The stability of treatment preferences among patients with advanced cancer

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ABSTRACT

Context

Stability of patients' treatment preferences has important implications for decisions about concurrent and future treatment.

Objectives

To examine the stability of treatment preferences and correlates among patients with advanced cancer.

Methods

In this cohort, 104 patients with metastatic cancer, progression after at least one chemotherapy regimen, and an oncologist-estimated life expectancy of six or fewer months participated in structured interviews after clinical visits in which patients' recent scan results were discussed. Interviews were repeated in three monthly follow-ups. At baseline, patients' age, education, sex, race, marital status, insurance status, and type of cancer were documented. At each assessment, patients reported their treatment preferences (i.e., prioritizing life-prolonging vs. comfort), quality of life, and current health status.

Results

At baseline (n = 104), 55 (53%) patients preferred life-prolonging care and 49 (47%) preferred comfort care. Patients were followed up for one (n = 104), two (n = 74), or three months (n = 44). Between baseline and Month 1, 84 patients (81%) had stable preferences. During follow-up, preferences of 71 patients (68%) remained stable (equally divided between a consistent preference for life-prolonging and comfort care). Treatment preferences of 33 (32%) patients changed at least once during follow-up. Direction of change was inconsistent. Patients' preferences at baseline strongly predicted preferences at Month 1 (odds ratio = 17.8; confidence interval = 6.7 – 47.3; P <.001). Description of the current health status at baseline was the only variable significantly associated with stability of preferences at Month 1.

Conclusion

Two-thirds of patients with advanced cancer had stable preferences. Changes of preferences were often inconsistent and unpredictable. Our findings suggest potential benefits of ongoing communication about preferences.

INTRODUCTION

Patients with cancer typically experience diverse symptoms and profound functional decline as their illness reaches an advanced stage.[1] Because there are often options to improve quality of life or survival,[2] patients confront decisions on the medical management of their illness.[1,3] Patients' preferences for potential interventions may vary. Timely discussions can support patients in identifying their options and prepare them for the actual decision-making.[2] Such discussions can increase the likelihood that the care is consistent with patients' (informed) preferences–a principle embedded in the patient's right to self-determination of treatment (e.g., the patient Self-Determination Act in the U.S.).[4] In practice, however, these discussions tend to occur not at all or late in the course of illness,[2] which involves the risk that patients have lost their capacity to engage in these discussions meaningfully.[3,5,6]

The American Society of Clinical Oncology acknowledges the complex nature of the discussions about patients' needs, goals and preferences.[2,7] Clinicians are in the difficult position of having to balance the fear and disappointment patients typically feel when they become aware of the progression of their illness, against an ethical duty to impart realistic information. Imparting this information is tied to fostering autonomy about the patient's prognosis and expected outcomes of treatment so that patients can make informed decisions about their treatment preferences.[8,9] Identifying the right moment in the disease trajectory to engage in these discussions is challenging.[7] One part of this challenge is tied to the stability of preferences. Clinicians must use their best judgment to decide how often preferences should be discussed to inform decision-making. They also have to determine if these preferences can be assumed to remain essentially stable and, therefore, serve as a reliable predictor for preferences in the future.

To date, evidence about the stability of general treatment preferences has been primarily based on studies outside of oncology and through the use of hypothetical scenarios.[10] In a recent review, Auriemma et al. found that treatment preferences are fairly stable among patients with illnesses other than cancer, and among students and physicians.[10] Stability of preferences was associated with the presence of an advance directive, higher level of educational attainment, and very mild and very severe health conditions. The published evidence on the association between changes in health status and stability is equivocal. Some patient groups were shown to have stable treatment preferences, despite a decline in daily activities or physical functioning. Other patient groups adjusted their preferences after a change in health status, either in favor of life-prolonging treatment or comfort care. Mixed results on stability were also found among racial/ethnic minority groups of patients.[10] A pilot study with healthy individuals on the stability of specific treatment wishes (among which cardiopulmonary resuscitation or kidney dialysis) showed a mixed pattern, with a stronger stability for cardiopulmonary resuscitation (CPR) preferences and lower stability for preferences for kidney dialysis.[11]

We identified one study explicitly investigating the stability of treatment preferences of patients with cancer.[12] The patients in this study had a life expectancy of less than two years and reported their attitudes concerning treatment on inclusion in the study, and after six and 12 months of follow-up. Overall, patients were found to have stable treatment preferences, except for patients with a recent diagnosis of cancer.[12] The extent to which they preferred treatment aimed at prolonging life decreased after six months.[12]

We aimed to extend previous findings about the stability of treatment preferences to patients with advanced cancer who are estimated to have a life expectancy of six or fewer months, a period in which patients typically experience profound functional decline.[1,3] Furthermore, we aimed to observe the stability of treatment preferences in patients actually at the end of life confronting decisions, as opposed to evaluating hypothetical scenarios.

METHODS

Sample

The Coping with Cancer-2 (CwC-2) study is a National Cancer Institute-funded, prospective, multi-institutional cohort study of patients with advanced cancer, their caregivers, and their oncology providers. It was designed to evaluate end of life communication processes and end of life care. Patients were recruited to this study to determine how clinical communication related to their coping with a serious illness. Patients were recruited from nine cancer centers across the U.S.: Dana-Farber/Harvard Cancer Center (DF/HC; Dana-Farber Cancer Institute, Brigham and Women's Hospital, and Massachusetts General Hospital, Boston, MA), Parkland Hospital (Dallas, TX), Simmons Comprehensive Cancer Center (Dallas, TX), Yale Cancer Center (New Haven, CT), Meyer Cancer Center at Weill Cornell Medical College (New York, NY), Memorial Sloan Kettering Cancer Center (New York, NY), Virginia Commonwealth University Massey Cancer Center (Richmond, VA), University of New Mexico Cancer Center (Albuquerque, NM), and Pomona Valley Hospital Medical Center (Pomona, CA). Review boards of all participating cancer centers approved the study procedures and all participating patients provided written informed consent. Patients received $25 gift cards for every post–clinical visit assessment that they completed.

Patients had to meet the following inclusion criteria: stage IV gastrointestinal, lung, or gynecologic cancer and select incurable and poor-prognosis stage III cancers (e.g., pancreas and lung); oncologist-estimated life expectancy of six or fewer months; and illness progression after at least one chemotherapy regimen or, in case of colorectal cancer, progression after at least two chemotherapy regimens. All patients were screened using the Pfeiffer Short Portable Mental Status Examine scores to determine severe cognitive impairment. Patients with severe cognitive impairments were excluded, as well as patients who appeared too weak or too ill. Children and young adults up to age 20 were ineligible.

Patients completed structured clinical baseline interviews with mostly close-ended responses after a clinical visit with their oncology provider in which their most recent scan results and treatment plans were discussed. During the baseline interviews, patients reported their treatment preferences (i.e. trade-offs of life-prolonging care vs. comfort care). The interviews occurred either in clinic (31%) or over the telephone (69%), whichever the patient preferred, between November 2010 and April 2015. Patients completed additional monthly follow-up interviews in the clinic. The follow-up interviews included questions about treatment preferences, quality of life, and their description of their current health status. For the present analysis, we selected patients from the CwC-2 cohort who completed baseline and one up to three consecutive monthly follow-up interviews (N = 104, see Figure 1 for a CONSORT flow diagram of the study).

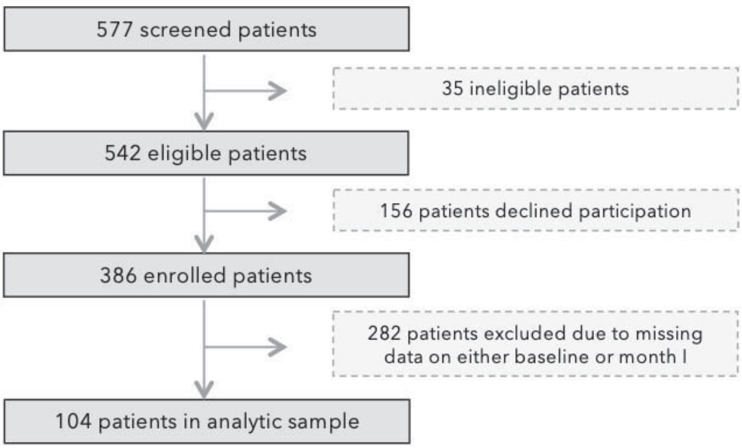


Figure 1. Flow diagram of patients.

Measures

Treatment preferences

Patients' treatment preferences were assessed with the question *"If you could choose, would you prefer A) a course of treatment that focused on extending life as much as possible, even if it meant more pain and discomfort, or B) (on) a plan of care that focused on relieving pain and discomfort as much as possible, even if that meant not living as long?"* Response options were (1) *extend life as much as possible* (classified as having a preference for life-prolonging care) or (2) *relieve pain or discomfort as much as possible* (classified as having a preference for comfort care). This question has been used in several studies of patients with terminal illnesses, including the SUPPORT trial.[13] It has been found to be associated with the number of therapeutic interventions received.[13]

We defined treatment preferences as stable when patients did not change their expressed preference throughout the follow-up period and/or until drop-out. We defined treatment preferences as unstable when patients changed their expressed treatment preference at least once during follow-up.

Predictors of the stability of treatment preferences

Patient characteristics

Patients provided information regarding their age and education (in years), sex, marital status (married or not married), and insurance status (insured or not insured). Patients also provided information on the race they consider themselves to be (white, Afro-American, or other). For the analysis, we recoded the answers into white or other.

Clinical characteristics included the type of cancer and whether patients were currently getting chemotherapy or radiation for their cancer. We summarized the answers on type of cancer into three categories: 1) lung cancer, 2) gastrointestinal cancer (also including bladder and gallbladder cancer), and 3) other cancer.

Quality of life

Patients' quality of life was assessed with the self-report McGill Quality of Life Questionnaire.[14] The questionnaire was designed for assessing quality of life of patients with life-threatening illnesses and has been validated in that setting.[14] The total quality-of-life score was calculated by taking the mean of the 15 self-report items of the questionnaire. Following guidelines, those who did not respond to four or more items were not included in the study as their scale was considered incomplete.[15] Higher scores indicate better self-reported levels of quality of life.

Description of the current health status

The patients' description of their current health status was assessed by asking *"How would you describe your current health status?"* Response options were 1) *relatively healthy,* 2) *relatively healthy and terminally ill,* 3) *relatively ill but not terminally ill,* 4) *seriously ill and terminally ill,* and 5) *do not know.* The responses 1) and 3) were re-coded into 1) *Does not understand that illness is terminal.* Responses 2) and 4) were re-coded into 2) *Understands that illness is terminal.* For this study we considered the response 5) *do not know* a missing response.

Statistical analyses

All statistical analyses were performed using SPSS, version 24 (Statistical Package for Social Sciences, Chicago, IL). *P*-values of <0.05 were considered statistically significant.

Descriptive statistics were used for analyzing patient demographics and baseline characteristics. Means and standard deviation (SD) were used for continuous variables, and frequencies and percentages for binary and categorical variables. Cross-tabulation and frequency counts were used to describe the sample and treatment preferences.

We used univariate logistic regression to calculate odds ratios (ORs) for the association between baseline treatment preferences and treatment preferences at Month 1. Given the restricted sample size at Months 2 and 3, the analysis focused on this particular study interval.

Subsequently, we created a variable on the stability of treatment preferences (stable preferences vs. unstable preferences) between baseline and Month 1 and used this variable in logistic regressions to estimate the association between the following predictors–treatment preferences, patient characteristics, quality of life, and description of the current health status, all at baseline–and stability of treatment preferences at Month 1. Owing to restrictions in sample size, multivariable analyses were not used.

RESULTS

Sample characteristics

The sample consisted of 104 patients who completed the baseline assessment and the assessment after one month of follow-up. Of these patients, 74 completed the questionnaire at Month 2, and 44 completed the questionnaire at Month 3 (see Supplementary Figure 1 for an overview of study participation). In New England, 73 patients were included, eight patients were included in Mid-Atlantic/South, and 23 patients in Southwest/West.

Most patients were female (70%), white (86%), and covered by health insurance (79%). Their average age was 61.3 years (SD 8.7 years). Most patients (89%) currently received chemotherapy or radiation for their cancer. Half of the patients described their current health status as "relatively healthy" or "seriously ill, but not terminally ill", and half of the patients described their current health status as "relatively healthy and terminally ill" or "seriously ill and terminally ill". At baseline, 55 patients (53%) preferred a course of treatment that focused as much as possible on prolonging life, whereas 49 patients (47%) preferred care that focused as much as possible on relieving pain and discomfort.

The patient characteristics are listed in Table 1, separately for patients with stable and unstable treatment preferences.

Stability of treatment preferences

In total, 71 patients (68%) had no observed changes in treatment preferences during the entire follow-up period (Month 1, Month 2, and Month 3). This stability of treatment preferences was equally divided between patients preferring life-prolonging care (35%) and patients preferring comfort care (34%, Table 2).

The remaining 33 patients (32%) changed their treatment preference over time. These patients either changed once or went back and forth between preferences (Figure 2a and 2b). Changes in treatment preferences were seen in patients who initially expressed preferences for life-prolonging care, as well as in patients who initially expressed preferences for comfort care. For instance, two patients who expressed their preference for life-prolonging care at baseline, Month 1, and Month 2, changed their preference towards comfort care at Month 3. Another patient indicated a preference for comfort care at baseline, subsequently changed the preference toward life-prolonging care at

Month 1, returned to a preference for comfort care at Month 2, whereas settled with a preference for life-prolonging care at Month 3.

Table 1. Patient characteristics and preferences at baseline (N = 104)

	Stable preferences after Month I (n = 84)	Unstable preferences after Month 1 (n = 20)
Characteristics	mean (SD)	mean (SD)
Age in years	61.4 (8.2)	60.9 (10.7)
Education in years	14.8 (3.3)	14.9 (3.3)
Quality of life[1]	7.6 (1.6)	7.1 (1.7)
	n (%)	n (%)
Sex		
Male	27 (87.1)	4 (12.9)
Female	56 (77.8)	16 (22.2)
Race		
Other	13 (92.9)	1 (7.1)
White	70 (78.7)	19 (21.3)
Marital status		
Not married	31 (81.6)	7 (18.4)
Married	50 (82.0)	11 (18.0)
Insurance status		
Uninsured	19 (86.4)	3 (13.6)
Insured	64 (79.0)	17 (21.0)
Type of cancer		
Gastrointestinal cancer	39 (88.6)	5 (11.4)
Other cancer	32 (74.4)	11 (25.6)
Lung cancer	39 (88.6)	5 (11.4)
Currently receiving chemotherapy or radiation		
No	10 (90.9)	1 (9.1)
Yes	73 (80.2)	18 (19.8)
Description of the current health status		
Not terminally ill	34 (70.8)	14 (29.2)
Terminally ill nature	42 (87.5)	6 (12.5)
Treatment preference at baseline		
Life-prolonging care	44 (83.0)	9 (17.0)
Comfort care	40 (78.4)	11 (21.6)

[1] McGill Quality of Life Questionnaire (range 0-10), higher scores indicate better self-reported levels of quality of life.

Table 2. Stability of treatment preferences during follow-up (n=104)

	n (%)
Stable preference for life-prolonging care	36 (34.6)
Stable preference for comfort care	35 (33.7)
Unstable preferences	33 (31.7)

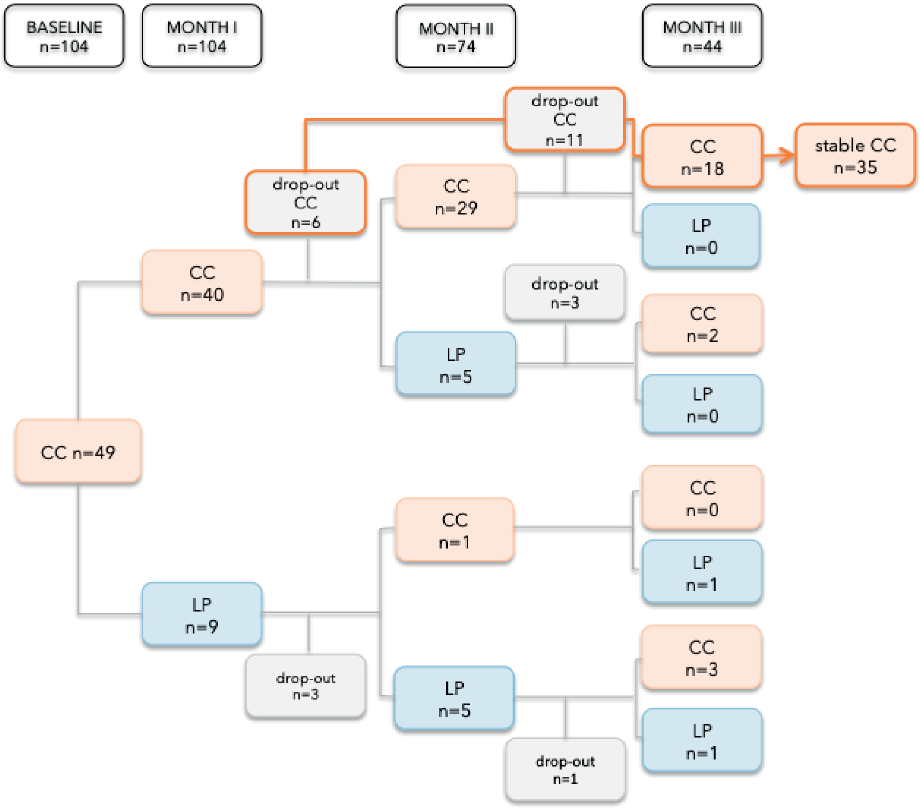


Figure 2a. Preferences over time, beginning with comfort care.
Abbreviations: CC=preference for comfort care; LP=preference for life-prolonging care; drop-out CC=stable preferences for comfort care until drop-out

Predictors of the stability of treatment preferences after one month of follow-up

Between baseline and Month 1, 84 patients (81%) had stable treatment preferences. Of 20 patients (19%) who changed their preference in this period, nine changed toward life-prolonging care (9%) and 1 changed toward comfort care (11%).

Patients' treatment preferences at baseline strongly predicted treatment preferences at Month 1 (OR = 17.8; CI = 6.7-47.3; *P* < .001).

Patients' sociodemographic and clinical characteristics, quality of life, and treatment preferences at baseline were not associated with stability of treatment preferences at Month 1 (Table 3). The association between the description of the current health status and stability of treatment preferences was significant (OR = 2.88; CI = 1.001-8.302; *P* = .05). Not describing the current health status as terminal was associated with unstable treatment preferences.

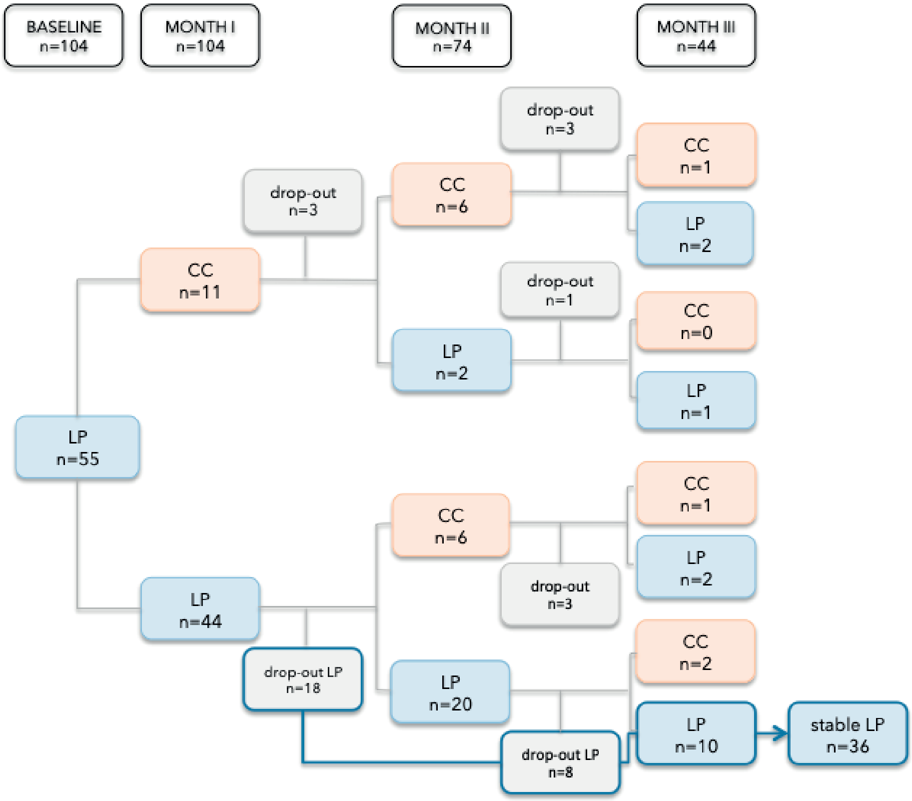


Figure 2b. Preferences over time, beginning with life-prolonging care.
Abbreviations: CC=preference for comfort care; LP=preference for life-prolonging care; drop-out LP=stable preferences for life-prolonging care until drop-out

DISCUSSION

We examined the stability of treatment preferences and predictors of stability in a cohort of patients with advanced cancer and an estimated life expectancy of six or fewer months. Most patients had stable treatment preferences during one to three months of follow-up. No patient characteristics, nor quality of life, predicted the stability of treatment preferences, except from the description of the current health status.

After discussing the most recent scan results during a clinical visit, 53% of patients preferred a course of treatment that focused as much as possible on prolonging life. The remaining 47% of patients preferred comfort care. Interestingly, previous studies found considerably lower rates (28% and 38%) of patients with advanced cancer wanting life-prolonging care.[12,16] The same applies to a study on attitudes of the Dutch general public towards the hypothetical scenario of becoming

Table 3. Predictors of stability of treatment preferences after one month of follow-up (n=104).

	Univariate OR	95% CI	*P*-value
Age (per year)	0.99	0.94-1.05	0.810
Education (per year)	1.01	0.87-1.18	0.887
Quality of life	0.82	0.57-1.16	0.263
Sex			
Male	0.52	0.16-1.70	0.279
Female	Ref		
Race			
Other	0.28	0.04-2.31	0.238
White	Ref		
Marital status			
Not married	1.03	0.36-2.93	0.961
Married	Ref		
Insurance status			
Uninsured	0.59	0.16-2.25	0.443
Insured	Ref		
Type of cancer			
Gastrointestinal cancer	0.37	0.12-1.19	0.373
Other cancer	0.90	0.24-3.33	0.869
Lung cancer	Ref		
Currently receiving chemotherapy or radiation			
No	0.41	0.05-3.38	0.404
Yes	Ref		
Description of the current health status			
Not terminally ill	2.88	1.00-8.30	0.050
Terminal ill	Ref		
Treatment preference at baseline			
Life-prolonging care	1.11	0.42-2.96	0.833
Comfort care	Ref		

Note:
OR: odds ratio, 95% CI: 95% confidence interval

seriously ill, which found 30% of people striving for life-prolonging care.[17] A potential explanation for the high proportion of patients in our study preferring life-prolonging care might be provided by Weeks et al.[13] They found that patients with metastatic cancer tend to overestimate their survival probabilities, which affected their treatment preferences.[13] Patients who thought that they would survive for at least six months were more prone to prefer life-prolonging care than patients who thought that they would survive less than six months.[13] Although the patients in our study had, according to their oncologist, an estimated life expectancy of six or fewer months, 50% of them did not describe their current health status as terminal, which might explain the large percentage of patients favoring life-prolonging treatment. In addition, the vast majority of patients in our study received chemotherapy or radiation at baseline. This might have led them to believe that they had longer survival than was the case, which would further make them want to remain on anti-cancer treatment. Throughout the follow-up period, which varied from one to three months, most patients (68%) had stable treatment preferences. This high proportion of patients with stable preferences is in accordance with a recent review on treatment preference stability in a variety of noncancer patient populations[10] and a study among Dutch patients with cancer who had a life-expectancy of less than two years.[12] Our study extends these findings towards a population of patients with advanced cancer and a life expectancy of six or fewer months, who de facto went through the process of having to make decisions on how to proceed.

Although most patients had stable preferences, one-third changed their preference at least once during follow-up. Some patients who initially repeatedly indicated a preference for comfort care subsequently changed toward life-prolonging care, whereas other patients changed their preference every month. Stability of treatment preferences was neither predicted by patient or clinical characteristics nor by quality of life. The OR for the description of the current health status was significant. The understanding of one's health status may thus play a role in the formation of preferences and patients who do not describe their health status as terminal might be more prone to change their treatment preferences. Besides, patients receiving chemotherapy are less likely to understand that they are terminal. Anticancer treatment may thus fuel a preference for more treatment. Overall, our findings extend and confirm the review by Auriemma et al., who found that the direction of changes in treatment preferences mostly seems inconsistent.[10] Although we did not detect such a difference, it is worth highlighting that patients may hold negative stereotypes towards palliative care/comfort care because these stereotypes (such as "giving up" or being "quitters") have been found in patients with cancer.[18,19] Taking the decision to stop life-prolonging care in favor of comfort care might be more challenging for patients to make. Health care professionals should be aware of this possible imbalance of treatment preferences during the decision-making process.

Our results highlight the need to view discussions of treatment preferences as a dynamic process. Despite guidelines highlighting the discussion of treatment preferences as an important component of high-quality patient care,[2] many physicians postpone these discussions with their patients with cancer who are incurably ill, but still free of symptoms.[20] It has been suggested that clinicians are uncertain as to how early and frequently they should discuss treatment preferences.[10] Our findings should encourage clinicians to engage in these conversations repeatedly because a considerable number of patients showed contradictory and fluctuating preferences as a part of their decision-making process. Clinicians therefore should be aware that preferences may change and that reevaluation of previously expressed treatment preferences during subsequent medical encounters is essential. This was also suggested in a recently published white paper on advance care planning, an increasingly used method that has been found to improve concordance between the care patients receive and the care they desire.[21,22] These repeated discussions may also help to overcome uncertainty with respect to the reliability of preferences of patients who have become incompetent. Because in that situation physicians cannot check the patient's actual preferences, they need to rely on the previously expressed ones. This will be easier to do when the physicians (and the family) have become convinced of the stability of the wishes, expressed at different moments by the then-competent patient. Following the recommendations of Rietjens et al.,[22] we would like to emphasize that advance care planning discussions should go beyond discussing treatment preferences alone and should be held in the context of assessing patients' illness understanding and discussing medical information, such as the diagnosis and prognosis. This is particularly important given the fact that half of the patients in our study did not describe their current health status as terminal and that low numbers of accurate illness understanding have been established elsewhere too.[23]

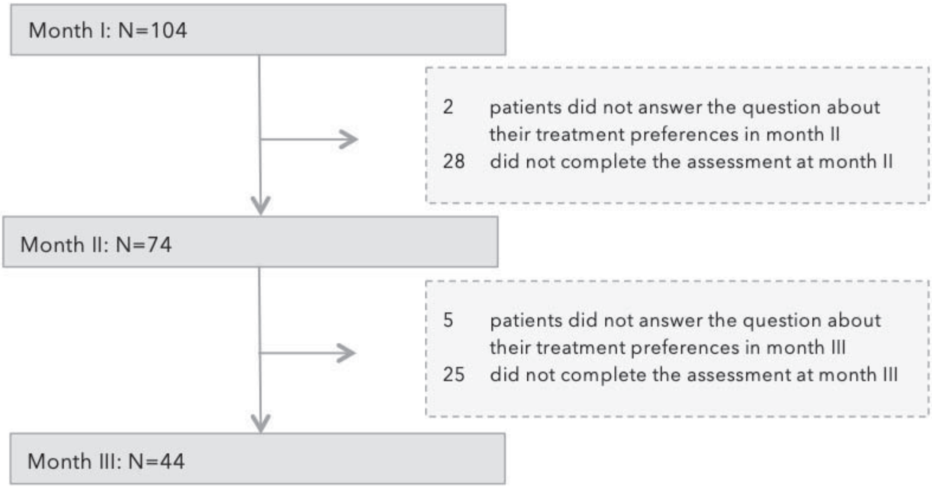
Our study is limited by the relatively small sample size and attrition of the sample during follow-up. Due to the restricted sample size at Months 2 and 3, we were only able to analyze the association between baseline treatment preferences and preferences at Month 1. Likewise, in-depth analyses on, for example, the impact of the description of the current health status on the change of treatment preferences could not be conducted because of a limited sample size and corresponding statistical power for multivariable analyses. Besides, we were unable to ascertain whether patients who dropped out thereafter had a change in treatment preferences. Because recruitment took place in academic hospitals, the patients were in treatment settings typically focused on aggressive cancer treatment.[24] Therefore, findings need to be confirmed in nonacademic oncology settings. The high attrition rate might have created a bias such that those with more stable illness were retained and those with more quickly advancing cancer dropped out. Based on findings of previous studies, in which stable disease was associated with stable preferences, this might have led to a possible overestimation of stability in our study. The preference question we used (i.e., care primarily aimed at life-prolongation vs. care primarily aimed at comfort) is a simplistic dichotomy of care options for patients near the end of life. We recommend more nuanced measures in future research, such as those used by Schubart et al.[11]

With these limitations in mind, our study provides evidence for the stability of treatment preferences of most patients with advanced cancer regarding life-prolonging versus comfort care in the last months of life. Our results suggest that early discussions about treatment preferences may be useful predictors for the type of treatment patients prefer when death approaches. It is however essential for clinicians to keep in mind that patients may change their treatment preferences and that continuous discussions about these preferences are crucial for the alignment of patients' preferences with the actual treatment.

REFERENCES

1. McCarthy EP, Phillips RS, Zhong Z, et al. Dying with Cancer: Patients' Function, Symptoms, and Care Preferences as Death Approaches. *J Am Geriatr Soc* 2000;48.
2. Peppercorn JM, Smith TJ, Helft PR, et al: American society of clinical oncology statement: toward individualized care for patients with advanced cancer. *J Clin Oncol* 2011;29:755-760.
3. Gao X, Prigerson HG, Diamond EL, et al: Minor cognitive impairments in cancer patients magnify the effect of caregiver preferences on end-of-life care. *J Pain Symptom Manage* 2013;45:650-659.
4. Omnibus Budget Reconciliation Act of 1990, Pub. Law No. 101-508, 1990.
5. Triebel KL, Martin RC, Nabors LB, et al: Medical decision-making capacity in patietns with malignant glioma. *Neurology* 2009;73;2086-2092.
6. Silveira MJ, Kim SYH, Langa KM. Advance Directives and Outcomes of Surrogate Decision Making before Death. *N Engl J Med* 2010; 362:1211-1218
7. Gilligan T, Coyle N, Frankel RM, et al: Patient-Clinician Communication: American Society of Clinical Oncology Consensus Guideline. *JCO* 2017;35.
8. Mack JW, Weeks JC, Wright AA, et al: End-of-life discussions, goal attainment, and distress at the end of life: predictors and outcomes of receipt of care consistent with preferences. *J Clin Oncol* 2010;28;1203-1208.
9. Street RL, Jr., Makoul G, Arora NK, et al: How does communication heal? Pathways linking clinician-patient communication to health outcomes. *Patient Educ Couns* 2009;74:295-301.
10. Auriemma CL, Nguyen CA, Bronheim R, et al: Stability of end-of-life preferences: a systematic review of the evidence. *JAMA Intern Med* 2014;174:1085-1092.
11. Schubart JR, Levi BH, Camacho F, et al: Reliability of an interactive computer program for advance care planning. *J Palliat Med* 2012;15:637-642.
12. Voogt E, van der Heide A, Rietjens JA, et al: Attitudes of patients with incurable cancer toward medical treatment in the last phase of life. *J Clin Oncol* 23:2012-9, 2005
13. Weeks JC, Cook EF, O'Day SJ, et al. Relationship between cancer patients' predictions of prognosis and their treatment preferences. *JAMA* 279:1709-1714, 1998;279:1709-1714.
14. Cohen SR MB, Strobel MG, et al: The McGill Quality of Life Questionnaire: a measure of quatliy of life appropriate for people with advanced disease. A preliminary study of validity and acceptability. *Palliat Med* 1995;9:207-219.
15. Cohen SR, Mount BM: Living with cancer: "good" days and "bad" days--what produces them? Can the McGill quality of life questionnaire distinguish between them? *Cancer* 2000;89:1854-1865.
16. Wright AA, Mack JW, Kritek PA, et al: Influence of patients' preferences and treatment site on cancer patients' end-of-life care. *Cancer* 2010;116:4656-4663.
17. Rietjens JA, van der Heide A, Voogt E, et al: Striving for quality or length at the end-of-life: attitudes of the Dutch general public. *Patient Educ Couns* 2005;59:158-163.
18. Shen MJ, Wellman JD: Evidence of palliative care stigma: The role of negative stereotypes in preventing willingness to use palliative care. *Palliat Support Care*2018:1-7.
19. Zimmermann C, Swami N, Krzyzanowska M, et al: Perceptions of palliative care among patients with advanced cancer and their caregivers. *CMAJ* 2016;188:E217-E227.
20. Keating NL, Landrum MB, Rogers SO, Jr., et al: Physician factors associated with discussions about end-of-life care. *Cancer* 2010;116:998-1006.
21. Brinkman-Stoppelenburg A, Rietjens JA, van der Heide A: The effects of advance care planning on end-of-life care: a systematic review. *Palliat Med* 2014;28:1000-1025.
22. Rietjens JAC, Sudore RL, Connolly M, et al: Definition and recommendations for advance care planning: an international consensus supported by the European Association for Palliative Care. *Lancet Oncol* 2017;18:e543-e551.
23. Epstein AS, Prigerson HG, O'Reilly EM, et al: Discussions of Life Expectancy and Changes in Illness Understanding in Patients With Advanced Cancer. *J Clin Oncol* 2016;34:2398-2403.
24. Earle CC, Landrum MB, Souza JM, et al: Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? *J Clin Oncol* 2008;26:3860-3866.

SUPPLEMENTARY MATERIAL



Supplementary Figure 1. Flow diagram of patients who completed the questions on treatment preferences throughout the follow-up period.