Cincinnati Children's

Best Evidence Statement (BESt)

Date: March 18, 2014

Title: Physical therapy during the hemopoietic stem cell transplant process to improve quality of life [1]

Clinical Question

P	*(Population/Problem)*	Among school aged children and adolescents receiving hemopoietic stem cell transplant (HSCT)*
I	*(Intervention)*	does physical therapy (PT) intervention (active participation in mobility, endurance, strength exercise)
C	*(Comparison)*	compared to no intervention
O	*(Outcome)*	improve the patient's quality of life (QoL)*?

***Definitions** for terms marked with * may be found in the Supporting Information section.*

Target Population for the Recommendation

School aged children, adolescents and young adults age 6 to 21 years receiving HSCT (during both inpatient and outpatient phases).

Exclusions

- Children aged 0 to 6 years old and adults older than 21 years
- Individuals unable to cognitively participate (unable to follow commands or instructions) in a structured exercise program

Recommendations

1. It is strongly recommended that physical therapists provide exercise therapy, including endurance and strength training, throughout the HSCT process to reduce/minimize the effects of immobility and consequences of the HSCT treatment, which contributes to improved QoL *(Wolin 2010 [1a], Wiskemann 2008 [1b], Baumann 2011 [2b], Hacker 2011 [2b], Baumann 2010 [2b], Hayes 2004 [Incl in Wiskemann, 2008-3b, Included in Wolin 2010.])*.

   Note 1: Side effects of immunosuppressive therapy and bed rest can include loss of muscle mass, strength and endurance *(Wolin 2010 [1a], Knols 2005 [1a], Wiskemann 2008 [1b], Baumann 2011 [2b])*.

   Note 2: Pediatric patients benefitted from frequent, supervised intervention, suggesting the need for higher frequency to achieve desired outcomes *(Wolin 2010 [1a])*.

   Note 3: Full recovery from HSCT is a 3 to 5 year process. Recovery may be accelerated by exercise interventions to increase work related capabilities, improve social support and manage depression *(Syrjala 2004 [4a])*.

2. It is recommended that a physical therapist provide the following interventions in the pre-transplant phase:
   a. Complete a physical therapy examination to establish a baseline level of function and QoL *(Local Consensus 2013 [5])*.
   b. Make recommendations for treatment (based upon) specific to the evaluation results, as appropriate *(Wiskemann 2011 [2b], Local Consensus 2013 [5])*.
   c. Educate families regarding the benefits of structured exercise therapy throughout the HSCT process to reduce the effects of immobility and consequences of the HSCT treatment *(Local Consensus 2013 [5])*.

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Note 1: It is preferred the physical therapy examination be completed, including assessments of strength, endurance and QoL, prior to the initiation of the preparative regimen and inpatient admission for HSCT in order to obtain an accurate baseline measurement and identify needs for physical therapy intervention *(Wiskemann 2011 [2b], Local Consensus 2013 [5])*.

Note 2: Caregiver and patient education should be provided using appropriate methods including, but not limited to instructional materials or 1:1 educational sessions *(Local Consensus 2013 [5])*.

3. It is strongly recommended that during the HSCT inpatient stay, starting at admission or the initiation of the preparative treatment regimen and continuing until discharge, a physical therapist provide a supervised, low to moderate intensity exercise program to positively affect QoL, including:
   a. aerobic endurance training *(Wolin 2010 [1a], Wiskemann 2008 [1b], Knols 2010 [2a], Baumann 2011 [2b], Baumann 2010 [2b], Jarden 2009 [2b], Jarden 2007 [2b])*
   b. exercises dealing with strength, balance/coordination and flexibility *(Wolin 2010 [1a], Wiskemann 2008 [1b], Knols 2010 [2a], Baumann 2011 [2b], Baumann 2010 [2b], Jarden 2009 [2b], Jarden 2007 [2b])*

   Note 1: During the inpatient stay for HSCT, the risk of infection is high and physical activity options may be restricted, therefore equipment and exercise options may be reduced *(Wolin 2010 [1a], Local Consensus 2013 [5])*.

   Note 2: A higher frequency exercise program (i.e. 5 times per week or daily) is beneficial in stabilizing physical performance *(Wolin 2010 [1a], Wiskemann 2008 [1b], Jarden 2009 [2b])*

   Note 3: A low to moderate intensity exercise program for 30-60 minutes (with rest intervals as needed) may include:
   a. aerobic exercise at 50 to 75% of the heart rate max and a Rate of Perceived Exertion (RPE) of 10 to 13
   b. strengthening/stretching exercises at an RPE of 10 to 13
   c. progressive relaxation exercises at an RPE of 6 to 9 *(Jarden 2009 [2b], Local Consensus 2013 [5])*
4. It is recommended that during the HSCT inpatient stay, a physical therapist provide interventions to promote functional mobility, including transfers, walking and stair climbing *(Baumann 2011 [2b], Local Consensus 2013 [5])* and relaxation through progressive relaxation exercises. *(Jarden 2009 [2b], Jarden 2007 [2b])*
5. It is strongly recommended that following discharge from the HSCT inpatient stay, a physical therapist provide a supervised, scheduled moderate intensity exercise program (with the goal to return the individual to functional baseline level or until progress is no longer demonstrated) including the following:
   a. aerobic endurance training *(Wolin 2010 [1a], Wiskemann 2008 [1b], Knols 2010 [2a], Wiskemann 2011 [2b])*
   b. exercises dealing with strength, balance/coordination and flexibility *(Wolin 2010 [1a], Wiskemann 2008 [1b], Knols 2010 [2a], Wiskemann 2011 [2b])*

   Note 1: The exercise program is designed to reduce fatigue, improve physical function and positively affect QoL *(Wiskemann 2011 [2b])*.

   Note 2: A minimum frequency and duration (i.e. 2x/week for 6 to 12 weeks) may be beneficial at this stage of recovery *(Knols 2005 [1a], Local Consensus 2013 [5], Hayes 2004 [Incl in Wiskemann, 2008-3b, Included in Wolin 2010.])*.

   Note 3: A moderate intensity exercise program for 30 to 60 minutes may include:
   a. aerobic exercise starting at 50 to 60% and increasing up to 70 to 80% of the heart rate max and a RPE up to 15
   b. strengthening/stretching exercises at an RPE of 10 to 13 *(Knols 2010 [2a], Local Consensus 2013 [5])*
6. It is recommended that during outpatient program following HSCT a physical therapist provide interventions to promote functional mobility, including transfers, walking and stair climbing *(Knols 2010 [2a], Local Consensus 2013 [5])*.

Discussion/Synthesis of Evidence related to the recommendations

The trend in the reviewed literature supports structured exercise throughout the HSCT process *(Wolin 2010 [1a], Wiskemann 2008 [1b], Knols 2010 [2a], Hacker 2011 [2b], Wiskemann 2011 [2b], Jarden 2009 [2b])*. Benefits to individual function and QoL were recognized in numerous studies in both inpatient and outpatient settings *(Wolin 2010 [1a], Baumann 2011 [2b], Hacker 2011*

[2b], Baumann 2010 [2b], Jarden 2009 [2b], Dimeo 1997 [2b]). Hayes (2004) identified a relationship between fitness and QoL, with individuals with higher levels of fitness experiencing higher QoL. In addition, Jarden (2009) identified trends suggesting benefits of supervised aerobic and resistive exercise on QoL, including improved psychological well being and reduced fatigue. Although more research to support the benefits of exercise would be beneficial, the existing preliminary data is promising *(Wolin 2010 [1a])*.

Although some of the evidence had limitations, such as a lack of strong methodology, heterogeneous diagnoses with different treatment protocols and predominantly adult subjects, there was sufficient consistency among the authors to support exercise throughout the HSCT process *(Wolin 2010 [1a], Knols 2005 [1a], Tsimicalis 2005 [1a], Tremolada 2009 [1b], Wiskemann 2008 [1b], Knols 2010 [2a], Baumann 2011 [2b], Hacker 2011 [2b], Wiskemann 2011 [2b], Baumann 2010 [2b], Jarden 2009 [2b], Syrjala 2004 [4a])*. This in-depth literature review established a strong and growing body of evidence to support the benefits of regular physical exercise/activity for adults undergoing HSCT*(Wolin 2010 [1a], Wiskemann 2008 [1b], Baumann 2011 [2b], Hacker 2011 [2b], Baumann 2010 [2b])*. A smaller body of evidence demonstrated the benefit of supervised exercise interventions with children undergoing HSCT *(Wolin 2010 [1a])*.

There is strong evidence to suggest that multimodal physical activity interventions during the HSCT process, including strength and aerobic training, are safe and positively impact functional outcomes and QoL *(Wolin 2010 [1a], Wiskemann 2008 [1b], Baumann 2011 [2b], Wiskemann 2011 [2b], Baumann 2010 [2b], Jarden 2009 [2b])*. Exercise performed during the inpatient HSCT admission can minimize loss of strength/physical function and benefit cardiorespiratory fitness/endurance performance *(Wolin 2010 [1a], Wiskemann 2008 [1b], Knols 2010 [2a], Baumann 2011 [2b], Baumann 2010 [2b], Jarden 2009 [2b])*. There was also strong evidence supporting the continuation of structured exercise, with a focus on strength, endurance and physical function, following discharge from the inpatient setting, which can lead to improved function and psycho-social well-being *(Wolin 2010 [1a], Wiskemann 2008 [1b], Knols 2010 [2a], Wiskemann 2011 [2b], Jarden 2009 [2b], Local Consensus 2013 [5])*. It was noted that patients generally did better when they participated in exercise at the facility where they received the transplant *(Wolin 2010 [1a])*.

Wolin (2010) found strong evidence reporting a benefit on body composition, with evidence also identified for benefit on cardiorespiratory fitness, fatigue, muscle strength, physical function and quality of life within the systematic review. Thirteen of the studies in this systematic review involved pediatric patients and demonstrated evidence that exercise intervention positively impacts muscle strength and cardiorespiratory fitness. Two of these 13 studies were high quality intervention studies involving pediatric patients undergoing HSCT. One of the two pediatric studies reported aerobic and strength activities done by children during inpatient HSCT hospitalization resulted in significantly increased fitness and muscle mass without affecting immune cell recovery *(Wolin 2010 [1a])*. The second study identified that pediatric survivors of hematologic cancers who received HSCT and underwent an outpatient aerobic and strength program demonstrated significant improvement in muscle strength, functional mobility, aerobic fitness and QOL *(Wolin 2010 [1a])*.

Similarly, in a systematic review by Knols (2005) general results of the reviewed studies indicate that exercise during and after cancer treatment is effective in reducing symptoms and improving physical and psychological functioning of adult patients *(Knols 2005 [1a])*.

Wiskeman (2008) noted physical exercise in adults undergoing HSCT may have a stabilization effect on physical performance during the inpatient admission, with significantly less loss of endurance compared to controls. Aerobic exercise and resistance training were related to improvements in endurance and strength performance during the outpatient period following HSCT. Overall, the reviewed studies showed improved QoL in HSCT patients who participated in exercise programs *(Wiskemann 2008 [1b])*.

Tremolada (2009) performed a systematic review related to short and long-term QoL and psychological effects in children who underwent a HSCT. The author suggested a child's isolation experience through HSCT may be traumatic and adversely impact QoL.

While there was no published evidence related to timing of initiation of an exercise program for this patient population, early education and awareness of the benefits of exercise can be beneficial when provided in the pre-transplant phase

(Local Consensus 2013 [5]). A baseline physical therapy assessment prior to the inpatient admission, accomplished in a less restricted environment prior to the effects of the preparative regimen, could result in a more accurate record of function and outcomes over time *(Local Consensus 2013 [5])*. Interventions can be offered earlier to address identified problem areas and therefore, impact QoL *(Wiskemann 2011 [2b], Local Consensus 2013 [5])*.

Individuals who participated in exercise during HSCT were found to have higher QoL scores on outcome testing than those who did not exercise *(Wolin 2010 [1a], Knols 2005 [1a], Baumann 2011 [2b])*. In addition, physical exercise interventions are feasible without adverse effects and well accepted during HSCT *(Wolin 2010 [1a], Wiskemann 2008 [1b], Jarden 2009 [2b])*. While there was no specific exercise program identified, there were common areas of focus, including strength, endurance and flexibility*(Wolin 2010 [1a], Wiskemann 2008 [1b], Knols 2010 [2a], Baumann 2011 [2b], Baumann 2010 [2b], Jarden 2009 [2b], Dimeo 1997 [2b])*. In addition, there was consistent support for high frequency, low intensity structured exercise during this portion of the HSCT process *(Knols 2005 [1a], Knols 2010 [2a], Jarden 2009 [2b], Local Consensus 2013 [5])*.

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IMPLEMENTATION

Applicability Issues

HSCT patients need to be identified early by members of the health care team in order to facilitate referral for PT evaluation of appropriate patients in the pre-HSCT phase. Hindrances to early referral may include patient geographic location, medical status and schedule conflicts within the HSCT work-up *(Local Consensus 2013 [5])*.

Exercise intervention should be provided by physical therapists who have knowledge of the HSCT process. Additional staffing resources need to be identified, to cover the demands for high utilization of therapy resources *(Local Consensus 2013 [5])*.

Collaboration and planning is required to expedite management of patient care across inpatient and outpatient settings, including appropriate notification, referral and sharing of information by inpatient and outpatient physical therapists *(Local Consensus 2013 [5])*.

Relevant CCHMC Tools for Implementation

- Bone Marrow Transplant-OT Knowing Note
- Bone Marrow Transplant-PT Knowing Note
- OTPTTR 1255 Immunosuppressed Patients, Management of
- ICRM-731 Standard Precautions
- ICRM-732 Airborne Precautions
- ICRM-733 N-95 Airborne Precautions
- ICRM-734 Droplet Precautions
- ICRM-735 Respiratory Precautions
- ICRM-736 Contact Precautions
- ICM-737 STRICT Precautions
- ICRM-738 Protective Precautions
- ICRM-739 STRICT Protective Precautions
- Best Evidence Statement: School-aged and Adolescent Bone Marrow Transplant (BMT) Recipients: Quality of Life Interventions

Outcome or Process Measures

There is an opportunity to improve patient outcome by providing comprehensive PT services to patients undergoing HSCT. PT intervention should be focused on maximizing functional abilities and providing appropriate education and support to facilitate an optimal return to home and community post HSCT. Possible outcome measures may include improved function and quality of life, as measured by standardized control measures, quality of life measurement scales and other disease/problem specific objective measures of health outcomes. Standardized measures to assess function include the 6 Minute Walk Test, the Pediatric Balance scale, the Pediatric Reach Test and the Timed Floor to Stand. Quality of life measures that may be useful include the PedsQL Cancer Module.

SUPPORTING INFORMATION

Background/Purpose of BESt Development

Hemopoietic stem cell transplant can have profound and lasting adverse effects on an individual's physical and psychological well-being *(Wolin 2010 [1a], Tsimicalis 2005 [1a], Baumann 2011 [2b], Jarden 2009 [2b])*. The HSCT treatment results in a decline in physical functioning related to loss of muscle mass and muscle strength and muscle atrophy is associated

with several transplant related problems, including immunosuppressive therapy, bed rest and drug toxicities *(Wolin 2010 [1a], Knols 2005 [1a], Wiskemann 2008 [1b], Baumann 2011 [2b])*. The experience of the isolated environment and the stress of a life threatening illness, resulting in fatigue, anxiety, depression and fear may also contribute to negative effects on physical function and QoL *(Tsimicalis 2005 [1a])*.

Chemotherapy results in anemia, which can affect cardiorespiratory fitness and cause skeletal muscle atrophy and weakness. Chemotherapy toxicities can impede adequate nutrition needed to maintain muscle mass. Radiation therapy can lead to lung fibrosis resulting in decreased pulmonary function. Cranial radiation in childhood has been strongly linked to physical inactivity during adulthood *(Wolin 2010 [1a])*. Individuals being treated for pediatric cancers in particular, tend to experience adverse effects of treatment including impaired growth, decreased neurological and/or cardiac function, endocrine complications, osteoporosis and obesity *(Wolin 2010 [1a])*. All of these side effects can lead to a decline in physical functioning and contribute to experiences of fatigue, anxiety and depression *(Wolin 2010 [1a])*.

In addition to the symptoms and side effects the treatment requires prolonged isolation, which can also impede functional activity and impair psychological well-being *(Tremolada 2009 [1b])*. Activity restrictions and limited exercise options hinder the individual's ability to sustain physical function throughout this process. Mentally, the challenges pediatric patients experience while undergoing HSCT may have a long lasting impact on QoL *(Tremolada 2009 [1b])*.

Because survival rates have increased, the need to address these quality of life issues and the impact of functional impairment has grown significantly. It is important to consider not only immediate survival, but also long term recovery of this patient population. Cincinnnati Children's Hospital Medical Center has a large hemopoietic stem cell transplant program and physical therapy that is a integral part of the intradiscplinary program including focus on functional long term recovery. The purpose of developing this BESt was to identify physical therapy interventions that can improve function and positively impact outcomes, thereby positively impacting HSCT pediatric patients' QoL.

Definitions

Hematopoietic stem cell transplantation (HSCT): also known as Bone Marrow Transplant, is the transplantation, or replacement, damaged or destroyed hematopoietic stem cells with healthy new stem cells. The HSCT process is divided into pre, during and post phases:

Pre-HSCT: is the period of time prior to HSCT admission. It is the time during which the individual may be undergoing evaluation as a candidate for HSCT.

During-HSCT: admission is the phase starting at hospital admission for HSCT and continues until hospital discharge. This phase includes the delivery of the preparative regimen. Days during the HSCT admission are characterized by negative numbers counting down to day zero, which signifies the day in which the new stem cells are infused and then counts up in positive numbers from the day of transplantation. During this time the patient is very immunocompromised and is limited to in-room activity.

Post–HSCT: begins after the patient is discharged from the hospital for the transplant process. The patient must usually remain in close proximity to the treating facility for at least 100 days post-transplant.

Quality of Life: A concept that focuses on the individual's perception of one's position in life, in the context of the culture and value system in which one lives and in relationship to goals, expectations, standards and concerns. Domains of quality of life are those that encompass physical, psychological, social, role functioning and spiritual issues. For children, quality of life measures should include assessment of cognitive functioning, autonomy, body image and family relationships, along with children's expectations and experiences.

In the health care context the most restricted concept of quality of life, the notion of health related quality of life (HRQoL), refers to the subjective and objective impact of dysfunction on the physical, psychological and social aspects of quality of life that are influenced by an individual's disease and its treatment *(Tanzi 2011 [1b])*.

Search Strategy

Databases: Trip, PubMed Clinical Queries, Pediatric Physical Therapy, Ebsco, Cinahl Plus with full text, PEDro, Medline, Cinahl, Cochrane, CAOT, OT Seeker, OTEvidence, Center for Evidence Based Medicine, National Guideline Clearing House, Google Scholar, Rehabilitative Reference Center, Cochrane library

Search Terms: exercise, bone marrow transplant, stem cell transplant, children, pediatric, childhood, physical therapy, quality of life, pediatric, cancer, physical activity, bone marrow transplant + physical therapy, bone marrow transplant + rehabilitation, bone marrow transplant + child + rehabilitation, bone marrow transplant + quality of life , brain tumors, therapy, occupational therapy, autologous bone marrow transplant, fatigue + bone marrow transplant, daily living + bone marrow transplant, self-care + bone marrow transplant

Limits and Filters: Limits and filters were applied randomly to individual databases by multiple people participating in the search. Those include: 2000-2011, pediatrics.

Last Search Date: 12/2013

Relevant CCHMC Evidence-Based Documents

Best Evidence Statement: School-aged and Adolescent Bone Marrow Transplant (BMT) Recipients: Quality of Life Interventions

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Conflicts of Interest were declared for each team member

☒ No financial conflicts of interest were found.
☒ No external funding was received for development of this BESt.
☐ The following financial conflicts of interest were disclosed:

Note: Full tables of the LEGEND evidence evaluation system are available in separate documents:

- Table of Evidence Levels of Individual Studies by Domain, Study Design, & Quality *(abbreviated table below)*
- Grading a Body of Evidence to Answer a Clinical Question
- Judging the Strength of a Recommendation *(dimensions table below)*

Table of Evidence Levels *(see note above)*

Quality level	*Definition*
1a† or 1b†	Systematic review, meta-analysis, or meta-synthesis of multiple studies
2a or 2b	Best study design for domain
3a or 3b	Fair study design for domain
4a or 4b	Weak study design for domain
5a or 5b	General review, expert opinion, case report, consensus report, or guideline
5	Local Consensus

†a = good quality study; b = lesser quality study

Table of Language and Definitions for Recommendation Strength *(see note above)*

Language for Strength	*Definition*
It is strongly recommended that… It is strongly recommended that… not…	When the dimensions for judging the strength of the evidence are applied, there is high support that benefits clearly outweigh risks and burdens. *(or visa-versa for negative recommendations)*
It is recommended that… It is recommended that… not…	When the dimensions for judging the strength of the evidence are applied, there is moderate support that benefits are closely balanced with risks and burdens.
There is insufficient evidence and a lack of consensus to make a recommendation…	

Given the dimensions below and that more answers to the left of the scales indicate support for a stronger recommendation, the recommendation statement above reflects the strength of the recommendation as judged by the development group.
(Note that for negative recommendations, the left/right logic may be reversed for one or more dimensions.)

Rationale for judgment and selection of each dimension:

1. Grade of the Body of Evidence	☒ High	☐ Moderate	☐ Low
Rationale: Strong evidence was found supporting structured exercise during the HSCT process, which can positively impact QoL *(Wolin 2010 [1a], Knols 2010 [2a], Hacker 2011 [2b], Wiskemann 2011 [2b], Jarden 2009 [2b], Hayes 2004 [Incl in Wiskemann, 2008-3b, Included in Wolin 2010.])*			
2. Safety/Harm (Side Effects and Risks)	☒ Minimal	☐ Moderate	☐ Serious
Rationale: Exercise intervention resulted in no adverse outcomes or injuries *(Wiskemann 2008 [1b], Knols 2010 [2a], Jarden 2009 [2b], Jarden 2007 [2b]).*			
3. Health benefit to patient	☐ Significant	☒ Moderate	☐ Minimal
Rationale: Trends suggest intervention during HSCT hospitalization to be feasible, safe, well tolerated and of possible benefit to QoL *(Jarden 2009 [2b], Jarden 2007 [2b])*.			
4. Burden on patient to adhere to recommendation	☐ Low	☐ Unable to determine	☒ High
Rationale: During the HSCT process, patients may be critically ill and have many side effects (i.e. emesis, nausea, pain and diarrhea) that interfere with exercise participation *(Wolin 2010 [1a], Baumann 2011 [2b])*.			
5. Cost-effectiveness to healthcare system	☐ Cost-effective	☒ Inconclusive	☐ Not cost-effective
Rationale: Improved function and quality of life may contribute to decreased costs of medical care and use of health resources over time *(Local Consensus 2013 [5])*.			
6. Directness of the evidence for this target population	☐ Directly relates	☒ Some concern of directness	☐ Indirectly relates
Rationale: The majority of studies were completed using adult subjects, which may limit the ability to apply the findings to a pediatric population.			
7. Impact on morbidity/mortality or quality of life	☐ High	☒ Medium	☐ Low
Rationale: Regular physical exercise has been shown to be effective in reducing symptoms/side effects of the HSCT treatment and improving the physical and psychological function, including quality of life of patients *(Wolin 2010 [1a], Knols 2005 [1a], Baumann 2011 [2b], Hacker 2011 [2b], Wiskemann 2011 [2b], Baumann 2010 [2b], Jarden 2009 [2b], Hayes 2004 [Incl in Wiskemann, 2008-3b, Included in Wolin 2010.])*.			

Copies of this Best Evidence Statement (BESt) and related tools (if applicable, e.g., screening tools, algorithms, etc.) are available online and may be distributed by any organization for the global purpose of improving child health outcomes.
Website address: http://www.cincinnatichildrens.org/service/j/anderson-center/evidence-based-care/bests/
Examples of approved uses of the BESt include the following:

- Copies may be provided to anyone involved in the organization's process for developing and implementing evidence based care;
- Hyperlinks to the CCHMC website may be placed on the organization's website;
- The BESt may be adopted or adapted for use within the organization, provided that CCHMC receives appropriate attribution on all written or electronic documents; and
- Copies may be provided to patients and the clinicians who manage their care.

Notification of CCHMC at **EBDMinfo@cchmc.org** for any BESt adopted, adapted, implemented, or hyperlinked by the organization is appreciated.

Please cite as: Strenk, M., Cincinnati Children's Hospital Medical Center: BESt Evidence Statement Physical therapy during the hemopoietic stem cell transplant process to improve quality of life, http://www.cincinnatichildrens.org/service/j/anderson-center/evidence-based-care/recommendations/default/, BESt 177, pages 1-9, 3/18/14

This Best Evidence Statement has been reviewed against quality criteria by two independent reviewers from the CCHMC Evidence Collaboration. Conflict of interest declaration forms are filed with the CCHMC EBDM group.

Once the BESt has been in place for five years, the development team reconvenes to explore the continued validity of the guideline. This phase can be initiated at any point that evidence indicates a critical change is needed. CCHMC EBDM staff perform a quarterly search for new evidence in an horizon scanning process. If new evidence arises related to this BESt, authors are contacted to evaluate and revise, if necessary.

For more information about CCHMC Best Evidence Statements and the development process, contact the Evidence Collaboration at EBDMinfo@cchmc.org.

Note

This Best Evidence Statement addresses only key points of care for the target population; it is not intended to be a comprehensive practice guideline. These recommendations result from review of literature and practices current at the time of their formulation. This Best Evidence Statement does not preclude using care modalities proven efficacious in studies published subsequent to the current revision of this document. This document is not intended to impose standards of care preventing selective variances from the recommendations to meet the specific and unique requirements of individual patients. Adherence to this Statement is voluntary. The clinician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.