intent of the answer (e.g., "This experience has been really bad, but I don't think I've changed," coded as "unchanged"). For answers that did not address the question, the coders chose the category (4) "cannot judge."

Using these coding definitions, each transcript was then examined by two independent coders, one who had undergone a minimum of 3 weeks of formal training and a master coder with at least 1 year of experience in qualitative coding. The initial coding sheets for each coder were converted into a spreadsheet to assess the agreement between the evaluators using kappa statistics. Coders attained a high degree of intercoder reliability (kappa > .65)—a score that Landis and Koch (1977) described as "substantial" agreement—and then continued to meet and process the codes for each case until agreement was achieved between them. All cases were judged by two coders with the differences adjudicated within the pair of coders. A master coding dataset containing the agreed-upon codes was then used for the subsequent analysis. The categories were then converted to numerical values (1–4). These data were entered into a spreadsheet as a single ordinal variable and analyzed following the quasi-statistical qualitative approach as outlined by Miller and Crabtree (1992).

Statistical Evaluation

Descriptive frequencies were examined and χ^2 statistics were used to assess differences in mortality between subgroups by stage of disease and by scores on the view of self. Bivariate logistic regressions were performed to assess the relationship between case characteristics and either view of self or long-term mortality outcomes. Hierarchical multivariable logistic models were used to

assess the cumulative impact on mortality of age and gender first, stage of disease next, and then improved view of the self last. All statistical analyses were conducted in Stata SE 12 (Statacorp, College Station, TX, 2012).

RESULTS

Sample Characteristics

Between February 1999 and July 2003, a total of 909 patients diagnosed with cancer were enrolled into the study (Table 1). Of the 909 participants, 881 (97 percent) answered the "view of self" question of whom 825 (94 percent) had a codable response and were included in the statistical analyses. Mortality outcomes for the entire cohort were extracted in June of 2009. There was no significant difference in age, race, marital status, education, anxiety, depression, number of psychiatric diagnoses, number of comorbidities, stage of cancer at interview, or mortality between participants with and without a codable response regarding change in view of self. The sample was comprised predominantly of older, female Caucasian participants. Half of the sample had at least some college education, and nearly half were working at the time of the interview. Half of the sample had stage 4 cancer (Table 1).

Qualitative Analysis of "View of Self"

Roughly half of the participants had a stable view of themselves, with the remaining patients being nearly equally divided into an improved (23 percent) or worsened outlook (28 percent). In the group with an improved view of self, the most common theme involved some redeeming quality of the cancer experience. One woman expressed such an experience, using the metaphor of a journey reflecting a more spiritual side of the illness progression: "I'm back to realizing that I do have an internal strength; that it will take me wherever I need to go in this journey. And it will be a good journey, whatever the end outcome is." Other patients described themselves as becoming emotionally and socially enriched: "I was a person who was always pretty hard on myself. Pretty demanding. And I think for the same reason, very demanding of other people. And I saw the world very narrowly. And I can see that there are many very good alternatives in life to doing things outside of the narrow point of view that I had. And I find myself being much more forgiving of myself and much more forgiving of people who used to irritate me (Laughs). You know, you just become more accepting." Still others emphasized a growing

Table 1:   Sample Characteristics

	N	%	Median	IQR
Age			58	48–67
Male	348	40		
White	833	95		
Education				
Some college	222	25		
College	128	15		
Professional	92	10		
Working	393	45		
Married	566	64		
HADS anxiety			6	4–9
HADS depression			4	2–7
SIP physical category			5.98	1.35–16.05
SIP psychosocial category			6.34	1.70–14.68
SIP total			13.68	4.51–30.30
Cancer stage (N = 758)				
1	92	12		
2	129	17		
3	157	21		
4	380	50		
View of self (N = 825)				
Improved	186	23		
Unchanged	411	50		
Worse	228	28		

awareness of how precious life is: "I appreciate each day. I don't take them for granted. I think I've got this to do, I've got so much to do, I better get busy. It kind of crowds your heart."

In the group with a worsened view of self the most common themes involved description of physical harm or damage and the resulting mental anguish that came from the disease. Such a view was expressed in the statement of a young woman: "I am not the person that I was (Cries). Just to grasp the concept that at a young age you're disabled, just like overnight, is very hard to swallow. That's a very hard thing to tell someone: 'Too bad, your life is ruined; you just better learn to go on.' And at 37, you're thinking: 'Oh my gosh, I just had a baby.'" Others focused more on the limitations either physically or in their life goals. One patient shared the frustrations that arose from the cancer diagnosis: "I went outside with my husband yesterday, out in the courtyard and could see my reflection in the glass windows and thought: 'This is pathetic! I'm an active person and I am sitting here in a hospital gown hardly moving around.' So, yeah, I guess I look at myself a little differently." Others

described their cancer as a type of judgment rendered upon them: "All I keep saying is I'd like to know what I did to cause all this trouble, you know? I always thought I was a good, hard worker and all that. And I keep saying why should I have to do so much suffering?"

The group with an unchanged view of self gave statements that described stability in the face of disease, mostly using short answers to reject the idea that anything had changed. "No. Why should I [have changed]? What is to be, is to be." A few participants made statements about ways that they had stayed the same, such as one patient who noted: "Not really [changed]. I've had a few trials and tribulations through my life, different kinds of things. And I already know that I'm a survivor."

Mortality Outcomes

A total of 538 patients from the cohort had died: a mortality rate of 61.1 percent. As shown in Table 2a and b, there was a significant association between mortality and both cancer stage and view of self. Analyses of group differences indicated that participants with an improved view of self had a significantly lower death rate than those whose view of self was either unchanged or worse ($\chi^2 = 10.33$; $p = .001$). These latter groups had equivalent death rates (66 and 63 percent, respectively; see Table 2b). Further analyses therefore used a binary variable to distinguish between those with an improved view of self versus those with either an unchanged or worsened view of self.

We examined the bivariate relationships between other case characteristics and an improved view of self and mortality, using logistic regression (Table 3). Participants in the most advanced age group had a decreased likelihood of an improved view of self, while having at least a college degree and being employed were positively associated with an improved view of self. High levels of anxiety and moderate to high levels of depression were associated with a lower likelihood of having an improved view of self. Cancer stage was not significantly associated with an improved view of self.

With regard to mortality, being in the middle to older age group, being male, and having a more advanced stage of cancer were associated with death. Conversely, having a college degree, but not a professional degree, and being actively employed were associated with a lower likelihood of death. Having stage 3 or stage 4 cancer was positively associated with death, while an improved view of self was associated with decreased likelihood of death.

We next examined hierarchical multivariable logistic models that included basic demographic variables (age and gender as one block), cancer

Table 2:   (a) Mortality Rate in Cancer Patients by Stage of Disease. (b) Mortality Rate in Cancer Patients by Change in View of Self

	Deceased		Alive			
	N = 480	63%	N = 278	37%	χ^2 test	p-value
(a) Cancer Stage						
1	36	39	56	61	94.38	<.001
2	53	41	76	59	3 df	
3	90	57	67	43		
4	301	79	79	21		

	Deceased		Alive			
	N = 509	62%	N = 316	38%	χ^2 test	p-value
(b) View of self						
Improved	96	52	90	48	10.88	0.004
Unchanged	270	66	141	34	2 df	
Worse	143	63	85	37		

stage as the next step, and improved view of self as the final step (Table 4). Age and clinical stage were both significantly associated with mortality. An improved view of self contributed to the prediction of mortality (OR = .67, CI [.45–1.00], p = .051), even when the demographic control variables of age and gender and the cancer stage were included first as separate blocks in the model. It remained an independent predictor when all the variables were considered in the model (Δ LR χ^2 = 3.77, p = .052).

DISCUSSION

Our study examined the predictive value of a qualitatively derived variable on cancer mortality in a large patient cohort and showed that an improved view of self was associated with lower mortality. This finding was stable when tested in models including known prognostic variables, such as age or stage of disease. Our results suggest that having a positive outlook may be independently associated with cancer survival. Should this finding persist in future studies, the next challenge will be investigating how health services can positively influence the patient's view of self.

Our findings also illustrate the utility of the quasi-statistical (Miller and Crabtree 1992) analysis of qualitative data, highlighting several key points. First, the qualitative coding provided distinct categories with high intercoder

Table 3:   Bivariate Relationships of Predictors to Improved View of Self and Mortality

	View of Self			*Mortality*		
	OR	*SE*	*95% CI*	*OR*	*SE*	*95% CI*
Age						
Age ≥65	0.71	0.14	0.49–1.04	**1.63***	**0.27**	**1.17–2.25**
Age >50 and <65	**0.45***	**0.10**	**0.29–0.68**	**2.81***	**0.51**	**1.97–4.00**
Male	1.04	0.18	0.75–1.45	**1.33***	**0.19**	**1.01–1.76**
White	0.63	0.21	0.33–1.20	0.78	0.24	0.42–1.44
Education						
Some college	1.23	0.25	0.82–1.84	0.99	0.17	0.71–1.38
College	**1.72***	**0.41**	**1.08–2.75**	**0.58***	**0.12**	**0.39–0.86**
Professional	**1.75***	**0.47**	**1.03–2.97**	0.77	0.18	0.49–1.22
Working	**2.19***	**0.37**	**1.57–3.05**	**0.52***	**0.07**	**0.40–0.68**
Married	1.41	0.25	0.99–2.00	0.91	0.13	0.69–1.21
HADS anxiety						
2	0.79	0.19	0.50–1.25	0.73	0.14	0.51–1.06
3	**0.54***	**0.17**	**0.29–1.00**	0.76	0.17	0.49–1.18
HADS depression						
2	**0.34***	**0.12**	**0.17–0.69**	1.43	0.34	0.90–2.27
3	**0.34***	**0.15**	**0.14–0.82**	1.26	0.35	0.73–2.16
SIP physical category	0.91	0.06	0.80–1.03	1.09	0.06	0.98–1.21
SIP psychosocial category	0.92	0.06	0.81–1.05	0.99	0.05	0.89–1.10
SIP total	0.96	0.03	0.90–1.02	1.00	0.03	0.95–1.06
Cancer stage						
2	1.00	0.34	0.51–1.96	1.08	0.30	0.63–1.87
3	1.47	0.47	0.78–2.77	**2.09***	**0.56**	**1.24–3.53**
4	0.83	0.25	0.46–1.49	**5.93***	**1.47**	**3.64–9.64**
Improved view of self				**0.58***	**0.10**	**0.42–0.81**

Note. *$p < .05$.
Bold entries indicate significant entries.

reliability, and these codes were then used in statistical models along with other demographic, clinical, and survey-based variables. Second, we demonstrated that the qualitative categorical variable not only functioned as an independent predictor within the model but even outperformed commonly used measures of mood state (e.g., HAD and SIP Psychosocial) and physiological functioning (e.g., SIP Physical) in this study (Bergner et al. 1981; Zigmond and Snaith 1983; see Table 3). Third, a single categorical code based on a thematic analysis of the participants' assessment of the subjective impact of their disease provided relevant prognostic information above and beyond the impact of disease stage. Such subjective factors may thus be important tools that may be used clinically as predictors.

Table 4:   Hierarchical Logistic Regression: Relationship of Predictors to Death Outcomes in Patients with Cancer ($N = 709$)

	Demographic		With Clinical Predictors		With Improved View of the Self	
	OR	95% CI	OR	95% CI	OR	95% CI
Age						
>50 and <65	1.65*	1.14–2.39	1.64*	1.10–2.44	1.60*	1.07–2.39
≥65	2.44*	1.64–3.63	2.65*	1.73–4.07	2.51*	1.63–3.87
Male	1.49*	1.08–2.07	1.25	.88–1.78	1.25	.88–1.78
Cancer stage						
2			1.32	.74–2.36	1.31	.73–2.35
3			2.39*	1.36–4.21	2.47*	1.40–4.35
4			7.03*	4.16–11.90	7.00*	4.13–11.84
Improved view of self					.67**	.45–1.00
LR χ^2 (p-value)	26.19 (p < .001)		116.61 (p < .001)		120.38 (p < .001)	
Δ LR χ^2 (p-value)	–		90.42 (p < .001)		3.77 (p = .052)	

Note. *$p < .05$; **$p = .05$.

The strengths of qualitative and mixed methods research lies with its ability to provide in-depth insights into participants' viewpoints and their clinical decision-making patterns (Bradley et al. 2001; O'Cathain, Murphy, and Nicholl 2007; Newgard et al. 2012; Zier et al. 2012). These methods focus on clarifying important contextual factors that can help describe and define situations (Pope, Ziebland, and Mays 2000; Creswell 2007). In most traditional studies, insights gained through the detailed, iterative capturing of participants' expression are important and sufficient as a qualitative approach to the data. We sought to explore whether under certain circumstances the application of the quasi-statistical approach could provide further insights to questions that may involve a probability estimate.

In our study, we prospectively addressed a question involving a critical disease outcome with special health services' implications and employed the qualitative code as a potential predictor, using a long follow-up time to measure mortality. The results may serve as a proof of concept, showing the potential of a quasi-statistical approach to enrich the applications of mixed methods research in particular studies and to encourage researchers conducting prospective, longitudinal research to consider the predictive value of qualitatively derived categories. The application of the quasi-statistical approach also suggests that under the right conditions, qualitative methods can be effectively used to examine empirically based research questions that usually require a statistical answer.

Beyond showing that qualitatively derived categories can indeed provide important and possibly unique insights into clinically relevant questions, our findings also demonstrate that study design is critical for the success of the quasi-statistical approach. We used a complex dataset with qualitative, demographic, and clinical variables obtained concurrently and from the same subjects. The convergent or concurrent design (Creswell and Plano Clark 2006; Fetters, Curry, and Creswell 2013) enabled us to integrate qualitative and quantitative variables analytically into a single model.

In addition, testing the association with a health outcome required a sample size much larger than the numbers usually required by thematic saturation (Sandelowski 1995; Guest and Johnson 2006). Indeed, the coding scheme that emerged could have reached saturation in less than 20 patients, which would have made it impossible to examine the predictive value of these categories. The statistical analysis of qualitative data will require study designs that have sufficient power to examine defined endpoints of interest, taking into account likely rates of these outcomes in the targeted study population (Zickmund et al. 2004).

In addition to suggesting methodological innovations in data collection and analysis, the quasi-statistical approach can effectively highlight the multifaceted role that qualitative research can play within the health care system. When integrated appropriately, qualitative data may provide a source of information that can be used to stratify cohorts to assess risks, predict outcomes, or address other potentially relevant endpoints. The quasi-statistical methodology may encourage researchers to investigate subjective experience using qualitative methods in novel ways, such as the approach used here or in other promising avenues involving open-response speech samples (Yang, Mulvey, and Falissard 2012). By combining the more open approach of qualitative data acquisition, we provide an opportunity for patient voices to affect results outside of predefined variables that typically constitute standardized questionnaires or other routinely administered instruments. Viewed more generically, variables derived from patient perspectives might point toward new and salient factors that could effectively modify health, treatment choices, treatment adherence, and ultimately treatment outcomes.

The present study provides important support for the utility of a quasi-statistical mixed methods approach. Based on our iterative coding of patients' answers to our key question, we focused on a series of codes describing the view of self. However, this choice, by definition, reduced the complexity of themes to a few major categories, thereby reducing the richness of the information, a major emphasis of interpretative analyses in qualitative research.

Another limitation involved the extensive transcription and coding burden that came from reviewing the qualitative material from such a large cohort. This must be acknowledged as an inherent challenge in our approach. Having a large sample of patient interviews linked to survey and mortality data afforded us the opportunity to explore the insights derived from a qualitative predictive variable, but only after the investment of considerable energy and resources. However, our results are not meant to indicate that all qualitative studies should seek to use this approach. Also, it is not clear whether similar results could have been gained from conducting fewer interviews and then creating a survey item. It is uncertain whether such an item could capture the narrative patterns we coded or whether it requires participants to have a chance to talk through their feelings in an open-response format. A future study including both closed, and open-ended responses might clarify how transferable information on a complex topic like view of self might be. Finally, our study sample did not include sufficient racial and ethnic minorities to allow for us to generalize beyond the more homogenous population included in this study.

In conclusion, our study provides an example of quasi-statistical mixed methods analysis with a robust, qualitatively derived variable associated with mortality and with health services ramifications in a large sample of cancer patients. Prospective studies in the future should be able to build upon and extend these findings so that more can be learned about the strengths and limitations of this analytic approach and how such results can be used to improve the experience of patients in the health care system.

ACKNOWLEDGMENTS

unconstrained. All remaining authors have no conflicts of interest (i.e., financial and personal relationships between themselves and others that might bias their work).

Disclaimer: The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States Government.

Disclosures: None.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article:

Appendix SA1: Author Matrix.