



Meaningful Change in the Ability to Perform Physical Activities for Patients with Cachexia and Cancer

Abstract
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INTRODUCTION

Cachexia is a multifactorial, multi-organ syndrome with ongoing loss of skeletal muscle mass (with or without the loss of fat mass), resulting in subsequent weight loss as well as fatigue, that is one of the main causes of morbidity and mortality in late stages of chronic conditions such as cancer.^{1,2} The ongoing weight loss, loss of skeletal muscle, and physical fatigue results in progressive functional impairment, including reduced physical activity/function limiting activities of daily living.³

In a recent Phase 2 clinical trial, patients with cancer and cachexia had increased digital health technology (DHT)-derived physical activity following 12 weeks of ponegromab (400 mg, Q4W) as compared to placebo (increase in non-sedentary physical activity: 71.7 min/day modeled mean difference from placebo).⁴ (Table 1)

Digital health technologies (DHTs) can quantify changes in physical activity in cachexia clinical studies. But what is a meaningful change to patients with cachexia and cancer? We estimated the meaningfulness of incremental changes in ability to perform physical activities of different intensity and time spent each day doing non-sedentary activity that can be measured with DHTs.

Table 1. DHT-derived physical activity in cancer patients with cachexia treated with Ponsegromab compared to placebo at Week 12¹

Digital endpoint	Baseline		Change from Baseline at Week 12			
Nonsedentary physical activity – min/day	N1 Ψ	Observed Mean (±SD)	N2 Ψ	Observed Mean (±SD)	Modeled Mean (95% Credible Interval)	Modeled Mean Difference from Placebo (95% Credible Interval)
Placebo	44	228.1±109.8	12	-29.9±100.5	-41.09 (-67.59 to -15.55)	NA
Ponsegromab, 100 mg	46	220.1±119.3	17	-13.9±58.8	-20.19 (-44.88 to 3.57)	20.89 (-15.49 to 57.25)
Ponsegromab, 200 mg	43	214.8±115.1	16	-27.0±38.7	-76.51 (-101.91 to -53.19)	-35.42 (-70.57 to 0.60)
Ponsegromab, 400 mg	46	243.7±104.1	14	31.6±75.5	30.61 (8.48 to 52.70)	71.70 (37.01 to 107.21)
• Plus-minus values are means ±SD. The listed analyses are based on post hoc Bayesian joint longitudinal analysis after adjustment for the competing risk of death. No adjustments for multiple comparisons were made, and credible intervals should not be used in place of hypothesis testing. NA denotes not applicable. • Ψ N1 indicates the number of patients who underwent randomization and had available data at baseline; N2 indicates the number of patients who had available data regarding the change from baseline to week 12.						

METHODS

A cross-sectional online survey was conducted among US adults (≥18 years) with cancer and cachexia. Participants had to report unintentional weight loss consistent with the following criteria: (a) report lowest weight since cancer diagnosis or within past six months (whichever was shorter); and (b) have a calculated weight loss greater than 5% over past six months or since cancer diagnosis (whichever was shorter).

Activities included in the survey were identified based on a review of existing qualitative and quantitative data (Figure 1). Meaningfulness of 14 changes in ability to perform physical activities and 3 increases in daily time spent in non-sedentary activity were assessed on a 5-point rating scale (not at all meaningful to extremely meaningful) (Figure 2). Subgroups (tumor type, cancer stage, self-reported ECOG performance status [PS]) were compared using chi-square tests (or Fisher's exact tests for sparse data in which observed cell counts were <5).

Figure 1. Identifying physical activities that are important to patients

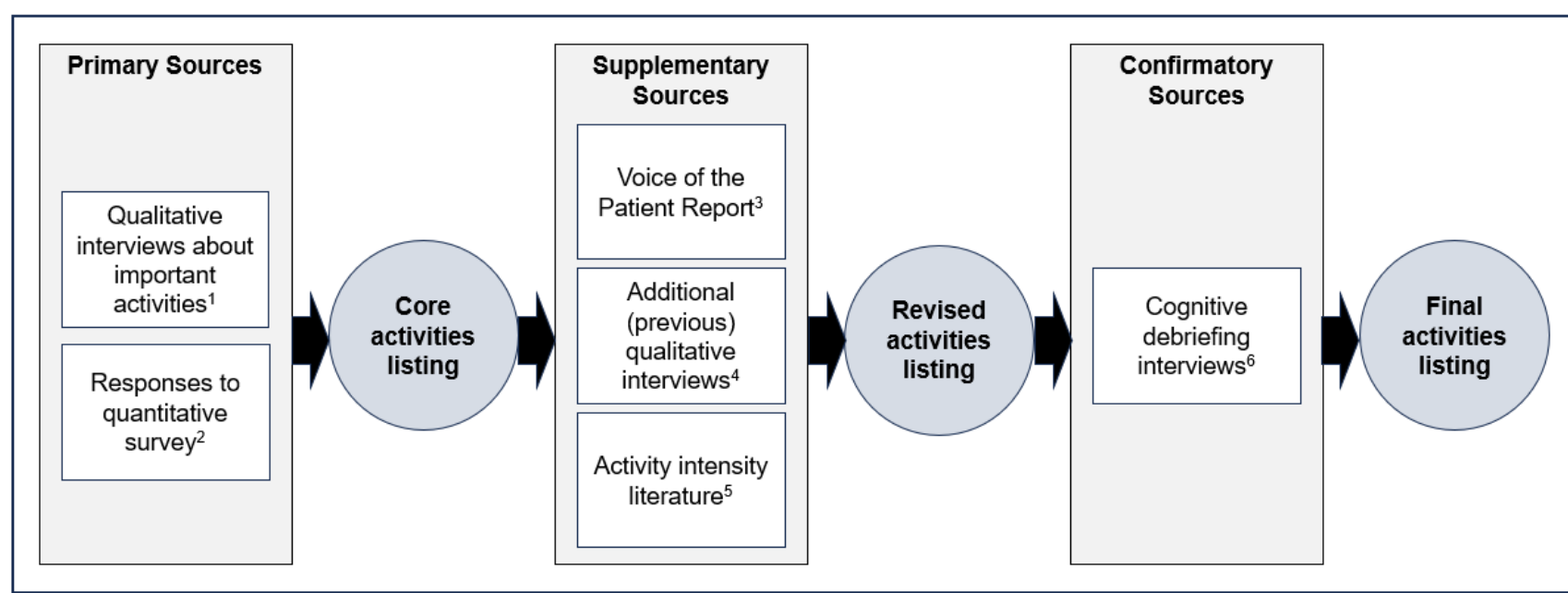


Figure 2. Establishing the Meaningfulness

Identifying changes in the ability to do physical activities that could be captured using Digital Health Technologies (DHTs)

From	To
1. Cannot go walking outside	→ Able to walk a short distance like around a city block or a quarter mile (~1000 steps)
2. Able to walk a short distance like around a city block or a quarter mile (~1000 steps)	→ Able to walk a long distance like several city blocks or a mile (~4000 steps)
3. Cannot walk, even at a slow pace	→ Able to walk at a slow pace (1.5 miles per hour)
4. Able to walk at a slow pace (1.5 miles per hour)	→ Able to walk at an average adult walking pace (3 miles per hour)
5. Able to walk at an average adult walking pace (3 miles per hour)	→ Able to walk at a fast pace (4.5 miles per hour)
6. Cannot be up and about	→ Able to be up and about for less than an hour a day
7. Able to be up and about for less than an hour a day	→ Able to be up and about for 3 hours a day
8. Able to be up and about for 3 hours a day	→ Able to be up and about for at least 6 hours a day
9. Cannot move from sitting to standing	→ Able to move from sitting to standing, but with a lot of effort
10. Able to move from sitting to standing, but with a lot of effort	→ Able to move from sitting to standing easily
11. Cannot do any activities, even while sitting	→ Able to do activities (such as using a computer or reading) while sitting
12. Able to do activities (such as using a computer or reading) while sitting	→ Able to do light activities (such as dusting or doing laundry)
13. Able to do light activities (such as dusting or doing laundry)	→ Able to do moderate activities (such as walking uphill or carrying groceries)
14. Able to do moderate activities (such as walking uphill or carrying groceries)	→ Able to do vigorous activities (such as running, playing tennis)

How meaningful would this increase be to you?

Not at all meaningful	Somewhat meaningful	Moderately meaningful	Very meaningful	Extremely meaningful
1	2	3	4	5

Measure meaningfulness of changes (Above) and the amount of time spent (Below) doing the physical activities using a 5-point verbal rating scale

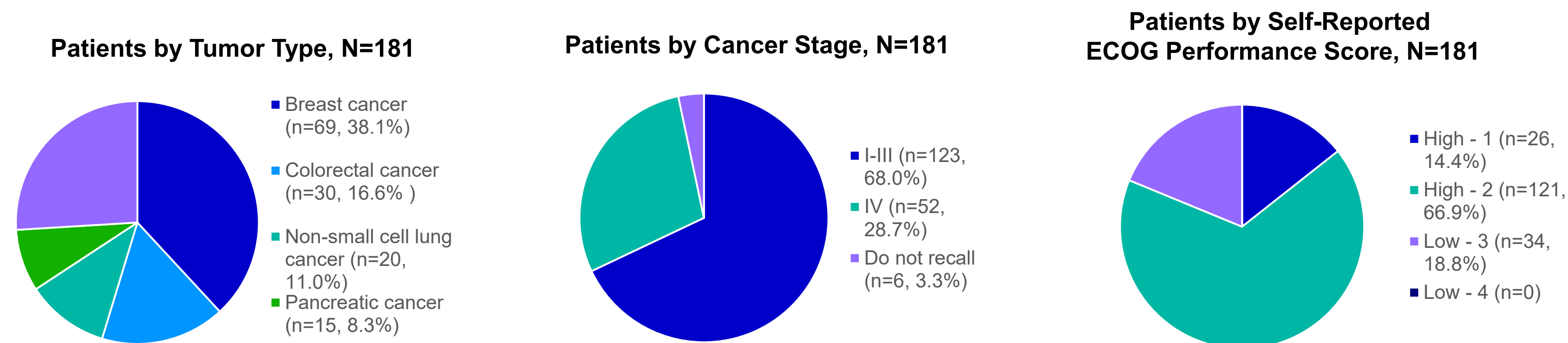
You mentioned that you do light activities for **INSERT TIME FROM QUESTION D1, C ABOVE, IF "0" SELECTED, PIPE IN: "3 minutes"** each day. Imagine this changed, and you now do light activities for an additional 4 minutes each day. How meaningful would this change be to you?

Not at all meaningful	Somewhat meaningful	Moderately meaningful	Very meaningful	Extremely meaningful
1	2	3	4	5

RESULTS

In total, 181 patients with cancer and cachexia participated [tumor types: breast n=69 (38.1%), colorectal n=30 (16.6%), non-small cell lung n=20 (11.0%), pancreatic n=15 (8.3%), other solid tumors n=47 (26.0%); stage: I-III n=123 (68.0%), IV n=52 (28.7%), don't recall/not sure n=6 (3.3%); higher performance status (n=147) [self-reported ECOG PS of 1 (14.4%) and 2 (66.9%], lower self-reported performance status PS of 3, n=34 (18.8%)]. (Figure 3)

Figure 3. Participant Characteristics



All changes in physical activity intensity, and both a 14-min and a 30-min increase in time spent in non-sedentary activity/day, were at least moderately meaningful to most patients, regardless of tumor type, cancer stage, or patient reported ECOG PS (Table 2 and Figure 4). Some meaningfulness ratings differed significantly by tumor type (both walking pace and distance were less meaningful in NSCLC and sitting to standing was less meaningful in pancreatic) and self-reported performance status (walking pace was less meaningful in patients with self-reported ECOG PS 3). Majorities of patients (60.9% to 86.7%), except for those with colorectal cancer (48.1%), rated a 4-min increase/day in non-sedentary activity as at least moderately meaningful (Figure 5).

TABLE 2. Changes in Physical Activity Intensity

Change in Ability to do Physical Activities	Proportion of Patients Rating Each Change as at Least Moderately Meaningful									
	All Patients N=181	Tumor Type					Cancer Stage		Self- Reported Performance Status	
		NSCLC N=20	Breast N=69	Colorectal N=30	Pancreatic N=15	Other N=47	Stage I-III N=123	Stage IV N=52	Higher (1 and 2) N=147	Lower (3) N=34
Cannot go walking outside to Able to walk a short distance	93.9%	95.0%	94.2%	93.3%	93.3%	93.6%	92.7%	98.1%	93.9%	94.1%
Able to walk a short distance to Able to walk a long distance	90.6%	65.0%*	91.3%*	96.7%*	100.0%*	93.6%*	91.9%	88.5%	91.8%	85.3%
Cannot walk, even at a slow pace to Able to walk at a slow pace	94.5%	100.0%	95.7%	93.3%	93.3%	91.5%	93.5%	98.1%	95.9%	88.2%
Able to walk at a slow pace to Able to walk at an average walking pace	90.6%	70.0%*	92.8%*	93.3%*	100.0%*	91.5%*	89.4%	94.2%	93.2%*	79.4%*
Able to walk at an average walking pace to Able to walk at a fast pace	79.6%	70.0%	78.3%	93.3%	93.3%	72.3%	79.7%	78.8%	80.3%	76.5%
Cannot be up and about to Able to be up and about for <1 hour a day	93.9%	100.0%	92.8%	93.3%	100.0%	91.5%	94.3%	94.2%	94.6%	91.2%
Able to be up and about for <1 hour a day to Able to be up and about 3 hours a day	96.1%	100.0%	94.2%	90.0%	100.0%	100.0%	95.1%	100.0%	95.9%	97.1%
Able to be up and about 3 hours a day to Able to be up and about 6 hours a day	92.3%	80.0%	89.9%	93.3%	100.0%	97.9%	90.2%	98.1%	92.5%	91.2%
Cannot move from sitting to standing to Able to move from sitting to standing with effort	89.0%	95.0%*	91.3%*	100.0%*	60.0%*	85.1%*	88.6%	92.3%	89.8%	85.3%
Able to move from sitting to standing with effort to Move from sitting to standing easily	95.0%	100.0%	94.2%	100.0%	100.0%	89.4%	95.1%	96.2%	95.9%	91.2%
Cannot do any activities, even while sitting to Able to do activities while sitting	95.0%	95.0%	92.8%	100.0%	100.0%	93.6%	94.3%	98.1%	95.2%	94.1%
Able to do activities while sitting to Able to do light activities	96.1%	100.0%	94.2%	93.3%	100.0%	97.9%	97.6%	94.2%	97.3%	91.2%
Able to do light activities to Able to do moderate activities	91.2%	95.0%	87.0%	93.3%	93.3%	93.6%	91.1%	92.3%	92.5%	85.3%
Able to do moderate activities to Able to do vigorous activities	75.7%	60.0%	75.4%	80.0%	86.7%	76.6%	78.9%	67.3%	78.2%	64.7%
Able to do non-sedentary activities for an additional 4 minutes per day	65.2%	65.0%*	75.0%*	48.1%*	86.7%*	60.9%*	70.0%	62.7%	66.4%	69.7%
Able to do non-sedentary activities for an additional 14 minutes per day	76.2%	80.0%	77.9%	66.7%	93.3%	80.4%	79.2%	76.5%	79.0%	75.8%
Able to do non-sedentary activities for an additional 30 minutes per day	85.6%	90.0%	89.7%	85.2%	100.0%	82.6%	88.3%	88.2%	88.8%	84.8%
* indicates statistically significant differences (P<0.05) in proportion among subgroups										

Figure 4. Proportion of Patients Rating Each Change in Ability to do Physical Activities as at Least Moderately Important

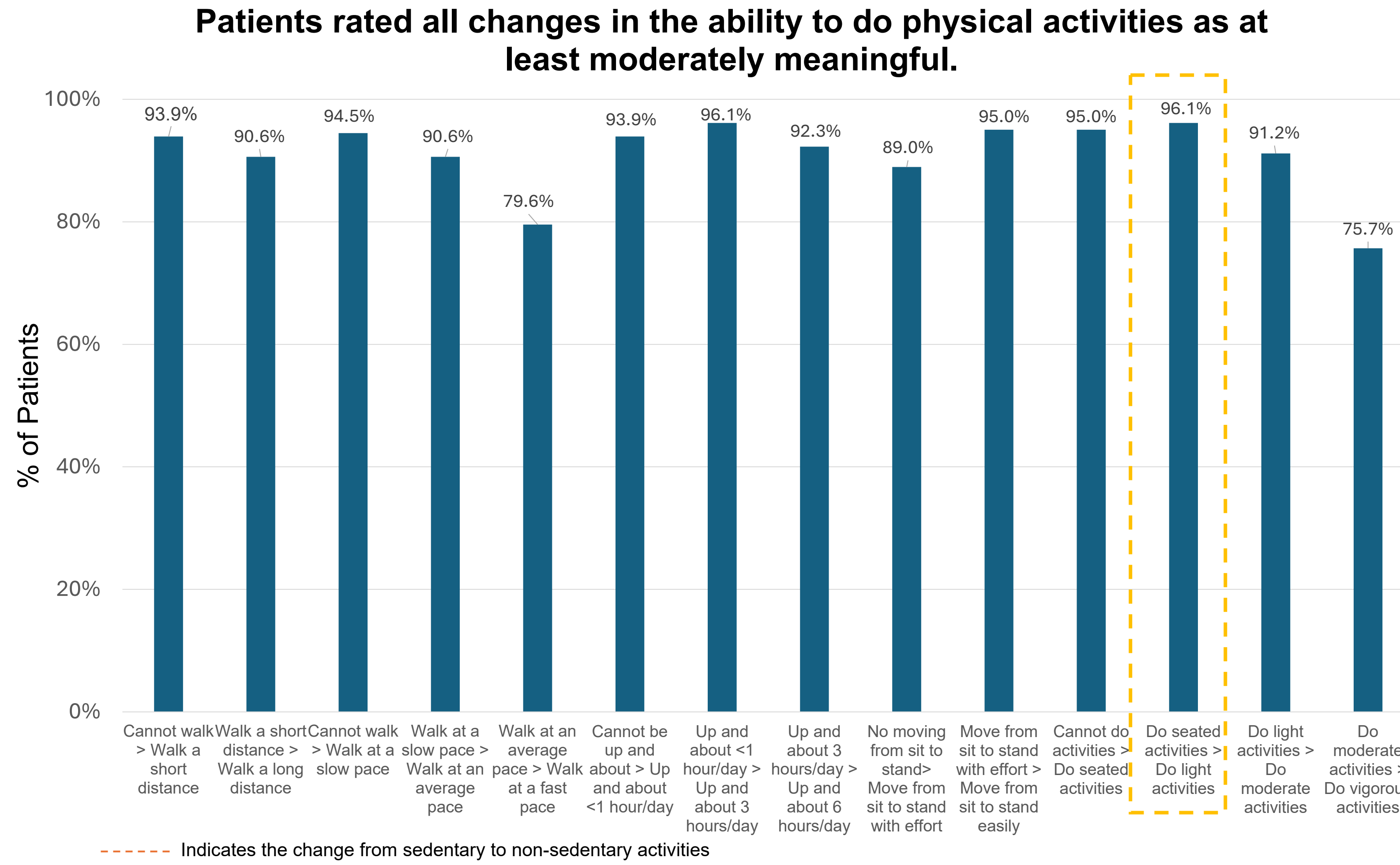
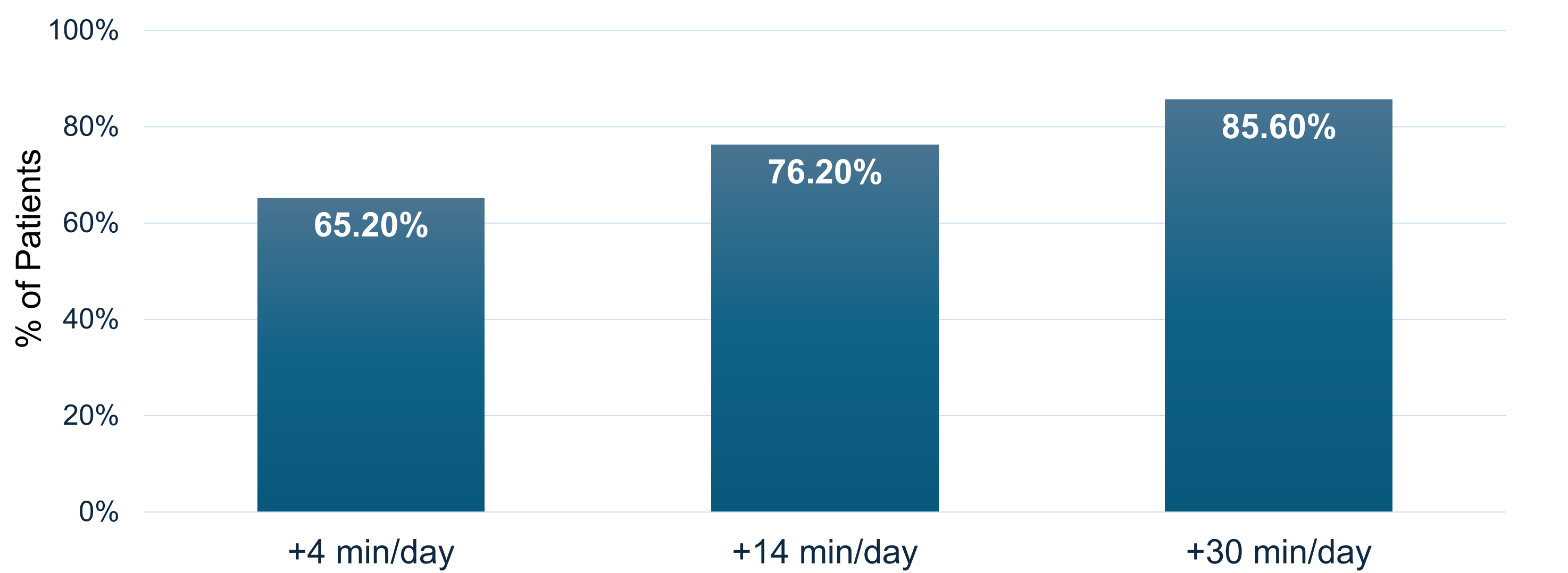


Figure 5. Proportion of Patients Rating Each Increase in Daily Non-Sedentary Time as at Least Moderately Meaningful

Overall, patients rated all changes in additional time each day (4 min, 14 min, 30 min) in non-sedentary activity as at least moderately meaningful.



CONCLUSIONS

Patients with cancer and cachexia perceived even small changes in physical activities and time spent in non-sedentary activity (as little as a +4 minute improvement) as being at least moderately meaningful, suggesting that DHTs that measure changes in movement duration can be used to capture important patient-centric endpoints in clinical studies.

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