Evaluation of pedometry as a patient-centered outcome in patients undergoing hematopoietic cell transplant (HCT): a comparison of pedometry and patient reports of symptoms, health, and quality of life

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Abstract

Aims We evaluated pedometry as a novel patient-centered outcome because it enables passive continuous assessment of activity and may provide information about the consequences of symptomatic toxicity complementary to self-report.

Methods Adult patients undergoing hematopoietic cell transplant (HCT) wore pedometers and completed PRO assessments during transplant hospitalization (4 weeks) and 4 weeks post-discharge. Patient reports of symptomatic treatment toxicities (single items from PRO-CTCAE, http://healthcaredelivery.cancer.gov/pro-ctcae) and symptoms, physical health, mental health, and quality of life (PROMIS® Global-10, http://nih.promis.org), assessed weekly with 7-day recall on Likert scales, were compared individually with pedometry data, summarized as average daily steps per week, using linear mixed models.

Results Thirty-two patients [mean age 55 (SD = 14), 63 % male, 84 % white, 56 % autologous, 43 % allogeneic] completed a mean 4.6 (SD = 1.5, range 1–8) evaluable assessments. Regression model coefficients (β) indicated within-person decrements in average daily steps were associated with increases in pain ($\beta = -852$; 852 fewer steps per unit increase in pain score, $p < 0.001$), fatigue ($\beta = -886$, $p < 0.001$), vomiting ($\beta = -518$, $p < 0.01$), shaking/chills ($\beta = -587$, $p < 0.01$), diarrhea ($\beta = -719$, $p < 0.001$), shortness of breath ($\beta = -1018$, $p < 0.05$), reduction in carrying out social activities ($\beta = 705$, $p < 0.01$) or physical activities ($\beta = 618$, $p < 0.01$), and global physical health ($\beta = 101$, $p < 0.001$), but not global mental health or quality of life.

Conclusions In this small sample of HCT recipients, more severe symptoms, impaired physical health, and restrictions in the performance of usual daily activities were associated with statistically significant decrements in objectively measured daily steps. Pedometry may be a valuable outcome measure and validation anchor in clinical research.

Keywords PRO-CTCAE · PROMIS Global-10 · Fitbit · Pedometry · Hematopoietic cell transplant · Oncology · Validation

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Introduction

Wearable devices that monitor daily steps are increasingly popular and of great interest in clinical research for assessing activity level, deconditioning, and symptom burden. This is particularly salient to populations with advanced disease or receiving toxic regimens. In this paper, we compare self-reported symptoms and function with

pedometry data from patients undergoing hematopoietic cell transplant (HCT) to explore the informational value of pedometry for better understanding the impact of disease and treatment on patients.

Although patient-reported outcome (PRO) measures are the standard approach for assessing symptoms, functional status, and quality of life [1–4], PRO assessment is not feasible for some patient populations, such as those with impaired cognitive function, limited literacy or fluency, lack of home Internet access, and those who are too ill or burdened to complete surveys [5]. Among patients who are able to complete PRO surveys, missing data are a common and critical issue. When patients are too sick to complete surveys, the validity of the PRO assessment is greatly reduced by the occurrence of missing data particularly because it is missing not at random (MNAR) [6]. Although observer-reported outcome measures have been designed to assess outcomes of patients who are unable to self-report, they are limited in scope to observable phenomenon, such as vomiting, cough, and difficulty with activities of daily living. Further, they are biased by the observers' own health and perspectives, and require additional effort from the caregiver [7, 8].

Wearable pedometers provide data that are not dependent on a patient's cognition, literacy, language, or health status and provide an objective measure of physical activity which may be complementary to self-reports. Further, the new-generation pedometry devices are low cost and comfortable enough to wear long term. Pedometry data captured and reported through newly existing platforms can potentially support the long-term, continuous, and real-time monitoring of patient function and well-being. This will create new opportunities to predict and understand treatment tolerance in physiologically vulnerable populations, to understand the impact of treatment on patient outcomes, and to explore reasons for treatment non-adherence or discontinuation [9]. Longitudinal pedometry data may also have value for tracking sarcopenia (wasting syndrome) and declines in functional capacity, which are predictive of survival in advanced cancer [10, 11].

A review of several small pilot studies of physical activity monitoring in patients with cancer found physical activity, specifically the number of daily steps, varied considerably based on treatment type and phase in the cancer continuum, comparing healthy controls, surgical resection with curative intent, and palliative chemotherapy or radiation [12].

The objective of this study was to identify the cross-sectional and longitudinal relationships between objectively measured daily steps and patient reports of symptoms and functioning in a well-defined and relatively homogenous patient population, in this case adult patients undergoing autologous or allogeneic HCT.

This research is a secondary analysis of data from a trial designed to evaluate the efficacy of a pre-transplant, interval exercise training (IET) intervention on the cardiorespiratory performance and functional outcomes of patients undergoing HCT. HCT is an intensive, high-risk procedure which patients receive for its curative or anti-tumor efficacy in the treatment for leukemia, lymphoma, myeloma, and other diseases. Despite selection of generally "fit" patients, transplant-related mortality occurs in up to 10–40 % of allogeneic transplant recipients and 2–5 % of autologous transplant recipients [13]. Further, transplantation is associated with significant short-term symptom burden and other morbidity. These side effects are usually attributable to the conditioning chemotherapy and/or radiation received prior to infusion of stem cells. In many centers, patients are hospitalized for 3–4 weeks following the infusion of stem cells, in order to allow for neutrophil and platelet recovery as well as the provision of supportive care for symptomatic toxicities from the conditioning regimen. During this period of time, patients are typically physically deconditioned with impaired functional status. Many of the symptomatic toxicities are not present immediately after infusion but appear and worsen in subsequent days. For those centers that perform inpatient transplantation, patients are usually discharged once they are able to meet basic self-care needs, maintain adequate oral intake and hydration, have achieved minimal blood counts, and are no longer at risk of neutropenic fever. Other treatment-related complications that may occur in the first 100 days following transplant include graft versus host disease (for allogeneic transplant recipients), infections, and organ dysfunction. Both early and late post-transplant complications are associated with significant quality-of-life impairment, and some long-term survivors continue to report quality-of-life deficits for at least 5–7 years following transplantation [14].

Methods

Data were drawn from an exercise intervention study, specifically a single-arm feasibility study of an interval exercise training (IET) program to be completed by participants from home in the 6 weeks prior to transplant (clinicaltrials.gov identifier NCT02577939) [15]. As part of the IET study protocol, participants were subsequently followed during hospitalization lasting approximately 3–4 weeks and for 4 weeks after discharge from the hospital. It is from this follow-up period that the pedometry and PRO data used in this analysis were collected; these data are described in detail below.

The IET study sought to enroll autologous ($n = 20$) and allogeneic ($n = 20$; 10 full intensity and 10 reduced

intensity conditioning) transplant patients deemed appropriate for exercise intervention by their treating physician. Eligible patients were 18–75 years of age, not currently participating in an interval exercise training program, willing and able to participate in a 6-week intervention program prior to transplant, and willing and able to provide written informed consent. Patients were not eligible if they had dementia, altered mental status, or psychiatric condition, had received erythropoiesis-stimulating proteins within 4 weeks prior to enrollment, had a comorbid condition that would contraindicate exercise testing or participation in a regular exercise program, or concurrent non-transplant-related chemotherapy or radiation. The study was conducted at the University of North Carolina Cancer Hospital. Institutional review board approval was obtained at the University of North Carolina at Chapel Hill, and all participants provided written informed consent.

As part of usual care, all patients hospitalized in the bone marrow transplant unit—including those who did and those who did not participate in the IET study, are encouraged by the nursing staff to walk as much as possible. Ribbons are awarded to patients who complete a "marathon" (26 miles) of walking during their 3–4 week hospital stay. The number of laps around the unit that corresponds to a mile is posted on the wall.

Data of interest to this research were the daily steps recorded by continuously worn physical activity trackers that recorded daily steps and the weekly symptom and health-related quality-of-life assessments completed after the exercise intervention was complete, during the approximately 3- to 4-week hospitalization and the 4-week period following discharge from the hospital. Daily steps were recorded by the Fitbit™ Flex (Fitbit Inc., San Francisco, CA), a consumer-grade activity tracker that is wireless and worn on the wrist. The Fitbit™ Flex uses a triaxial accelerometer and proprietary algorithm to estimate steps, which has been found to be reliable [16–18]. 2000 steps are approximately one mile of walking.

Self-reported symptoms, functioning, and health were assessed via 35 items from the NCI PRO-CTCAE measuring severity of relevant symptoms (pain, fatigue, chills, gastrointestinal problems, and other potential symptomatic treatment toxicities; see Table 3) and the PROMIS Global-10. The NCI PRO-CTCAE is a library of items measuring symptomatic treatment toxicities for adult patients undergoing cancer treatment [19, 20]. Items selected for this study had a 7-day recall period and employed a Likert scale response option, in which 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe, and 4 = Very Severe. Items are scored individually (range 0–4), and higher scores indicate greater symptom severity. The PROMIS Global-10 is a brief measure of health status that is not disease specific [21, 22]. The 10 items have a 7-day recall period or the recall period is not specified, and Likert scale response options are used for all items except pain which is measured via 11-point numeric rating scale. Items are scored on a scale of 1–5 where higher scores indicate better health, e.g., better functioning or less severe symptoms. Standardized T-scores (range 0–100) are calculated for the subscales global physical health and global mental health and higher scores indicate better health.

To be included in the analysis, an evaluable week, i.e., a case, required both a completed survey item and daily steps measured in at least four out of 7 days during the recall period of the item. The daily steps were summarized as the average of the 7-day period. Patients were included in the analysis who had at least one case.

The demographic and clinical characteristics of patients in the study sample were summarized using descriptive statistics; data were collected from the medical record. To provide a general illustration of changes in average daily steps, symptoms, functioning and health, the sample average was plotted across study weeks. To describe the prevalence of symptoms within this sample, the proportion of cases with symptom score >0 was calculated for each PRO-CTCAE symptom item. To further assist with the interpretation of findings in this sample of patients undergoing HCT, the symptom items were categorized by investigators as those likely to directly impact the amount of walking, e.g., fatigue, vomiting, shortness of breath, diarrhea, and those which are not likely to directly impact the amount of walking, e.g., problems tasting, hair loss, rash, but will be associated with changes in steps because they are part of the array of treatment toxicities that increase during the weeks of post-transplant hospitalization. This conceptual model is illustrated in Table 1.

To estimate the difference in average daily steps associated with a one-unit difference in a symptom, function, or health score—i.e., a cross-sectional analysis, cases from all patients and from all weeks were pooled, and the difference in average daily steps was estimated using linear mixed models, with patient-level random effects. To estimate the change in average daily steps associated with a one-unit change in symptom, function, or health score——i.e., change from prior week, within each patient the change in average daily steps and in item score from 1 week to the next was calculated for each available pair of weeks for that patient, e.g., Week 1–Week 2, Week 2–Week 3. These change scores were pooled across patients, and the change in average daily steps was estimated using linear mixed models, with patient-level random effects. Adjustment to the level of statistical significance to account for multiple comparisons, i.e., one model per PRO-CTCAE item, was not made because the analysis was exploratory. Because of the small sample size, we did not test whether patient characteristics such as transplant type—autologous or

Table 1 Conceptual model of relationships between patient-reported symptoms and daily steps among patients undergoing HCT

SYMPTOM	IMPACT ON WALKING	ASSOCIATION WITH DAILY STEPS
Symptoms likely to directly impact walking		
Fatigue Shortness of breath Shaking/chills Blurry vision Dizziness	Limit physical ability to walk	May directly impact number of daily steps May be negatively associated with daily steps
Joint aches Nausea Numbness/tingling Arm/leg swelling Headache	Cause physical discomfort while walking	
Vomiting Diarrhea Frequent urination	Require proximity to bathroom	
Depression Anxiety Urinary leakage	Limit willingness to walk	
Symptoms not likely to directly impact walking		
Cough, Problems tasting, Decreased appetite, Hair loss, Dry skin, Itchy skin, Rash, Dry mouth, Mouth sores, Difficulty swallowing, Constipation , Bloating, Bruising, Memory problems, Concentration problems, Insomnia	No direct impact on walking, but symptoms change during post-transplant period	Correlated with the symptoms which may directly impact number of daily steps May be negatively associated with daily steps

Note: Among symptoms likely to directly impact walking, some may be rightfully classified into more than one subgroup regarding their impact on walking. E.g. Numbness/tingling has been classified here as *causing physical discomfort while walking*, although severe numbness/tingling may also be classified as *limiting physical ability to walk.* Consideration of symptom severity and context of measurement, e.g. built environment, is recommended.

allogeneic, gender, age, and race/ethnicity—modified the relationship between self-reported symptoms, functioning, health, and average daily steps. The amount of variance in average daily steps explained by each PRO is described via *R*-squared statistic.

Results

191 patients were identified via the medical record as potentially eligible, and permission was sought from the treating physician to recruit the patient onto the study. Ninety-eight patients were approached about participating in the study. Forty-nine patients (50 %) provided written informed consent and were enrolled in the study. Of these, 17 participants did not contribute data to this analysis; two were lost to follow-up, nine were withdrawn due to lack of interest, change in treatment plan, or transition to hospice, and five had substantial missing data. Thirty-two participants had at least 1 week of evaluable data and were included in this analysis. Participants had a mean of 4.6 (SD = 1.5, range 1–8) evaluable weeks, for a total of 148 cases. The distribution of cases per study week is shown in Table 1. Note that patients still in hospital at week 4 were those not yet well enough to be discharged.

Participants had a mean age of 55 (SD = 14). Twenty (63 %) were male. Twenty-seven (84 %) were white and five (16 %) were African American. The highest level of education for 10 (31 %) participants was high school, four (13 %) completed an undergraduate degree, and 18 (56 %) completed graduate school. Eighteen (56 %) received autologous transplant, of whom 14 (78 %) had multiple myeloma and 14 (43 %) received allogeneic transplant (50 % full intensity, 50 % reduced intensity), of whom two (14 %) had acute lymphocytic leukemia, four (29 %) had acute myeloid leukemia, and four (29 %) had chronic lymphocytic leukemia (Table 2).

The average daily steps of participants during week 1 of hospitalization were 4824 (SD = 2774) and during week 1 following discharge from the hospital was 2783

Table 2 Demographic and clinical characteristics of the study sample

Patient characteristics	Total sample
N (%)	$N = 32$
Age, mean (SD)	55 (14)
Gender	
Male	20 (63 %)
Female	12 (38 %)
Race	
White	27 (84 %)
African American	5 (16 %)
Education—highest level completed	
High school graduate	10 (31 %)
Associates degree/vocational	3 (9 %)
Graduate school	18 (56 %)
Missing	1 (3 %)
Disease	
ALL	2 (6 %)
AML	4 (13 %)
Aplastic anemia	1 (3 %)
CLL/PSS	3 (9 %)
CML	1 (3 %)
Multiple myeloma	14 (44 %)
Myelodysplastic syndrome	4 (13 %)
Non-Hodgkin's lymphoma	2 (6 %)
Other solid tumor	1 (3 %)
Transplant type	
Autologous	18 (56 %)
Allogeneic	14 (43 %)

ALL acute lymphocytic leukemia, *AML* acute myeloid leukemia, *CLL* chronic lymphocytic leukemia, *CML* chronic myeloid leukemia, *PSS* progressive systemic sclerosis, SD standard deviation

Among patients receiving allogeneic transplant, seven (50 %) received full intensity (myeloablative) and seven (50 %) received reduced intensity conditioning regimen

(SD = 1935). The average daily steps over all study weeks included in this analysis was 3595 (SD = 2477). The average daily steps decline during hospitalization and recover in the weeks following discharge from the hospital (Fig. 1). Figures 2 and 3 illustrate changes over time for a subset of symptoms measured by PRO-CTCAE. The severity of symptoms increases during hospitalization and improves following discharge from the hospital, in particular fatigue, pain, nausea, diarrhea, decreased appetite, problems tasting, dry mouth, and hair loss. The PROMIS® Global-10 items measuring general health, quality of life, and functioning are fairly constant over time, while fatigue improves in the weeks following discharge from the hospital (Fig. 4).

Among symptoms likely to directly impact the amount of walking, cross-sectional regression model coefficients

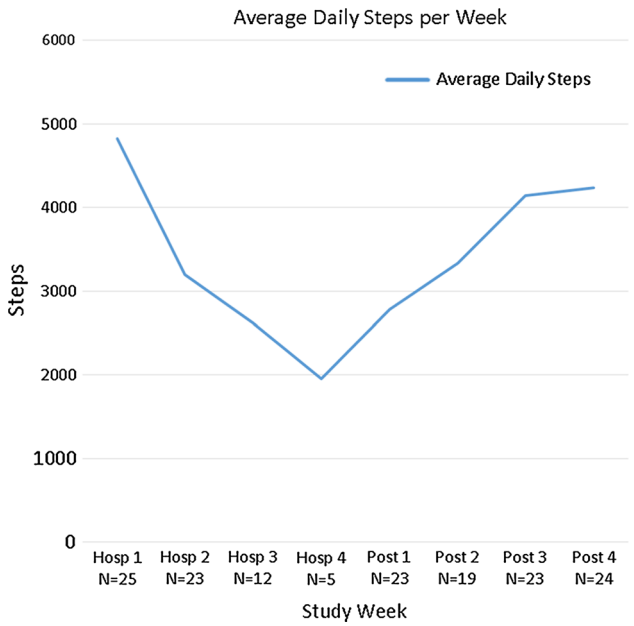

Fig. 1 Average daily steps per week, by study week. *Note* Study weeks include up to 4 weeks in hospital ("Hosp") and up to 4 weeks post-discharge ("Post")

(β) indicated lower levels of average daily steps were associated with higher levels of pain ($\beta = -720$, i.e., 720 fewer steps per unit increase in pain score, $p < 0.001$), fatigue ($\beta = -608$, $p < 0.001$), vomiting ($\beta = -575$, $p < 0.01$), shaking/chills ($\beta = -476$, $p < 0.05$), and diarrhea ($\beta = -409$, $p < 0.05$), but not with shortness of breath, muscle aches, dizziness, or other symptoms (Table 3). Within-person decrements in average daily steps from the prior week were associated with an increase in symptom severity of pain ($\beta = -852$, $p < 0.001$), fatigue ($\beta = -886$, $p < 0.001$), vomiting ($\beta = -518$, $p < 0.01$), shaking/chills ($\beta = -587$, $p < 0.01$), diarrhea ($\beta = -719$, $p < 0.001$), shortness of breath ($\beta = -1018$, $p < 0.05$), nausea ($\beta = -701$, $p < 0.001$), dizziness ($\beta = -931$, $p < 0.01$), and depression ($\beta = -598$, $p < 0.05$), but not muscle aches, arm/leg swelling, or others.

Among symptoms not likely to directly impact the amount of walking, in cross-sectional analysis lower levels of average daily steps were associated with greater severity of dry skin ($\beta = -913$, $p < 0.001$), problems tasting ($\beta = -606$, $p < 0.001$), decreased appetite ($\beta = -588$, $p < 0.001$), hair loss ($\beta = -526$, $p < 0.001$), itchy skin ($\beta = -524$, $p < 0.05$), difficulty swallowing ($\beta = -469$, $p < 0.01$), and rash ($\beta = -411$, $p < 0.05$), but not mouth sores, bloating, or insomnia (Table 3). Within-person decrements in average daily steps from the prior week were associated with an increase in severity of dry skin ($\beta = -903$, $p < 0.001$), problems tasting ($\beta = -678$, $p < 0.01$), decreased appetite ($\beta = -566$, $p < 0.01$), hair loss ($\beta = -448$, $p < 0.001$), rash ($\beta = -615$, $p < 0.01$),

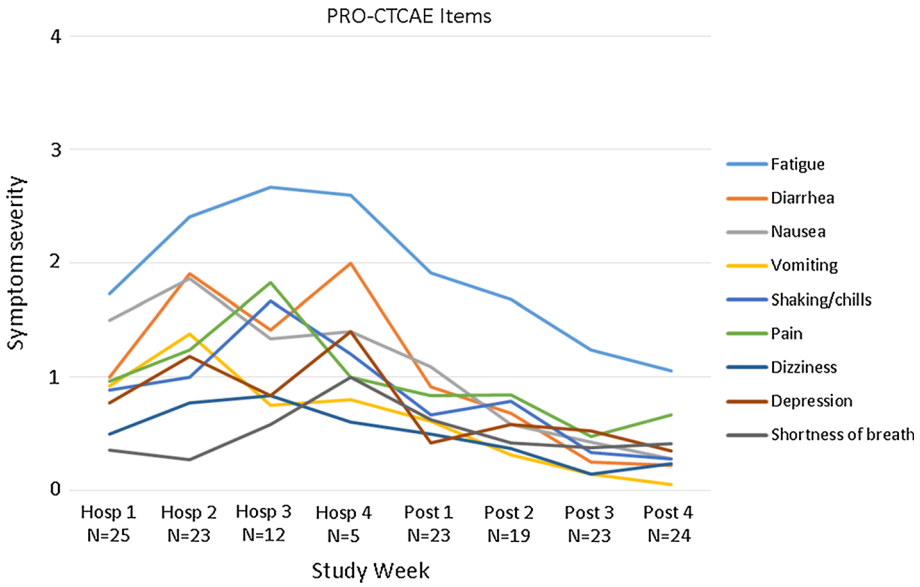

Fig. 2 Symptom severity by study week, measured by PRO-CTCAE: Subset of items likely to directly impact walking. *Abbreviations PRO-CTCAE* The Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events. *Note* PRO-CTCAE items measuring symptom severity are scored on a scale of 0–4 where higher scores indicate greater symptom severity. Study weeks include up to 4 weeks in hospital ("Hosp") and up to 4 weeks post-discharge ("Post")

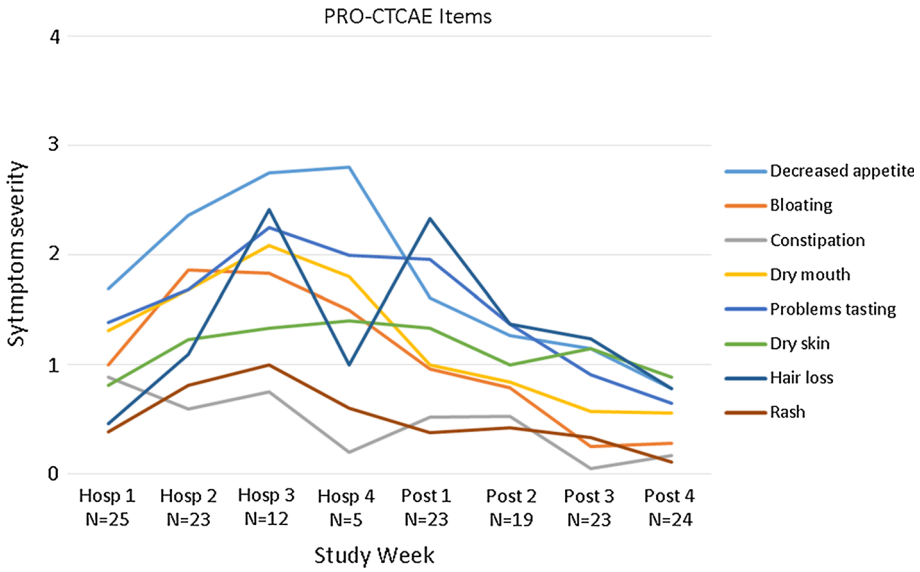

Fig. 3 Symptom severity by study week, measured by PRO-CTCAE: Subset of items not likely to directly impact walking. *Abbreviations PRO-CTCAE* The Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events. *Note* PRO-CTCAE items measuring symptom severity are scored on a scale of 0–4 where higher scores indicate greater symptom severity. Study weeks include up to 4 weeks in hospital ("Hosp") and up to 4 weeks post-discharge ("Post")

dry mouth ($\beta = -489$, $p < 0.05$), bloating ($\beta = -529$, $p < 0.05$), and constipation ($\beta = -661$, $p < 0.05$), but not difficulty swallowing, mouth sores, or other symptoms.

Among PROMIS® Global-10 items and global scores, in cross-sectional analysis, lower levels of average daily steps were associated with worse general health ($\beta = 932$, $p < 0.01$) and physical health ($\beta = 942$, $p < 0.001$); lower satisfaction with social activities ($\beta = 566$, $p < 0.01$); limitations in carrying out social activities ($\beta = 904$, $p < 0.001$) and in carrying out physical activities ($\beta = 1083$, $p < 0.001$); greater fatigue on average ($\beta = 669$, $p < 0.001$) and pain on average ($\beta = 930$, $p < 0.001$); and worse global physical health ($\beta = 193$, $p < 0.001$), but not with global mental health or quality of life (Table 4). Within-person decrements in average daily steps were associated with reductions in carrying out social activities ($\beta = 705$, $p < 0.01$) and in carrying out physical activities ($\beta = 618$, $p < 0.01$); greater fatigue on average ($\beta = 788$, $p < 0.001$) and pain on average ($\beta = 712$, $p < 0.01$); and worse global physical health ($\beta = 101$, $p < 0.001$); but not with general health, quality of life, physical or mental health (each single items), or global mental health.

The amount of variance in average daily steps explained by each PRO item or global score, i.e., the model *R*-squared, is presented in Tables 5 and 6. Many of the statistically significant PROs have *R*-squared values in the range of 0.13–0.18.

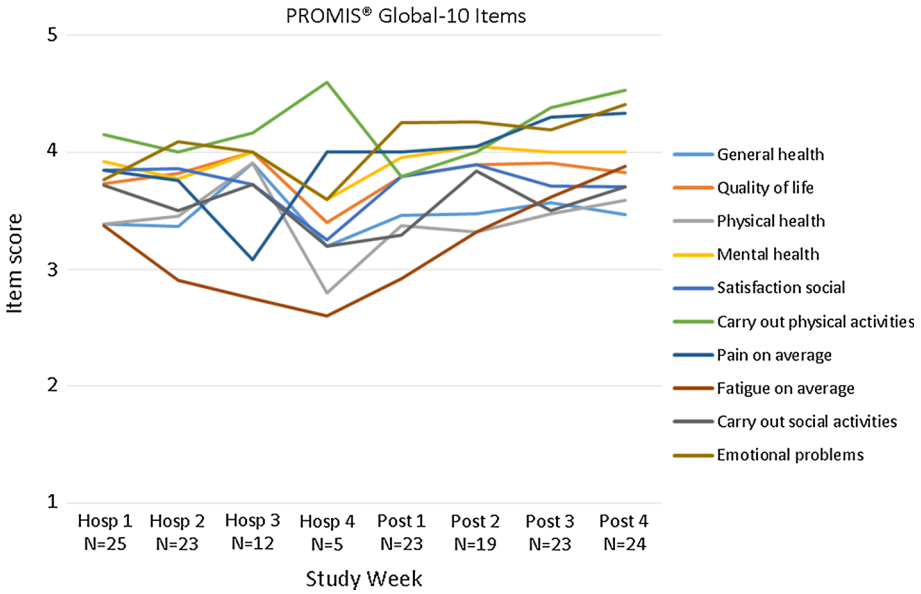

Fig. 4 Health status by study week, measured by PROMIS® Global-10 items. *Note* PROMIS® Global-10 items are scored on a scale of 1–5 where higher scores indicate better health, e.g., better functioning or less severe symptoms. Study weeks include up to 4 weeks in hospital ("Hosp") and up to 4 weeks post-discharge ("Post")

Discussion

This analysis of objectively measured daily steps and self-reported symptoms and functioning among patients undergoing HCT found that changes in pain, fatigue, vomiting, shaking/chills, diarrhea, shortness of breath, nausea, dizziness, depression, dry skin, problems tasting, decreased appetite, hair loss, rash, dry mouth, bloating, and constipation, as well as limitations in carrying out physical activities and social activities, and global physical health, were significantly associated with changes in average daily steps.

These results highlight that the interpretation of the changes in steps and changes in symptoms and function over time are context specific. Among patients undergoing transplant, mucositis is a common side effect of therapy. However, it is interesting to note that patient-reported mouth sores were not associated with daily steps, whereas pain was associated with decreases in daily steps. This suggests potentially that pain may have been a descriptor that was more clearly linked by patients to the sensation of mucositis, whereas mouth sores may not have adequately captured the experience of mucositis, since step decreases were observed during the period of time that was expected to correlate with symptomatic mucositis from conditioning chemotherapy or radiation. In this way, the pedometry data aid in interpreting the relationship of individual PRO items with the patient experience.

The increase in dry skin with decrements in daily steps may have been confounded by the length of time spent in the hospital, or be due to the presence of acute GVHD. Participants may have interpreted the question about dry skin as asking about mild forms of rash—a toxicity of treatment. Constipation is anecdotally experienced by patients at the beginning of hospitalization, which might explain why more severe constipation was associated with higher daily step counts.

Quality of life, general health, and global mental health were not associated with average daily steps in this sample. Quality of life is a difficult construct to interpret during an acute transplant hospitalization and may not have been expected to show much change much during this short period of time. However, components of quality of life (e.g., physical health) were affected. This may tell us something about how acutely ill populations interpret the phrase "quality of life"—these data suggest that quality of life is not significantly impacted by short-term decrements in physical health. Patient reports of general health were also remarkably stable over time. Patients were aware that the transplant process would include a short-term period of poor health which would resolve prior to discharge. Participants may have reported good general health relative to their expectations for the transplant period and because of the potential for transplant to significantly improve their health. We believe the strong mental health reported by patients may be an artifact of the sample being composed of those willing to participate in an exercise intervention program in order to make the most out of the transplant process, and that walking as much as possible could improve mood and outlook. The single-item measure of depression from the PRO-CTCAE was statistically significant ($p = 0.02$); however, the global mental health score composed of multiple items may be a more reliable measure of mental health; therefore, it is the one on which we are basing conclusions.

The within-person analyses comparing changes in each construct to changes in average daily steps found more statistically significant associations than the cross-sectional

Table 3 Model coefficients for cross-sectional and prior week control models of PRO-CTCAE symptom items

PRO-CTCAE symptom items[a] $N = 32$ Total cases = 148	Proportion of cases with symptom[b]	Cross-sectional[c]	Change from prior week[c]
Symptoms likely to directly impact amount of walking[d]			
Pain	0.55	−720***	−852***
Fatigue	0.93	−608***	−886***
Vomiting	0.36	−575**	−518*
Shaking/chills	0.46	−476*	−587*
Diarrhea	0.55	−409*	−719***
Shortness of breath	0.32	−359	−1018*
Blurry vision	0.36	−354	78
Muscle aches	0.44	−353	−446
Nausea	0.56	−338	−701***
Dizziness	0.36	−296	−931**
Depression	0.47	−255	−598*
Joint aches	0.51	−131	−26
Urinary leakage	0.09	−32	274
Numbness/tingling	0.60	5	46
Arm/leg swelling	0.28	35	227
Anxiety	0.43	35	510
Headache	0.47	57	−647
Frequent urination	0.55	227	−337
Symptoms not likely to directly impact amount of walking[d]			
Dry skin	0.74	−913***	−903***
Cough	0.24	−636	−341
Problems tasting	0.80	−606***	−678**
Decreased appetite	0.80	−588***	−566**
Hair loss	0.55	−526***	−448***
Itchy skin	0.60	−524*	−209
Difficulty swallowing	0.23	−469**	−498
Rash	0.28	−411*	−615*
Concentration problems	0.50	−349	−18
Dry mouth	0.65	−282	−489*
Mouth sores	0.28	−279	−389
Bruising	0.34	−275	−399
Bloating	0.57	−214	−529*
Memory problems	0.46	−115	−222
Constipation	0.31	112	661*
Insomnia	0.82	307	−77

[a] PRO-CTCAE items measuring the severity of each symptom via Likert scale (None/Mild/Moderate/Severe/Very Severe)

[b] *Proportion of cases with symptom* is the number of cases in which the symptom severity was greater than "None." Symptoms with low prevalence may not have observable associations with daily steps due to sample size

[c] *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$

[d] Symptoms have been divided into those likely and those not likely to *directly* impact the amount of walking, to assist the reader in interpreting these study results

analysis. This may be because the within-person analyses control for the individual's level of activity in the prior week. Because of the substantial between-person variation in average daily steps, within-person analyses are recommended for research or clinical interpretation of pedometry data.

Participation in the IET study was limited to patients willing and able to exercise and provided encouragement to

Table 4 PROMIS Global-10 model coefficients for cross-sectional and prior week control models

PROMIS Global-10 $N = 32$ Total cases = 148	Cross-sectional[a]	Change from prior week[a]
General health	932**	599
Quality of life	595	203
Physical health	942***	274
Mental health	528	214
Satisfaction social	566*	407
Carry out social activities	904***	705**
Carry out physical activities	1083***	618**
Emotional problems	−44	73
Fatigue on average	669**	788***
Pain on average	930***	712**
Global physical health (T-score)	193***	101***
Global mental health (T-score)	53	28

[a] *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$

exercise during the 6 weeks prior to transplant and thus may limit generalizability of this analysis. It is our impression that among BMT units at institutions in the USA, practice patterns vary regarding encouragement to walk. However, this analysis focused on the degree of within-person change across study weeks. A potential source of error in the data is that the Fitbit device may not have been worn the entire day, and thus, daily steps may have been undercounted. This is partially addressed by summarizing daily steps as a seven-day average. The PRO-CTCAE and PROMIS ® Global-10 have not been validated specifically among patients undergoing HCT; however, the PRO-CTCAE was developed and validated to measure symptomatic toxicities of cancer therapy, and both are commonly used to evaluate the health and experience of patients with cancer. Many of the significant associations observed had p values <0.001; a Bonferroni adjustment for multiple comparisons would not alter the conclusions of the paper. The lack of statistical significance observed for some comparisons may have been due to the small sample size.

The Fitbit™ Flex has a battery life of 5–7 days; therefore, in this study, research staff would regularly assist the participant with charging the device while in hospital. When the participant was at home, they were reminded by research staff to charge the device themselves. Although the Fitbit™ Flex does not lose data stored in memory once it has no more charge, it cannot collect additional data until it is recharged. An additional limitation of the device was that it cannot be determined from the data whether the participant was at rest or whether the device was not being worn. Devices with a touch capacitive feature, or a heart rate monitor, can indicate whether it was being worn. We found the wrist bands on the Fitbit™ Flex occasionally fail and need to be replaced. The strengths of the Fitbit™ Flex are the much lower price than many older accelerometry-based pedometers, the availability of validation data for device accuracy, and that it is waterproof and worn on the wrist, which enables it to be worn continuously. Anecdotally, devices worn on the hip, which clip to the belt of pants or other clothing, are lost in the laundry. The Fitbit™ individual online user accounts and data upload/download were easy for research staff and many patients to use. Research data collection platforms may also import study participant data from the Fitbit user account via connections provided by a third party such as Validic, Inc. We encourage Fitbit and other device makers to produce subsequent generations of these activity trackers with longer battery life, such as 6 months or more, more durable components, and a method of detecting whether it is being worn.

The fields of patient-generated health data and mobile health are rapidly developing with the availability of new wearable devices and the proliferation of platforms that combine and present these data streams. Apple's new HealthKit supports applications that capture and display health and fitness data to consumers and their health care providers [23]. In September 2013, Vignet Inc. received NCI funding to create Fitninja, a Mobile Health Research Toolkit. It enables industry, health plans, and other health agencies, to create large-scale health interventions that integrate messaging, patient surveys and diaries, electronic health and medical records, and devices such as pedometers and blood pressure monitors [24]. At the University of North Carolina, Lineberger Comprehensive Cancer Center, we have recently integrated the automated capture of wearable device data into the Patient-Reported Outcome Survey System (PRO-Core) (http://pro.unc.edu) in order to support research studies collecting and displaying multiple types of patient-generated health data.

Table 5 R-squared values for cross-sectional and prior week control models of PRO-CTCAE symptom items

PRO-CTCAE symptom items[a] $N = 32$ Total cases = 148	Cross-sectional	Change from prior week
Symptoms likely to directly impact amount of walking[b]		
Pain	0.09	0.16
Fatigue	0.03	0.16
Vomiting	0.03	0.06
Shaking/chills	0.01	0.07
Diarrhea	0.03	0.18
Shortness of breath	0.01	0.07
Blurry vision	0.00	0.00
Muscle aches	0.00	0.03
Nausea	0.01	0.13
Dizziness	0.00	0.08
Depression	0.01	0.06
Joint aches	0.02	0.00
Urinary leakage	0.00	0.00
Numbness/tingling	0.00	0.00
Arm/leg swelling	0.00	0.01
Anxiety	0.00	0.02
Headache	0.00	0.04
Frequent urination	0.00	0.02
Symptoms not likely to directly impact amount of walking[b]		
Dry skin	0.07	0.16
Cough	0.03	0.01
Problems tasting	0.08	0.11
Decreased appetite	0.07	0.10
Hair loss	0.04	0.14
Itchy skin	0.02	0.01
Difficulty swallowing	0.01	0.03
Rash	0.01	0.08
Concentration problems	0.00	0.00
Dry mouth	0.00	0.07
Mouth sores	0.00	0.03
Bruising	0.02	0.02
Bloating	0.00	0.06
Memory problems	0.00	0.00
Constipation	0.01	0.07
Insomnia	0.00	0.00

[a] PRO-CTCAE items measuring the severity of each symptom via Likert scale (None/Mild/Moderate/Severe/Very Severe)

[b] Symptoms have been divided into those likely and those not likely to *directly* impact the amount of walking, to assist the reader in interpreting these study results

To appropriately leverage these new technologies for improving the quality of care and health of patients, we need an understanding of what data such as pedometry indicate about patient health and experience. This can be achieved through longitudinal and predictive modeling, and through interviews with patients regarding their perspective on the meaning and relevance of the information and the suitability of this type of data capture.

This study found average daily steps were indicative of patient symptoms and functioning during HCT. Pedometry is a potentially valuable anchor for PRO validation studies, especially for symptom interference items and measures of physical function and activity. Pedometry has promise as an acceptable and responsive measure of patient health and well-being during cancer treatment, suitable as a complement to PROs and for patients who are not able to self-report.

Table 6 R-squared of cross-sectional and prior week control models of PROMIS Global-10 items and global health T-scores

PROMIS Global-10 $N = 32$ Total cases = 148	Cross-sectional	Change from prior week
General health	0.12	0.12
Quality of life	0.05	0.01
Physical health	0.30	0.16
Mental health	0.06	0.00
Satisfaction social	0.05	0.03
Carry out social activities	0.08	0.00
Carry out physical activities	0.00	0.00
Emotional problems	0.02	0.14
Fatigue on average	0.22	0.08
Pain on average	0.14	0.02
Global physical health (T-score)	0.17	0.01
Global mental health (T-score)	0.13	0.10

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the Ethical Standards of the Institutional and/or National Research Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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