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Pediatric

## Transplant Energize Me Patient Outcome (TEMPO): A Quality Improvement Project that Maintains Functional Mobility in Pediatric Patients Admitted for Allogeneic Hematopoietic Cell Transplantation

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### A B S T R A C T

Allogeneic hematopoietic cell transplantation (HCT) remains the definite cure for many pediatric hematologic diseases but causes profound deconditioning, which impairs daily physical functioning and may lead to further health complications. The Transplant Energize Me Patient Outcome (TEMPO) project is a standard-of-care, quality improvement (QI) project whose primary objective is to maintain physical functional mobility and strength throughout admission for pediatric allogeneic HCT patients. Specifically, TEMPO incorporates individualized and developmentally appropriate exercises and activities that are administered by a multidisciplinary team, who objectively measure and record a patient's physical stamina at predetermined frequencies. Discipline-specific metrics at admission, at weekly intervals, at discharge, and at 100 days after graft infusion (D100) are recorded in templated flowsheets in the electronic medical record. As a secondary objective, resource utilization as measured by length of stay, duration of parenteral feeds and narcotics, readmission by D100, and infections was compared between TEMPO and historical control (pre-TEMPO) allogeneic HCT patients. TEMPO participation maintained physical endurance and functional strength throughout hospitalization, an effect that was significantly sustained or improved at D100. Resource utilization did not significantly differ between patient cohorts. Taken together, the TEMPO QI Project maintains physical functional mobility, strength, and endurance, thereby decreasing physical deconditioning in pediatric allogeneic HCT patients, an effect that is objectively sustained at D100.

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### INTRODUCTION

Hematopoietic cell transplant (HCT) patients often experience declines in physical functional mobility and strength that are commonly attributed to conditioning regimen, prior chemotherapy treatment, prolonged hospitalizations, and treatment-related fatigue [1–4]. Such physical decline often results in impaired daily physical functioning. Additionally, transplant patients often experience physical and psychological side effects including pain, nausea, fatigue, and depression as well as complications including infection and graft-versus-host

disease [5]. Together, these impairments and complications result in profound deconditioning, typically evident as declines in functional mobility [6,7], and an increased risk for nosocomial infection and use of analgesics, which often is associated with greater institutional resource utilization, including increased length of stay (LOS) [8,9].

Evidence supports the use of exercise as an adjunct therapy during HCT [5,10]. The safety and feasibility of an exercise program during and after HCT is well supported in the literature [1,11–14]. In addition, studies including physical activity have documented benefits including less fatigue, improved strength and cardiorespiratory fitness, and higher quality of life, and exercise intervention has been shown to decrease the loss of functional performance during admission for HCT [6,15,16]. Specifically, cardiorespiratory fitness, as assessed by measures such as the 6-minute walk test (6MWT), has been shown to

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have a stabilizing effect or statistically significant improvements in endurance with the use of exercise intervention during HCT for pediatric patients compared with control subjects from admission to follow-up [11,14]. The assessment of hand grip strength in pediatric patients undergoing HCT has shown similar statistically significant improvements in strength at time of discharge [17].

Finally, recent reviews support a strong correlation between moderate exercise and immune function with decreases in infection risk in cancer patients associated with improved outcomes [17–19]. However, no standardized exercise and activity recommendations for pediatric HCT patients exist, and ideal therapy frequency and intervention intensity remain unclear. Because of the lack of standardized physical activity and given the well-documented known declines in physical function during HCT, a cohesive program to reinforce the importance of functional mobility within the daily routine of each pediatric HCT patient is needed.

The Transplant Energize Me Patient Outcome (TEMPO) Quality Improvement (QI) project incorporates a multidisciplinary practice standard-of-care that emphasizes establishing routine and promoting physical mobility in pediatric patients admitted for allogeneic HCT. Therapy intervention is individualized, because it is both age and developmentally appropriate, and focuses on the child's primary functional deficits. We hypothesized that patients participating in the TEMPO project would maintain and/or improve functional mobility during hospitalization for HCT. Specifically, the project's primary objective was to maintain physical mobility, strength, and endurance as measured at the time of admission and compared with time of discharge. The project's secondary objective was to determine if patients who participated in TEMPO used less hospital resources than historical control (pre-TEMPO) patients.

## METHODS

### Patient Population

All pediatric allogeneic HCT patients were offered participation in standard-of-care TEMPO during HCT admission. Those patients who either

declined participation or met an exclusion criterion were not included in data analysis. Retrospective review was conducted on all patients who participated in TEMPO from its inception in August 2016 through November 2018. A retrospective review was also completed for a pre-TEMPO cohort of 89 historical control patients also receiving HCT from January 2012 through August 2016. Data for historical control subjects, defined as pediatric allogeneic HCT recipients admitted for transplant before TEMPO, were collected as approved by the Nationwide Children's Hospital Institutional Review Board. As a QI project, TEMPO patient data were exempt from institutional review board review.

Inclusion criteria for both TEMPO patient and historical control subject data analysis were as follows: (1) patients between 1 day and 21 years of age who received either reduced-intensity or myeloablative conditioning before transplant using any graft source and (2) patients receiving allogeneic HCT from haploidentical, matched related, and matched unrelated donors. Exclusion criteria from data analysis included (1) patients who had a prolonged pretransplant hospital admission > 120 days, (2) patients with any comorbidity that precluded participation in the TEMPO project (eg, neurologic deficits impeding physical exercise), and patients who died during HCT admission.

### Clinical Therapy and Psychosocial Services

The disciplines that participated in TEMPO were clinical therapy services (CTS; physical therapy, occupational therapy, massage therapy, therapeutic recreation, and speech therapy) and psychosocial services (Table 1). CTS are offered 5 days per week with a recommended 30-minute session on average. Before TEMPO, CTS were offered and averaged 2 to 3 times per week for each therapy. Each discipline uses specific outcome measures collected at admission, weekly during HCT, and at the time of discharge (Table 2). Physical therapy also completed follow-up evaluation at day 100 (D100) after allogeneic HCT. Each therapy service tailored treatment sessions to patients' level of functioning and tolerance throughout transplant admission, both within and between therapy sessions.

### Objective Mobility and Strength Metrics

The following discipline-specific metrics were assessed as a standard-of-care for pediatric HCT patients at defined times as previously described (Table 1).

#### Functional mobility score

The physical therapy functional mobility score (FMS) is a metric designed to objectively capture a patient's functional mobility with a developmentally appropriate tool. The HCT population has limited opportunities for functional mobility because of isolation restrictions, and currently no standard clinical tool exists to adequately capture functional mobility in these patients. Therefore, the FMS was designed to require only a portable step and be administered within the patient's room to meet these needs.

**Table 1**  
CTS Discipline-Specific Intervention Metrics

Service	Metrics	Description
Physical therapy	FMS*	Functional measure of 4 skills, each scored on a 7-point scale, equivalent for Bayley-3 gross motor skills for ages ≤ 42 months
	6MWT	Walk for 6 minutes and measure distance, pre/post heart rate, and oxygen saturation
	5STS test	Sit and stand 5 times, timed
	Bayley-3 gross motor skills	Assesses gross motor skills, ages ≤ 42 months, raw score and scaled score
Occupational therapy	ADL functional measure score*	Measures independence in 7 daily activities, each on a 7-point scale
	Bayley-3 fine motor skills	Assesses prehension, perceptual-motor integration, motor planning/speed, visual tracking, reaching, object grasping, object manipulation, functional hand skills, and responses to tactile information
	Grip strength	Maximum isometric strength of the hand and forearm muscles, in kilograms
	9 Peg hole test	Measure of fine motor skill, measured in minutes/seconds
Massage therapy	Massage therapy treatment index*	Composite of factors assessing patient, converts to a percentage and is measured each session
	Muscle texture/tension	Is the muscle hyper/hypotonic, spastic, rigid, or atrophy
	Pain/sensation	Is the pain/sensation normal, aching, throbbing, deep, or hyperesthesia
	Response	Response to treatment, relief, decreased pain, no change, irritated, or increased pain
Therapeutic recreation	Leisure engagement scale*	The total number and the percentage out of 100
	Pre/post mood score	Measures mood, 4-point scale
	Social engagement score	Measures socialization, 4-point scale
Speech therapy	Functional communication and swallowing score	Scale 1-7, criterion-based, no standardized scores

ADL indicates activities of daily living.

\* Discipline-specific outcome measure designed for TEMPO.

**Table 2**  
Timing of Functional Mobility and Strength Metric Evaluations

Measure	Admission	Weekly Assessment	Discharge	D100 Follow-Up
6MWT	x		X	x
FMS	x	x	x	x
5STS	x	x	x	x
Grip strength	x	x	x	

The FMS was intended for patients older than 42 months and assesses transfers of supine-to-sit and sit-to-stand, ambulation, and stair negotiation. Each of the 4 functional mobility categories is assessed in a single session by the physical therapist and scored on a 7-point ordinal scale (maximum score, 28) as follows: 0 = unable to complete, 1 = dependent, 2 = maximum assistance, 3 = moderate assistance, 4 = minimum assistance, 5 = contact guard assistance, 6 = stand by assistance, and 7 = independence. The score was converted into a percentage (patient score divided by 28 and multiplied by 100) to assess FMS changes over time.

The Bayley-3 gross motor subtest was used to assess gross motor milestones for patients ages 42 months and younger and is a developmental test that incorporates milestones including rolling, sitting, standing, and walking [20]. The test provides scaled scores that are calculated from raw scores and interpreted into descriptive categories of developmental level of skills. These scores were translated to an FMS (Supplemental Table 1).

*Six-m. inute walk test*

The 6MWT was used to assess aerobic endurance capacity. The test was administered by the patient’s primary treating physical therapist per the American Thoracic Society guidelines [21]. For infection control, the 6MWT was completed in the Bone and Marrow Transplant department hallway with a path of 125 feet. Vitals were assessed before and after test administration. If applicable and developmentally appropriate, patients were asked to manage their intravenous pole throughout the test. Assistive devices were used for safe ambulation as needed.

*Five . times sit-to-stand test*

The 5 times sit-to-stand (5STS) test assesses functional strength for patients [22,23] and is feasible for completing within a hospital setting. This outcome measure was used when the patient was able to be seated on a stable surface with knees and hips at a 90 degree angle and feet flat on the

floor. Without using upper extremities, the patient was instructed to complete 5 STS transfers as quickly as possible. The patient’s time was recorded in seconds.

*Grip strength*

Isometric hand grip strength is a valid, reliable, and feasible measure used in a pediatric hospital setting to assess functional strength [24,25]. Hand grip strength is measured with a hand-held dynamometer (B&L Engineering Division of Pincso, Inc. Santa Ana, CA). Each patient is seated with his or her back supported. Strength is recorded using the dominant hand, and the 1 repetition maximum is recorded in kilograms [26].

**Project Flow**

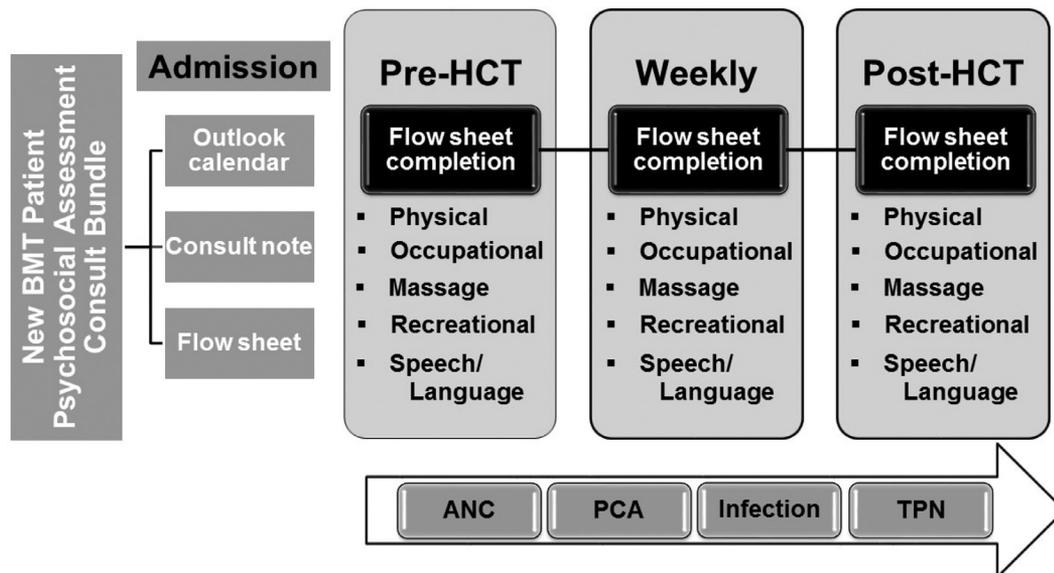
Patients and their families were informed about the TEMPO project at preadmission meetings and on admission. On admission for HCT a consult bundle, which includes CTS and psychosocial services, is entered for each patient (Figure 1). Each discipline establishes a scheduled therapy time and documents within the electronic medical record flowsheet as well as formally documents daily therapy as a discipline-specific note. Therapy frequency includes evaluations at beginning and end of hospital admission, daily treatment sessions, weekly assessments, and at D100 follow-up (Figure 1).

**Resource Utilization**

Resource utilization metrics included LOS, duration of total parenteral nutrition and patient-controlled analgesia, number of infections, and number of readmissions by D100. LOS was defined as the number of inpatient days from the date of admission for transplant until the date of discharge. Durations of total parenteral nutrition and patient-controlled analgesia were the number of inpatient days a patient received intravenous nutrition or pain medication, respectively. Number of infections included all microbiologically or radiographically documented infections for which antimicrobial therapy was started during admission for transplant.

**Statistical Analysis**

For the purpose of this study functional mobility, strength, and resource utilization were the primary focus of outcomes. All data were summarized using descriptive statistics. Frequency and percentages were given for qualitative variables and mean and standard error or median and range for continuous variables. Demographic and clinical information were compared between the historical and TEMPO cohorts using nonparametric statistical methods. To assess differences in TEMPO measurements, such as FMS, 6MWT, 5STS test, and grip strength, over the transplant admission from



**Figure 1.** Project flow during the TEMPO QI project. The TEMPO project is a multidisciplinary approach using standard-of-care practices among the CTS and psychosocial services to objectively measure physical stamina in pediatric patients admitted for HCT. All pediatric HCT patients are offered participation in TEMPO. At the time of transplant admission, services are consulted through a care bundle order within the electronic medical record (EMR), and baseline assessments are recorded in flowsheets within the EMR. Service disciplines coordinate care times for patient assessment using an Outlook (Microsoft, Redmond, WA) calendar. Disciplines perform daily treatment sessions and evaluations at the beginning and end of HCT admission, weekly during admission, and at D100 follow-up. Resource utilization was also captured retrospectively and included length of admission for initial HCT, time until neutrophil engraftment (absolute neutrophil count [ANC]), duration of patient-controlled analgesia (PCA) and total parenteral nutrition (TPN), number of microbiologically or radiographically documented infections for which antimicrobial therapy was started, and number of readmissions before D100.

evaluation to D100, linear mixed-effects models were used to account for the repeated nature of the data. Tukey-adjusted *P* values were calculated to compare time points. All *P* values were 2-sided, and *P* < .05 was considered to be statistically significant. Statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, NC) and GraphPad Prism, version 7 (GraphPad Software, La Jolla, CA).

## RESULTS

### Patient Demographics

Patient demographics and transplant information are presented in Table 3. Data from 89 pre-TEMPO and 41 TEMPO patients were available for statistical analyses. Median age, gender, race/ethnicity, disease indication for allogeneic HCT, conditioning regimen intensity, graft source, and time to neutrophil engraftment were similar between the patient cohorts. The only significant difference was more matched related donors in the pre-TEMPO transplant cohort. Of the 41 TEMPO patients, 34 completed at least 1 physical strength, functional mobility, or endurance metric at D100 at the time of data analysis.

**Table 3**  
Patient Demographics

Characteristic	Pre-TEMPO (n = 89)	TEMPO (n = 41)	<i>P</i>
Median age at transplant, yr (range)	7.0 (.1-25.0)	10.0 (.1-23.0)	.34
Age group			.67
<42 mo	26 (29.2)	9 (22.0)	
42 mo to 12 yr	30 (33.7)	16 (39.0)	
>12 yr	33 (37.1)	16 (39.0)	
Male	48 (53.9)	25 (61.0)	.45
Race/ethnicity			.47
Non-Hispanic white	55 (61.8)	28 (68.3)	
Black/African American	19 (21.3)	7 (17.1)	
Hispanic/Latino	3 (3.4)	1 (2.4)	
Asian	8 (9.0)	1 (2.4)	
Biracial or other	4 (4.5)	4 (9.8)	
Transplant disease indication			.76
Leukemia	40 (44.9)	20 (48.8)	
Lymphoma	3 (3.4)	3 (7.3)	
Solid cancer	1 (1.1)	1 (2.4)	
Bone marrow failure	10 (11.2)	4 (9.8)	
Nonmalignant disorder	35 (39.3)	13 (31.7)	
Graft source			.061
Bone marrow	70 (78.7)	30 (73.2)	
Peripheral blood stem cells	5 (5.6)	8 (19.5)	
Single umbilical cord blood	12 (13.5)	3 (7.3)	
Double umbilical cord blood	2 (2.3)	0 (.0)	
Donor type			.017
Matched related	30 (33.7)	6 (14.6)	
Matched unrelated	57 (64.0)	31 (75.6)	
Haploidentical	2 (2.3)	4 (9.8)	
Conditioning regimen intensity			.39
Myeloablative	59 (66.3)	24 (59.5)	
Reduced intensity/nonmyeloablative	30 (33.7)	17 (40.5)	
Total body irradiation-containing	26 (29.2)	10 (24.4)	.57
ANC engraftment	18 (8-52)	18.5 (6-28)	.67

Values are n (%) unless otherwise defined. Neutrophil engraftment was defined as the first 3 consecutive days that the absolute neutrophil count (ANC) was  $\geq 500/\mu\text{L}$ .

### TEMPO Therapy Intervention Is Safe

Patients participating in TEMPO completed therapeutic activities and exercises that were individualized, developmentally appropriate, and tailored to their level of functioning and tolerance. No patient experienced any detrimental physical injury during participation in TEMPO. Therapists followed current recommendations for intervention relative to their clinical status, including but not limited to hemoglobin levels and platelet counts [5,12].

### TEMPO Participation Maintains Functional Mobility, Endurance, and Strength

Because the TEMPO project's primary objective was to maintain functional mobility in patients during hospitalization, we compared each patient's FMS at the time of admission with those at the time of discharge. As depicted in Figure 2A, mean  $\pm$  SEM FMS at admission and discharge were  $83\% \pm 4\%$  and  $87\% \pm 3\%$ , respectively (*P* = .67). The mean FMS significantly improved from post-transplant peak to discharge ( $54\% \pm 6\%$  versus  $87\% \pm 3\%$ , respectively; *P* < .0001). Interestingly, mean FMS scores were maintained at D100 evaluation ( $95\% \pm 3\%$ ) and were not statistically different from those at either admission or discharge (each time point versus D100, *P* > .05) (Figure 2A).

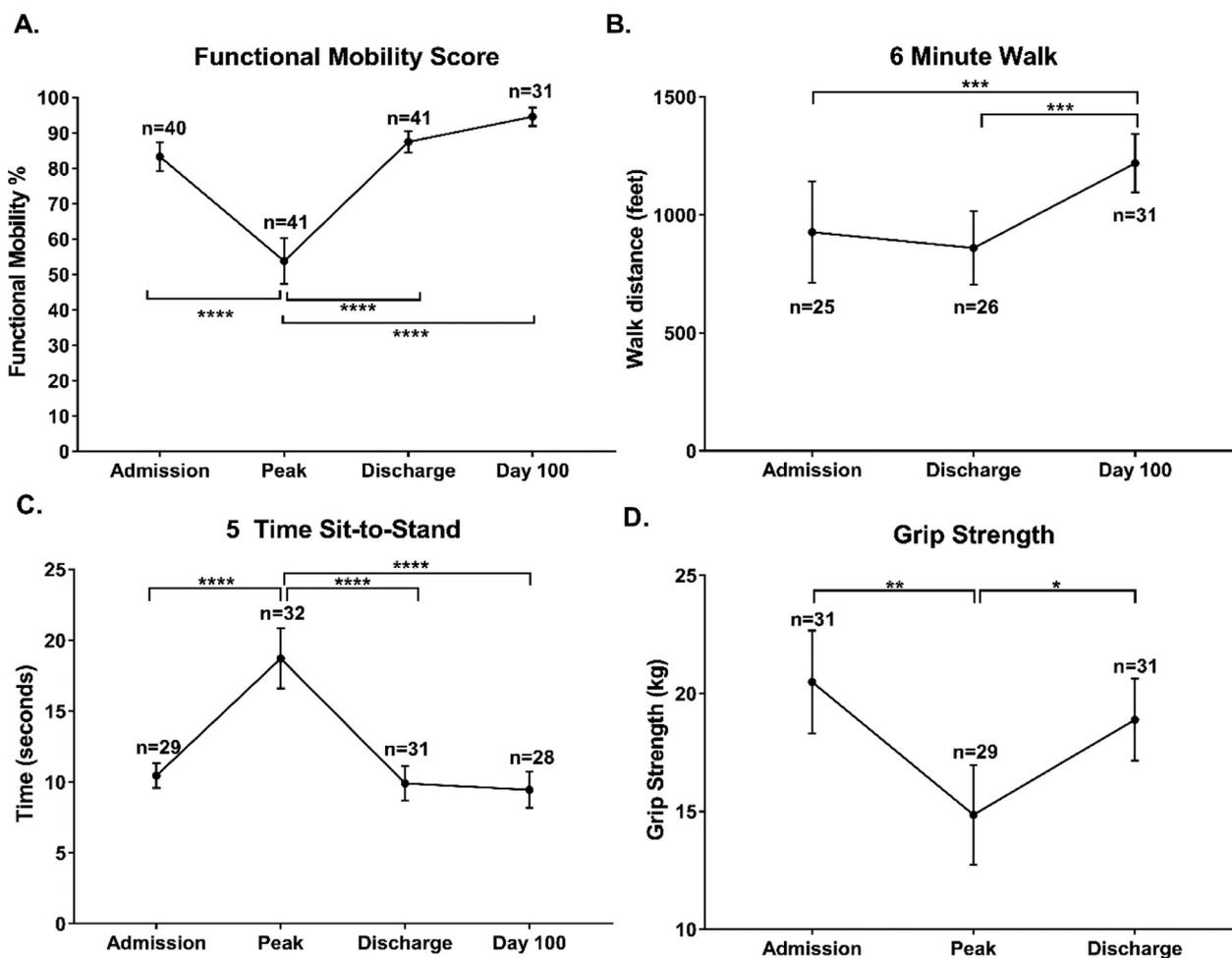
We next assessed whether other metrics of physical activity, functional mobility, strength, and endurance were maintained throughout hospitalization and at D100. Like FMS, cardiorespiratory fitness, as measured by distance (mean  $\pm$  SEM) achieved over a 6MWT, did not statistically differ between admission and discharge ( $927 \pm 104$  versus  $860 \pm 76$  feet, respectively; *P* = .94) (Figure 2B). However, a significant increase in the mean distance recorded for the 6MWT was noted at D100 compared with discharge ( $1219 \pm 60$  versus  $860 \pm 76$  feet, respectively; *P* = .007). Similarly, 6MWT distance at admission was significantly less than at D100 ( $927 \pm 104$  versus  $1209 \pm 60$  feet, respectively; *P* = .0023) (Figure 2B).

Lower extremity functional strength performance (mean  $\pm$  SEM), as measured by time (seconds) to perform 5STS movements, expectedly decreased from admission to post-transplant peak ( $10 \pm 1$  versus  $19 \pm 2$  seconds, respectively; *P* < .0001). Thereafter, 5STS time significantly improved from the peak post-transplant time to discharge ( $19 \pm 2$  versus  $10 \pm 1$  seconds, respectively; *P* < .0001) (Figure 2C). Like FMS and 6MWT, no significant difference was observed between admission and discharge (*P* = .98), and improvement in 5STS was sustained at D100 when compared with the peak post-transplant time ( $19 \pm 2$  versus  $9 \pm 1$  seconds, respectively; *P* < .0001) (Figure 2C).

Handgrip strength (mean  $\pm$  SEM), as measured by handheld dynamometry with a 1-repetition maximum, showed similar improvement from post-transplant nadir to discharge. Handgrip strength expectedly decreased from admission to post-transplant nadir ( $20 \pm 2$  versus  $15 \pm 2$  kg, respectively; *P* = .0022) and then significantly improved from nadir to discharge ( $15 \pm 2$  versus  $19 \pm 2$  kg, respectively; *P* = .0282) (Figure 2D). No measurements of handgrip strength were taken at D100.

### TEMPO Participation Was Not Associated with Significant Decreases in Resource Utilization

Next, we investigated the association of TEMPO participation with resource utilization. Data from 92 historical control subjects (pre-TEMPO) and 42 TEMPO transplant patients were available for resource utilization analyses. Compared with pre-TEMPO patients, the TEMPO cohort had a decreased median



**Figure 2.** Outcomes of functional endurance and strength for TEMPO participants. Physical performance of patients participating in TEMPO was evaluated over the course of the hospitalization to assess baseline, post-transplant drop, recovery, and maintenance of physical functioning as measured by (A) FMS, (B) 6MWT, (C) 5STS, and (D) grip strength. Figures are displayed as mean ± SEM. (C and D) “Peak” refers to the worst post-transplant measurement observed during weekly evaluations. The time point “Admission” is the initial pretransplant evaluation of physical function. D100 measurements of grip strength were not performed. Linear mixed-effects models were used for comparing measurements across time points, and *P* values were adjusted using the Tukey method for multiple comparisons. Statistical significance are denoted by asterisks: \**P* < .05, \*\**P* < .01, \*\*\**P* < .001, \*\*\*\**P* < .0001.

days of patient-controlled analgesia use, yet this difference was not statistically different (14 days [range, 0 to 63] versus 10 days [range, 0 to 40], respectively; *P* = .087) (Table 4). All other resource utilization metrics were not significantly different between pre-TEMPO and TEMPO patients. No differences were observed, even when controlling for donor type (data not shown). Further analyses incorporating data stratification by

conditioning intensity (Supplemental Table 2) or patient age (Supplemental Table 3) also did not reveal significant differences between the patient cohorts.

**DISCUSSION**

Studies support exercise through physical therapy intervention, resulting in positive outcomes for mobility, endurance, and strength during admission for HCT [6,7,27,28]. We implemented a multidisciplinary QI project for standardizing the approach to decreasing physical deconditioning in pediatric patients admitted for initial HCT. TEMPO emphasizes the importance of physical activity, mindfulness, and relaxation [29] through use of CTS and psychosocial services. Herein, results show that TEMPO demonstrated 3 main benefits. First, the project showed that a multidisciplinary team approach to mobility and exercise is safe for pediatric patients during HCT. Second, a standardized intervention throughout HCT admission demonstrates a strong correlation between an increase in functional mobility and strength during HCT admission and follow-up at D100. Third, this multimodal, standard-of-care approach for patients undergoing allogeneic HCT may ultimately decrease resource utilization with more patient participation.

**Table 4**  
Cohort Comparisons in Resource Utilization

Variable	Pre-TEMPO (n = 92)	TEMPO (n = 42)	<i>P</i>
LOS, days	32 (18-107)	35 (16-113)	.68
TPN use, <sup>a</sup> days	8 (0-70)	12 (0-82)	.66
PCA use, <sup>†</sup> days	14 (0-63)	9 (0-40)	.09
No. of infections	1 (0-5)	1 (0-5)	.93
Readmissions by D100	0 (0-6)	0 (0-3)	.78

Values are median (range). Mann-Whitney U test used for median comparisons, *P* values are unadjusted for multiple comparisons, due to nonsignificance. PCA indicates patient-controlled analgesia; TPN, total parenteral nutrition.

<sup>a</sup> TPN use: 64/92 (69.6%) pre-TEMPO patients vs. 28/42 (75.4%) TEMPO patients, *P* = .74.

<sup>†</sup> PCA use: 70/92 (76.1%) pre-TEMPO patients vs. 27/42 (64.3%) TEMPO patients, *P* = .16.

To our knowledge, TEMPO is the first multidisciplinary team approach for pediatric patients undergoing HCT that provides regular therapy intervention with a strong focus on developmentally appropriate education and establishing a culture of mobility. TEMPO confirms results of prior pediatric studies emphasizing the importance and positive effect of exercise and physical activity during HCT admission [2,7,11,14]. Whereas current literature highlights the effect of single discipline exercise programs, we present the success of a multidisciplinary project that focuses on exercise, functional mobility, strength, and physical activity; incorporates regular interventions 3 to 5 times per week for 60 minutes [2]; and uses validated assessment tools (ie, FMS) to track patient progress and task-specific sustainability.

Currently, published literature focusing on exercise during pediatric HCT reported difficulty in maintaining recommended physical activity outcomes or compliance at follow-up for cancer survivors [7,30]. Limited research is available for an inpatient exercise program with post-HCT follow-up. As the first pediatric structured exercise program during HCT with assessment time points at pre-HCT, discharge, and 1-month follow-up Yildiz Kabak et al. [7] demonstrated significant improvement in physical function and functional performance for the intervention group at the time of discharge. However, these beneficial results were not seen in the follow-up period. DeFor et al. [31] found in adults a greater compliance in physical activity in the follow-up period within the exercise group, compared with the control group, that was attributed to improved function. Specifically, our analysis at D100 shows significant improvement of endurance from discharge to D100. Similarly, DeFor et al. [31] demonstrated that a culture of mobility, physical activity, and exercise promoted during transplant admission led to improved outcomes at follow-up. In this regard, randomized controlled trials are needed to determine the effect of a multidisciplinary, pediatric inpatient exercise program within the follow-up period.

No clear recommendation on best-dosing practice for exercise exists for pediatric patients undergoing HCT [5]. Adult literature supports exercise 2 to 3 times a week for patients during HCT [6], which is consistent with usual care for therapies at our institution before TEMPO implementation. Current pediatric studies that explore therapy intervention for pediatric patients during HCT often include aerobic and strengthening activities [2,7,32], yet no consensus on an ideal exercise prescription exists [2]. By offering moderate-intensity therapy intervention through multiple disciplines 5 days per week, we hypothesized that functional mobility, endurance, and strength would be maintained throughout admission for HCT. In this regard, patients participating in TEMPO had measurable attenuation in physical deconditioning commonly measured in HCT patients. Patients' returns to baseline level of functional mobility and strength at time of discharge coupled with emphasis on physical activity provided during HCT admission may enable patients to further improve functional mobility, strength, and endurance at D100 follow-up. Many studies report that exercise leads to a stabilization effect on physical performance during the inpatient period of HCT [6,28]. Similar to these reports, patients participating in TEMPO showed improved endurance at D100. This finding highlights the novelty of TEMPO by providing a framework for maximizing physical function and embracing a culture of physical activity that combine to result in positive, sustainable patient outcomes.

TEMPO participation was not associated with significant decreases in resource utilization. As a QI project, TEMPO was not adequately powered to observe differences in patient

cohorts, because lower patient numbers limited further data stratification analyses (Supplemental Table 3). Notwithstanding, potential cost savings may be observed in future analyses using larger numbers of patients. For example, at our institution the daily Bone and Marrow Transplant department inpatient room and board charge is \$8500 per day, a price that does not include nursing, pharmacy, and physician charges. The estimated total charge for CTS for consult evaluation and aggregate follow-up throughout TEMPO is approximately \$11,238.25 for an average 4-week bone and marrow transplant admission. Hence, any potential decrease in LOS alone noted in TEMPO-participating patients would equate to a cost savings when compared with the total CTS care charge.

TEMPO itself and its reported results have several limitations. First, as a QI project, TEMPO data were not captured with the rigor of a clinical trial. Second, we could not adequately perform statistical analyses incorporating data stratification by age and conditioning regimen because of the small numbers of patients. As the project continues these numbers will increase, and additional results will be available. Third, the inability to provide comparison for functional mobility, strength, and endurance in pre-TEMPO participants precludes direct comparisons between the patient cohorts. Fourth, relative to physical therapy intervention, TEMPO does not protocol strengthening or aerobic activity. Fifth, we found that within the pediatric population, it is difficult to fully comply with a specific protocol because of the vast differences in physical and cognitive development between ages among patients. Finally, TEMPO did not address quality of life metrics in its assessments. To this end, TEMPO is currently gathering quality of life data to address this limitation.

In summary, TEMPO provides a novel approach to regular multidisciplinary therapy intervention to establish a standard-of-care for pediatric patients during HCT admission that demonstrates improved functional mobility, functional strength, and endurance while potentially reducing resource utilization. Future directions include revision of the FMS to identify greater sensitivity in differentiating changes in functional mobility and validating the FMS as a reliable and valid instrument to measure functional mobility for pediatric patients undergoing HCT; establishing a plan for consistent, timed quality of life measures to provide further insight into the effect of functional mobility on quality of life; and tracking aerobic activity minutes in physical therapy treatment sessions to determine optimal dosing in this specific pediatric population. In conclusion, the TEMPO project highlights the opportunity to provide an integrative standard-of-care for pediatric allogeneic HCT patients, which optimizes functional mobility through regular physical activity.

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#### SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.bbmt.2019.05.004.

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