

**HOW I APPROACH**

# The Italian consensus conference on the role of rehabilitation for children and adolescents with leukemia, central nervous system, and bone tumors, part 1: Review of the conference and presentation of consensus statements on rehabilitative evaluation of motor aspects

Francesca Rossi<sup>1,\*</sup> | Federica Ricci<sup>2,\*</sup> | Stefano Botti<sup>3</sup> | Daniele Bertin<sup>4</sup> |  
Simona Breggiè<sup>5</sup> | Roberto Casalaz<sup>6</sup> | Marta Cervo<sup>7</sup> | Paola Ciullini<sup>7</sup> |  
Monica Coppo<sup>8</sup> | Annalisa Cornelli<sup>9</sup> | Maria Esposito<sup>1</sup> | Miriana Ferrarese<sup>8</sup> |  
Marina Ghatti<sup>10</sup> | Lucia Longo<sup>8</sup> | Mattia Morri<sup>11</sup> | Gabriella Naretto<sup>12</sup> |  
Nicoletta Orsini<sup>13</sup> | Franca Fagioli<sup>4</sup> | the AIEOP Rehabilitation Working Group Members<sup>†</sup>

<sup>1</sup> Rehabilitation Service, Public Health and Pediatric Sciences Department, A.O.U. Città della Salute e della Scienza-Regina Margherita Children's Hospital, Turin, Italy

<sup>2</sup> Division of Child Neurology and Psychiatry, A.O.U. Città della Salute e della Scienza, Regina Margherita Children's Hospital, Turin, Italy

<sup>3</sup> Haematology Unit, Oncology and Advanced Technology Department, Azienda USL-IRCCS Reggio Emilia, Reggio Emilia, Italy

<sup>4</sup> Pediatric Oncohematology, Stem Cell Transplantation and Cell Therapy Division, A.O.U. Città della Salute e della Scienza-Regina Margherita Children's Hospital, Turin, Italy

<sup>5</sup> Palliative Care, Pain Therapy and Rehabilitation Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

<sup>6</sup> Paediatric Oncohematology Unit Institute for Maternal and Child Health-IRCCS Burlo Garofolo, Trieste, Italy

<sup>7</sup> Functional Rehabilitation Unit-A.O.U. Meyer, Florence, Italy

<sup>8</sup> Health Professions of Rehabilitation Sciences, Clinical and Biological Sciences Department, University of Turin, Turin, Italy

<sup>9</sup> Pediatric Oncology Department, ASST Papa Giovanni XXIII, Bergamo, Italy

<sup>10</sup> Pediatric Hematology Department, A.O.U. Policlinico Umberto I-Rome, Rome, Italy

<sup>11</sup> IRCCS Rizzoli Orthopedic Institute, Nursing, Technical and Rehabilitation Assistance Service, Bologna, Italy

<sup>12</sup> Rehabilitation Department of Pediatric Orthopedics Unit, A.O.U. Città della Salute e della Scienza, Regina Margherita Children's Hospital, Turin, Italy

<sup>13</sup> Physical Therapy and Rehabilitation, Department Children's Hospital Giannina Gaslini, Genoa, Italy

**Correspondence**

Francesca Rossi, Rehabilitation Service, Public Health and Pediatric Sciences Department, A.O.U. Città della Salute e della Scienza-Regina Margherita Children's Hospital, Piazza Polonia 94, 10126, Turin, Italy.  
Email: [francesca.rossi@unito.it](mailto:francesca.rossi@unito.it)

\* Authors contributed jointly to the drafting of this article.

† See Appendix for participant members of the AIEOP Rehabilitation Working Group.

**Abstract**

Because of increasing survival rates in pediatric oncology, attention is focusing on cancer and its treatment-related side effects. Rehabilitation may reduce their impact. However, the literature does not provide strong evidence regarding rehabilitation pathways. Therefore, the Italian Association of Pediatric Hematology and Oncology organized a consensus conference on the role of rehabilitation of motor impairments in children/adolescents affected by leukemia, central nervous system, and bone tumors

**Abbreviations:** AIEOP, Italian Association of Pediatric Hematology and Oncology; ALL, acute lymphoblastic leukemia; CC, consensus conference; CNS, central nervous system; GRADE, grading of recommendation assessment, developing and evaluation; HCPs, health care professionals; HSCT, hematopoietic stem cell transplantation; MJ, Multidisciplinary Jury; PoE, panel of experts; ROM, range of movements; TNPEE, development neuro- and psychomotor therapist; TSC, Technical Scientific Committee

to define recommendations for daily practice. The grading of recommendation assessment, developing and evaluation (GRADE) method was used in order to formulate questions, select outcomes, evaluate evidence, and create recommendations. This paper includes the results on the rehabilitation assessment.

#### KEYWORDS

functional assessment, pediatric oncology, rehabilitation, rehabilitative evaluation

## 1 | INTRODUCTION

In Europe, pediatric cancer is the first cause of death for diseases in children over 1 year. One child every 413 develops a tumor in the first 15 years of life, with around 1400 children and 800 adolescents being diagnosed with cancer in Italy<sup>1</sup> every year.

The incidence of these neoplasms corresponds to 16.5 cases/year/100 000 children, with the majority surviving into adulthood. For this consensus conference (CC), we referred to the most frequent cancers in the pediatric population: leukemia, central nervous system (CNS) tumors, and bone tumors. Acute lymphoblastic leukemia (ALL) is the most common tumor in pediatric age with an incidence of about four cases/year/100 000 children.<sup>1</sup> The prognosis for children has improved to an overall survival rate of 90% due to increases in early diagnosis and chemotherapy treatments. CNS tumors are the most common solid neoplasms. In children between 0 and 15 years, they represent 20-25% of all neoplasms. Osteosarcomas make up 40% of bone tumors and 2% of neoplastic cases in children, with an incidence rate of 0.33 cases/year/100 000 children.<sup>1</sup> The estimated survival rate for all neoplasms in 2003-2008 was close to 80% at 5 years.<sup>1</sup> However, the treatment is long and intense and the price of survival often results in long-term chronic conditions with potentially adverse impacts on nearly every organ system<sup>2</sup> and physical functioning.<sup>3</sup> Patients affected by leukemia can develop chemotherapy-induced peripheral neuropathy (CIPN),<sup>4,5</sup> reduced bone mineral density, osteoporosis, and osteonecrosis related to corticosteroid treatment,<sup>6-8</sup> cardiotoxicity related to anthracyclines,<sup>9</sup> and neurocognitive late effects for those who underwent CNS-penetrating chemotherapy or cranial radiation.<sup>8</sup> In patients with CNS tumors, the side effects depend on the histology, size, and location. Neurological deficits including dysarthria, dysphagia, impaired vision and hearing, ataxia, apraxia, hemiparesis, sensory loss, spasticity, seizures, and cognitive deficits may occur.<sup>10</sup> Posterior fossa syndrome may follow posterior fossa tumor resection. Patients undergoing craniospinal irradiation may experience spinal deformities.<sup>11</sup> Subjects with bone tumors may have negative physical sequelae related to chemotherapy regimen: weakness, neuropathy, impaired balance, and cardiac dysfunction.<sup>12</sup> The surgery used for local control (limb-salvage procedure, rotationplasty, or amputation)<sup>12</sup> may result in wound dehiscence, pain, and weight-bearing and activity restrictions.<sup>10</sup> All these problems may limit physical performance and functional capacity, thus interfering with social participation.<sup>3</sup> Early rehabilitation that restores function, promotes compensatory

strategies, or provides environmental adaptations is critical because it impacts quality of life.<sup>2</sup> Therefore, prevention and rehabilitation should become an integral part of the treatment plan for these patients.<sup>13</sup>

To achieve this, a hand-picked multidisciplinary care team might be required depending on the needs of the patients and their families, and could include a physiatrist, child neuropsychiatrist, physiotherapist, development neuro- and psychomotor therapist (TNPEE), and occupational therapist.<sup>13</sup> Professionals who deal with rehabilitation vary across national health systems. It is worth mentioning that in Italy, the physiotherapist and the TNPEE work with other specialists (occupational therapist, speech therapist, orthoptist) in the rehabilitation of patients during the developmental age. Therefore, in this paper the term "physiotherapist" refers to the physiotherapist and the TNPEE, whereas "rehabilitation" refers to the sensorimotor, neuro-, and psychomotor field. Rehabilitation may be required from diagnosis, during chemotherapy, and after surgery, and must be continued after completion of therapies to minimize any long-term side effects. Therefore, the rehabilitation evaluation should be carried out from diagnosis to define the rehabilitative needs of each child/adolescent and the rehabilitation program.

Considering the lack of available guidelines for an evidence-based rehabilitation practice, the main goal of this CC was to define the role of the rehabilitation team and of the physiotherapist in the assessment (part 1) and treatment (part 2) of sensorimotor, neuro-, and psychomotor impairments in children/adolescents affected by leukemia, CNS tumors, and bone tumors. This paper includes the results on the general role of rehabilitation and the assessment process.

### 1.1 | Rationale of the consensus conference

Difficulties in the development of clinical trials and a lack of good quality scientific evidence in the rehabilitation treatment of children with cancer have generated variable clinical approaches,<sup>14</sup> giving rise to the need for a clear model and definition for rehabilitation treatment, and for a clear definition of what constitutes health care professionals' (HCPs) roles, such as physiotherapists, with the support of a broad consensus of experts.<sup>15</sup>

Moreover, the European Standards of Care for Children with Cancer,<sup>13,16</sup> recognized by the European Society of Oncological

Pediatrics (SIOP Europe), promoted the implementation of HCPs networks to support care activities and research and training to create innovative, high-quality models of care.

Consequently, the Rehabilitation Working Group of the Italian Association of Pediatric Hematology and Oncology (AIEOP) undertook this CC<sup>17</sup> with the aim of integrating current evidence and providing expert-based recommendations on the role of rehabilitation assessment and treatment for children/adolescents affected by leukemia, CNS tumors, and bone tumors.

## 2 | METHODS

In this consensus, a systematic approach based on the Italian National System for Guidelines was used.<sup>17</sup>

The process was coordinated by a research nurse (Stefano Botti) with expertise in the development of CCs.

### 2.1 | Consensus conference composition

The promoter (AIEOP) established a lead committee (Francesca Rossi, Federica Ricci, Stefano Botti) who selected two panels of experts: a Technical Scientific Committee (TSC) and a Multidisciplinary Jury (MJ), composed of 10 and 19 professionals, respectively, including experts from oncology (pediatricians, oncologists, psycho-oncologists, nurses, pediatric nurses) and rehabilitative medicine (child neuropsychiatrist, physiatrist, physiotherapist, speech therapist, orthoptist), social workers, and patient representatives. A panel of experts (PoE) was selected by TSC and included 31 experts in pediatric cancer rehabilitation (they included pediatric neuropsychiatrists, oncologists, and physiotherapists and the TNPEE was selected by the TSC). The PoE was then divided into three subgroups: leukemia, CNS tumors, and bone cancers.

The criteria for selection into each subgroup were as follows: (a) experts in pediatric oncology, (b) an active role within the AIEOP national network, and (c) a balance of competencies across the three subgroups. In Figure S1, the role of each team involved in the CC process is reported.

### 2.2 | Topics and question building

The promoter opted to focus the CC on leukemia, CNS tumors, and bone cancer, which represent the most frequent oncological diseases affecting pediatric patients as well as the major illnesses requiring rehabilitation.<sup>10</sup>

Initially, the TSC formed background questions that were divided into three parts: (a) the role of rehabilitation HCPs, (b) assessment, and (c) treatment of sensorimotor, neuro-, and psychomotor function impairments. The PICO method was then used to establish suitable clinical questions for each subgroup. The resulting outcomes were divided into those that were considered “critical,” “relevant but not

critical,” or “not relevant” according to the grading of recommendation assessment, developing and evaluation (GRADE) method<sup>18</sup> and, following that, a final list of questions was chosen by the PoE.

### 2.3 | Literature review

The selected questions were inserted into the PubMed, CINAHL, PsycINFO, and Scopus databases for a review of the literature and included general information, rehabilitation HCPs role, rehabilitation assessment, and treatment in children with cancer in papers published in English up to July 2018. A complete list of the principal search strategies is provided in Table S1.

The PoE subgroups reviewed and selected the retrieved papers for their relevance to their population, design, intervention, comparison, outcomes, methodological issues, and results by categorizing the reviews, clinical trials, observational studies, and gray literature. The final database included 77, 54, and 65 records, respectively, from a total of 1940 articles retrieved for leukemia, 484 for CNS tumors, and 1885 for bone cancers subgroups.

### 2.4 | Appraisal of the evidence and building recommendations

A member of the lead committee (Stefano Botti) assessed the papers for their quality of evidence, and the GRADE method was used to up-/downgrade the evidence accordingly,<sup>18</sup> with any disagreements being resolved through discussion.

Where no comprehensive data were found in the pediatric literature, the PoE used evidence from systematic reviews and randomized clinical trials in adults. However, in the case where recommendations were based on evidence obtained from adult literature only, the piece was downgraded due to its indirectness (Figure S2) in agreement with other authors.<sup>19</sup>

A 3-day PoE meeting was organized in October 2018, where each subgroup produced the first draft of 15 recommendations and 51 statements. Any common recommendations between groups were unified and a rewording edited by the PoE was discussed in a plenary meeting. Agreement was obtained by voting on those recommendations and statements using a 1-9 scale (Figure S3), with the results analyzed for central tendency values (average, median, mode) and ranges.

The consensus report was submitted to MJ for peer review, and following the jury's recommendations the PoE performed a second review, voting on the quality, equity, feasibility, acceptability, relevance, risks-benefits balance, and costs (economic and social) for each recommendation. The final set of recommendations was shared at the CC in Turin in November 2018 to which the medical experts, representatives from science societies, and patients were invited. The CC process is described in Figure S1.

In this paper, the role of rehabilitation HCPs and motor rehabilitation assessment is presented (CC part 1). CC part 2 describes the findings following treatment.

### 3 | RESULTS AND RECOMMENDATIONS

For the role of HPCs in rehabilitation assessment, the CC produced eight general recommendations (Table 1) and 19 statements (Table 2): 10 for children/adolescents affected by all cancer types and nine specific statements (Table 1) for the three subpopulations.

*Question 1: "What kind of rehabilitative care should pediatric patients, with a diagnosis of cancer, receive?"*

- Recommendation: "The child/adolescent with cancer should be placed under the care of a multidisciplinary team, including rehabilitation professionals, from diagnosis."

Rehabilitation treatment in each developmental age has to take into account the multiplicity of altered motor, perceptive, cognitive, affective, communicative and relational functions, their mutual interactions, and variables such as age and role of the family while respecting the individuality of each child.<sup>20</sup>

The modalities of care<sup>21</sup> are influenced by the level of dependence that children/adolescents have on their families and the effect that a cancer diagnosis has on other family members. Therefore, the multidisciplinary team needs to promote family-centered care, thus establishing a partnership between the patient/family and HCPs.<sup>22</sup>

The multidisciplinary team should include medical specialists (oncologist, pediatrician, neurosurgeon, orthopedist, child neuropsychiatrist, physiatrist, radiotherapist, hematologist, ophthalmologist, cardiologist, pulmonologist, pathologist), nurses, physiotherapists, occupational therapists, speech therapists, orthoptists, psychologists, neuropsychologists, and social workers.<sup>13,14,16,23-26</sup> The composition of the rehabilitation team will vary according to the cancer type and phase of treatment. Most children affected by leukemia and bone tumors require a physiotherapist and occupational therapist. However, those affected by CNS tumors require a physiotherapist, occupational therapist, neuropsychologist, and speech therapist. Other HCPs that can contribute to restoring motor functioning include exercise physiologist to improve physical literacy and physical fitness and to promote a reintegration into physical activities in the community,<sup>27</sup> and an orthopedic technician to provide orthopedic aids.

Rehabilitation may be delivered before (prehabilitation), during, or following cancer treatment.<sup>28</sup> Prehabilitation aims to enhance a child's physical functioning and general health, and improve tolerance of cancer treatments, overall outcomes, and recovery.<sup>29</sup> Therefore, rehabilitation should be an integral part in the care of these patients from the point of diagnosis.<sup>30</sup> We believe that preventive rehabilitation programs should be developed with available resources that capitalize on the skills of the multidisciplinary team in the promotion of physical activity at all phases of the cancer trajectory.<sup>31,32</sup> This could be achieved by introducing alternative modes of service delivery (eg, telemedicine)<sup>31</sup> and strategies to improve adherence to preventive behavior (eg, mobile phone app).<sup>33</sup>

The multidisciplinary team should be coordinated by a clinical manager, who would generally be the referring doctor at each phase of the

treatment (oncologist, neurosurgeon, orthopedist, child neuropsychiatrist, physiatrist).

*Question 2: "What is the role of the physiotherapist?"*

- Recommendation: "The multidisciplinary team should include rehabilitation professionals (such as physiotherapist or neuro- and psychomotor therapist) with the appropriate skills and competences to manage the rehabilitation of children/adolescents with cancer."

In oncology rehabilitation, physiotherapists manage musculoskeletal and neuromuscular impairments.<sup>29</sup> In Italy, the physiotherapist generally deals with the motor aspects, including neurological and orthopedic rehabilitation (often mediated through play),<sup>34</sup> while the TNPEE supports the neuro-evolutive development in the integration of neuro- and psychomotor skills.<sup>35</sup>

The presence of these specialists within the multidisciplinary oncological team is supported by international papers on the subject.<sup>13,26,36</sup> The specialists should possess the appropriate skills and competences to undertake the rehabilitation treatment of pediatric patients and manage the variables of the oncological pathology.<sup>24,25,37</sup> A proposal of competences and knowledge required for pediatric oncology physiotherapists is reported in Figure 1.<sup>82,83</sup>

*Question 3: "Which children/adolescents affected by cancer should be evaluated to identify who should receive rehabilitative care?"*

- Recommendation: "The clinical evaluation of children/adolescents with cancer should include the identification of the patients who need a rehabilitation assessment and the possible development of a prevention and/or treatment rehabilitation intervention plan."

Cancer and the antineoplastic therapies can cause a number of symptoms of rehabilitative interest, ranging from fatigue and motor function deficits to cognitive impairments, as observed in patients affected by CNS cancers<sup>10</sup> and ALL patients.<sup>8</sup> It is important that all patients undergo screening for their possible rehabilitative needs during medical assessments performed by the pediatric oncologists<sup>38,39</sup> or other specialists (eg, neurosurgeons).

The clinical evaluation in rehabilitative optics is intended as an assessment of the potential need for rehabilitative care (the rehabilitation evaluation will reveal whether they are presumed or actual). Unfortunately, there is a lack of standardized measures to evaluate these side effects and a lack of referral guidelines.<sup>38</sup> Some authors propose performing a clinical evaluation by the treating oncologist for CIPN in women with breast cancer (history examination focused on symptoms and functional activities).<sup>40</sup> A proposal for a checklist that could be used by the pediatric oncologists for a full assessment of functional mobility impairments in patients aged >36 months affected by leukemia has been developed from the clinical patterns of glucocorticoid-induced myopathy and of CIPN<sup>41-43</sup> (Figure 2). The clinical evaluation of all pediatric patients affected by cancer in rehabilitative optics is a necessary condition for care at the beginning of their oncological journey, since not all patients need an immediate

**TABLE 1** Summary of recommendations for rehabilitation of children and adolescents affected by cancer

Question	Recommendations	Level of evidence	Degree of consent	Strength of the recommendation
Question 1: "What kind of rehabilitative care should pediatric patients, with a diagnosis of cancer, receive?"	"The child/adolescent with cancer should be placed under the care of a multidisciplinary team, including rehabilitation professionals, from the diagnosis."	Low	Average 8.4; range 1-9	Strong
Question 2: "What is the role of the physiotherapist?"	"The multidisciplinary team should include rehabilitation professionals (such as the physiotherapist or the TNPEE) with the appropriate skills and competences to manage the rehabilitation characteristics of children/adolescents with cancer."	Low	Average 8.4; range 1-9	Strong
Question 3: "Which children/adolescents affected by cancer should be evaluated in terms of who receives rehabilitative care?"	"The clinical evaluation of children/adolescents with cancer should include the identification of the patients who need a rehabilitation assessment and the possible development of a prevention and/or treatment rehabilitation intervention plan."	Low	Average 8.6; range 6-9	Strong
Question 4: "Who should carry out the rehabilitative evaluation of children/adolescents with cancer?"	"The rehabilitation assessment of children/adolescents affected by cancer should be carried out by rehabilitation professionals, based on the patient's needs."	Low	Average 8.6; range 1-9	Strong
Question 5: "When should children/adolescents affected by cancer be evaluated for rehabilitation?"	"The rehabilitation assessment of children/adolescents with cancer should be performed as soon as possible after diagnosis, according to the clinical and psychosocial conditions of the patient, the family context, and the scheduled antineoplastic treatment plan."	Low	Average 8.6; range 7-9	Strong
	"Subsequent assessments should be carried out periodically, based on the needs of the patient, the clinical conditions, and the stages of the antineoplastic treatment, to evaluate the results of the rehabilitation intervention plan and make any changes."	Very low	Average 8.6; range 7-9	Strong
Question 6: "Which aspects must be evaluated in children/adolescents affected by cancer and with what tools?"	"Rehabilitation assessment should cover sensorimotor functions, cognitive and psychosocial aspects, and should take into account the clinical status, comorbidities, and previous lifestyle of the patient."	Very low	Average 8.7; range 7-9	Strong
	"The assessment of rehabilitation needs should be carried out using appropriate tools and scales."	Very low	Average 8.5; range 7-9	Strong

**TABLE 2** Statements for the motor rehabilitation assessment of children and adolescents affected by cancer in general, and by leukemia, CNS tumors, and bone tumors in particular

Question	Statements for all children/adolescents affected by cancer	Statements for children/adolescents affected by leukemia	Statements for children/adolescents affected by CNS tumors	Statements for children/adolescents affected by bone tumors
Question 1: "What kind of rehabilitative care should pediatric patients, with a diagnosis of cancer, receive?"	<ul style="list-style-type: none"> <li>- The multidisciplinary team should include specialist doctors, nurses, physiotherapists, psychologists, social workers, and other relevant professionals according to the child's needs</li> <li>- The multidisciplinary team should be coordinated by a clinical case manager, who is chosen according to the type of cancer and treatment phase</li> <li>- The multidisciplinary care of children and adolescents affected by cancer should also include the surveillance and management of the psychosocial effects of the disease throughout the child's development and include a close alliance with the family and management of their transition to adulthood<sup>21</sup></li> <li>- In subjects who develop a cancer in developmental age, management, particularly in the rehabilitation area, should take into consideration the interrelations between affective, cognitive, and sensorimotor functions to support the child in their various evolutionary phases</li> </ul>			
Question 5: "When should children/adolescents affected by cancer be evaluated for rehabilitation?"	<ul style="list-style-type: none"> <li>- Rehabilitation assessment in children/adolescents with cancer should not be performed if the hemoglobin is less than 8 g/dL and/or the body temperature is above 38°C and/or platelets are less than 20 000/mm<sup>3</sup><sup>69-71</sup></li> <li>- In all children/adolescents suffering from cancer, rehabilitative evaluations at the "end of life" phase should be carried out according to the goals of palliative medicine, namely by seeking the best possible quality of life in relation to the cost-benefit ratio for the patient<sup>72</sup></li> </ul>	<ul style="list-style-type: none"> <li>- The rehabilitation assessment of children/adolescents affected by leukemia is feasible in all treatment phases<sup>64</sup></li> </ul>	<ul style="list-style-type: none"> <li>- The rehabilitation assessments for children/adolescents with CNS tumors, and those who have to be operated on, should be carried out immediately after the operation, as soon as the clinical conditions allow it</li> <li>- In children/adolescents suffering from CNS cancer, the rehabilitation evaluation, in the phase of adjuvant therapies, would be advisable at least at the beginning and at the end</li> <li>- In children/adolescents with CNS tumors who have completed antineoplastic treatments, rehabilitation assessment would be advisable annually at preschool age and every 6 months at school age</li> </ul>	<ul style="list-style-type: none"> <li>- For children/adolescents affected by bone tumors, the rehabilitation evaluation should be performed before surgery, in order to compile an intervention plan preparatory to surgery<sup>24,66</sup></li> <li>- For children/adolescents with bone tumors, the rehabilitation assessment should be performed at regular intervals after surgery (eg, 1, 3, 6, 9, 12, and 24 months after surgery)<sup>57-67</sup></li> </ul>

(Continues)

TABLE 2 (Continued)

Question	Statements for all children/adolescents affected by cancer	Statements for children/adolescents affected by leukemia	Statements for children/adolescents affected by CNS tumors	Statements for children/adolescents affected by bone tumors
Question 6: "Which aspects must be evaluated in children/adolescents affected by cancer and with what tools?"	<ul style="list-style-type: none"> <li>- In all children/adolescents with cancer, their pain, skin and mucosal status, fatigue, respiratory function, and the need to adopt aids and orthoses should be evaluated</li> <li>- In children/adolescents suffering from cancer and subjected to treatments that may have adverse neuropathic or myopathic effects, or who have anatomical lesions of the neuromuscular system, the minimum necessary requirements are the evaluation of the active and passive range of movement (ROM) and muscle strength:               <ul style="list-style-type: none"> <li>range of excursion in ankle dorsiflexion (ROM)</li> <li>range of excursion in wrist extension (ROM)</li> <li>dorsiflexion strength of the ankle (strength)</li> <li>extension strength of wrist (strength)</li> <li>strength of knee (strength)<sup>62,63,73-81</sup></li> </ul> </li> <li>- Rehabilitation assessment should be carried out using validated assessment scales for the pediatric cancer population, if these are available, or through the use of validated tools in the pediatrics field</li> <li>- Rehabilitation assessment should be carried out, where possible, through the use of quantitative scoring systems</li> </ul>	<ul style="list-style-type: none"> <li>- In children/adolescents with leukemia, global and fine functional abilities, balance, ROM, and muscle strength should be evaluated<sup>19</sup></li> </ul>	<ul style="list-style-type: none"> <li>- In children/adolescents with CNS cancer, rehabilitation assessment should be adapted based on the patient's clinical needs, the type of surgery, and the location of the tumor. This assessment should always include global aspects (balance, muscle tone, sensitivity, neuromotor and psychomotor functions) and, as needed, site-specific aspects (eg, ataxia and cranial nerve function for tumors of the posterior cranial fossa and brainstem, spasticity for tumors involving the cortico-spinal tracts, sphincter functions for medullary tumors)<sup>21,24,37,66,68</sup></li> </ul>	<ul style="list-style-type: none"> <li>- In children/adolescents affected by bone cancer, muscle strength, ROM, skin, functional abilities, possible peripheral deficits, and the need for prostheses should be evaluated</li> </ul>

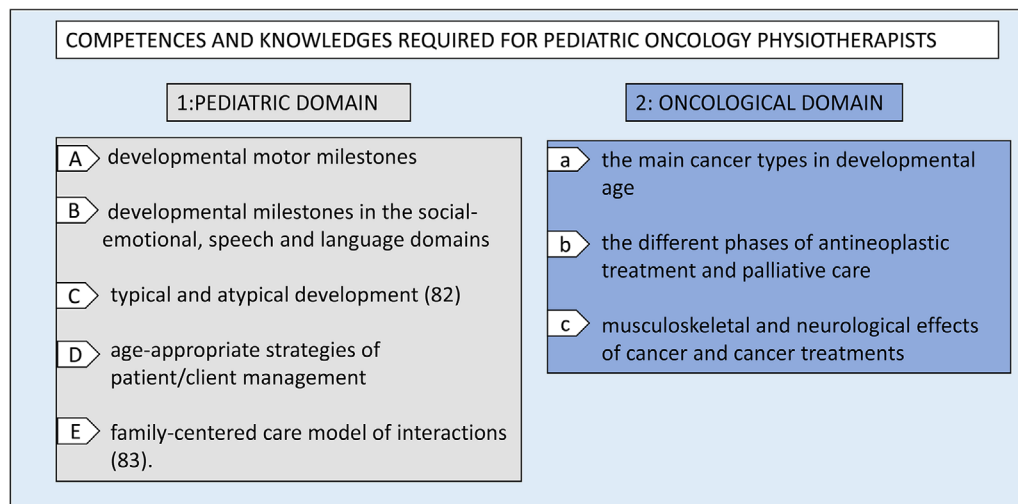
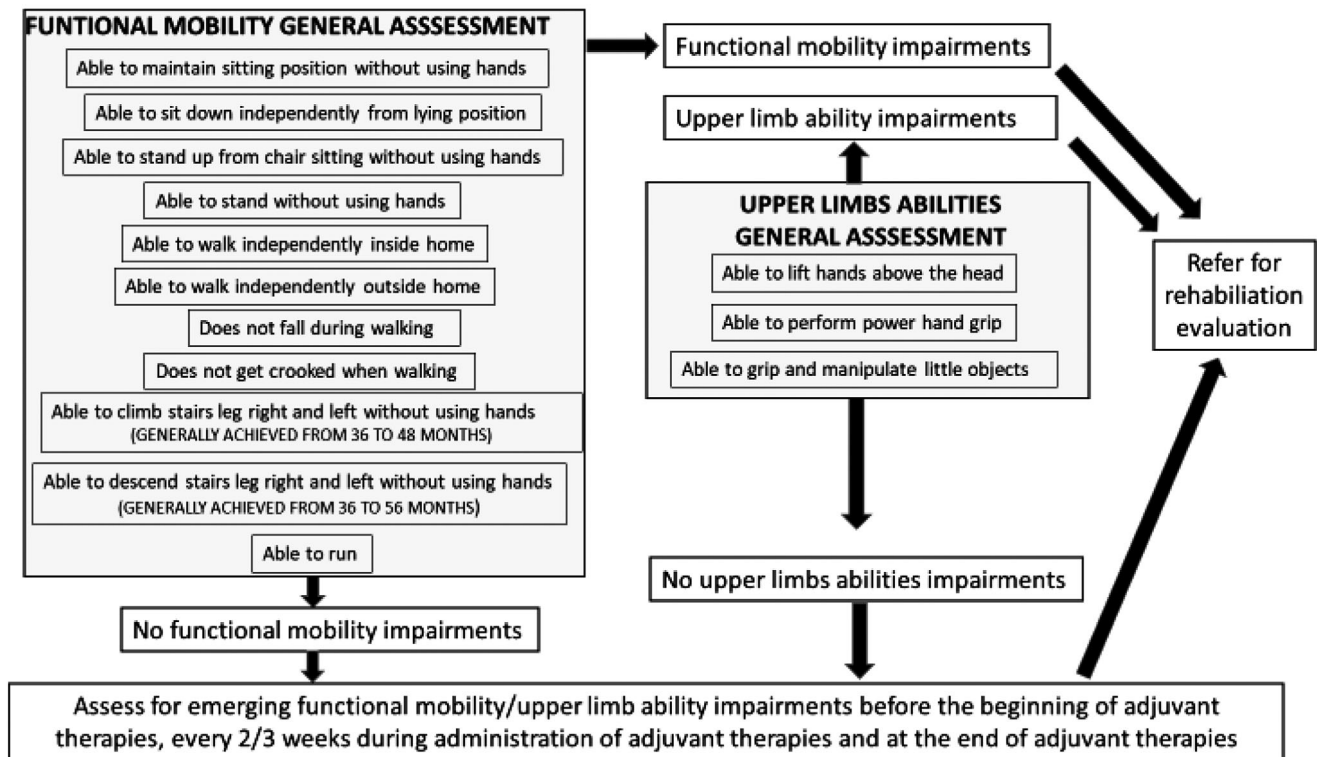


FIGURE 1 A proposal of the competences and the knowledge required for pediatric oncology physiotherapists

## CHECKLIST OF FUNCTIONAL MOBILITY IMPAIRMENTS IN PATIENTS WITH LEUKEMIA AGED >3 YEARS



**FIGURE 2** A proposal of algorithm for a checklist of functional mobility impairments in patients with leukemia aged >3 years

rehabilitation assessment and/or treatment, and resources can be limited. The multidisciplinary team would then define when the patient should next be evaluated, specifying the timing, or if they should begin a rehabilitation program.

*Question 4: "Who should carry out the rehabilitative evaluation of children/adolescents with cancer?"*

- Recommendation: "The rehabilitation assessment of children/adolescents affected by cancer should be carried out by rehabilitation professionals, based on the patient's needs."

Following clinical evaluation, if variables in musculoskeletal and neurological systems are found, the patient should be referred to a physiotherapist to carry out a functional assessment for pain, fatigue, weakness, limitations in range of movements (ROM), deficits in balance and walking, and psychomotor aspects.<sup>24,34,44,45</sup>

If problems arise, the physiotherapist will arrange a rehabilitation program with the clinical manager. The evaluation of different rehabilitation specialists or the intervention of the rehabilitation doctor may be needed. Periodical assessments by the physiotherapist, speech therapist, or other professionals may be required.<sup>46</sup>

*Question 5: "When should children/adolescents affected by cancer be evaluated for rehabilitation?"*

- Recommendation: "The rehabilitation assessment of children/adolescents with cancer should be performed as soon as possible after diagnosis, in relation to the clinical and psychosocial conditions of the patient, the family context, and the scheduled antineoplastic treatment plan."
- Recommendation: "Subsequent assessments should be carried out periodically, based on the needs of the patient, the clinical conditions, and the stages of the antineoplastic treatment, to evaluate the results of the rehabilitation intervention plan and make any changes."

In Figures S4-S6, the algorithm trees proposed for the habilitation evaluation of children and adolescents affected by leukemia, CNS tumors, and bone tumors are reported.

In rehabilitation, the importance of early intervention is now widely recognized.<sup>47-50</sup> It is also known that besides the clinical conditions, psychological and social factors and issues related to the organization of services and availability of resources can also influence the timing of the first rehabilitation assessment.



In pediatric oncological patients undergoing surgery (CNS tumors and bone tumors), postsurgical evaluation is important, as the deficit caused by surgical removal is added to the primary deficit caused by the tumor itself.

In patients with bone cancer, it is important to perform an assessment and plan treatment in the preoperative phase to preserve muscular strength, autonomy, and mobility.<sup>51</sup>

Following surgery, or even as an alternative, adjuvant therapies including chemotherapy or radiotherapy may be necessary. If rehabilitation treatment is ongoing, it is advisable to perform at least two rehabilitation assessments at the beginning and at the end of the treatment.

In children/adolescents undergoing hematopoietic stem cell transplantation (HSCT), a rehabilitative assessment in the pretransplant phase is strongly recommended to establish the patient's basic functional level.<sup>44</sup>

Children and adolescents who die of cancer (end of life stage) experience many physical symptoms, including pain, fatigue, dyspnea, and reduced mobility.<sup>52</sup> It may, therefore, be useful to administer scales to monitor levels of pain to better assist the patient according to the principles of palliative medicine.<sup>53</sup>

#### 4 | FOLLOW-UP REHABILITATIVE ASSESSMENT

According to CC, rehabilitation assessment for patients with leukemia who developed a CIPN should be performed during the oncological follow-up visits in order to track persisting CIPN-related problems and to define rehabilitation strategies.<sup>54</sup> For patients who undergo allogeneic HSCT, some authors suggest performing a functional evaluation after transplantation at 4, 8, 12, 15, 18, and 21 weeks.<sup>55</sup>

In patients with CNS cancers, the CC recommends follow-up rehabilitative assessments every 6 months for preschool children and annually in school age.

In patients with bone tumors, the CC recommends follow-up rehabilitative assessments every 3 months up to 1 year after surgery and then 2 years later. In assessing the results obtained, the type of surgery and the chemotherapy treatment should be taken into consideration. Some of the most pertinent reference values for the first-year postsurgical treatment for patients with mega-prosthesis of the knee are as follows: the possibility of recovering 90° of knee flexion in 50% of the patients, 3 months after surgery; for quadriceps strength recovery in 25% of patients, 12 months after surgery, the values are less than three according to the manual muscle test (0-5)<sup>56</sup> but with the chance of improving motor function even 12-24 months postsurgery.<sup>57,58</sup>

Beyond the oncological phases, further assessments are carried out periodically by the physiotherapist to monitor progress. This assessment is done at the beginning and at the end of the rehabilitation process, and also when clinical conditions change. The effectiveness of the rehabilitation intervention is measured in relation to preestablished goals. Resources used must always be in line with goals that can be achieved and/or that are reasonably achievable.<sup>21,34</sup>

*Question 6: "Which aspects must be evaluated in children/adolescents affected by cancer and with what tools?"*

- Recommendation: "Rehabilitation assessment should cover sensorimotor functions, cognitive and psychosocial aspects, and take into account the clinical status, comorbidities, and previous lifestyle of the patient."
- Recommendation: "The assessment of rehabilitation needs should be carried out using appropriate tools and scales."

The difficulties in validating assessment tools in pediatric oncology are due to the extreme variability and low number of cases. Therefore, a recommendation in the use of validated instruments for this specific population is not currently applicable. The PoE has considered this, for which the term "appropriate" instead of "validated" is used.<sup>59</sup> The term "appropriate" first indicates the use of validated tools for the setting of the specific disease, followed first by those validated for the pediatric world, and second those for measuring observed phenomenon while clearly taking into account that only instruments validated for the specific setting can guarantee reliability.

The following are validated rehabilitative assessment tools for children/adolescents with cancer:

- Gross motor function scale-acute lymphoblastic leukemia (GMFM-ALL).<sup>60</sup>
- Motor performance in pediatric oncology (MOON).<sup>61</sup>
- Pediatric modified Total Neuropathy Scale (Ped-mTNS).<sup>62</sup>

In the absence of validated assessment tools in the pediatric oncological population, the use of scales validated in other populations of developmental age and useful in the detection of the sign/symptom of interest is suggested. A qualitative observation should be made if there are no standardized assessment tools and in noncollaborating patients. The implementation of new studies for the validation of rehabilitation assessment scales on this population would be desirable.

For patients suffering from bone tumors, there is no homogeneity in the literature on areas of the body and movements to be evaluated. In the articles reviewed, the most widely researched areas on the lower limb are the hip and the knee. With ROM, the extension/flexion of the hip and knee are measured. For muscle strength, the flexion/abduction of the hip and the flexion/extension of the knee are evaluated. For the upper limb, the literature does not provide precise indications regarding evaluation of ROM and muscle strength. Although the Musculoskeletal Tumor Society Scale is frequently used to assess functional abilities, pain, and emotional acceptance, there are numerous studies that emphasize that its use is not always appropriate, particularly in the pediatric age group.<sup>23,63,64</sup>

In Table 2, an example of the rehabilitative assessment tools that can be used in pediatric cancer patients is reported.

#### 5 | CONCLUSIONS AND FUTURE DIRECTIONS

In part 1 of this two-part consensus conference on the role of rehabilitation for children and adolescents with leukemia, CNS, and bone tumors, recommendations and statements on rehabilitation

assessment focusing on motor impairments are presented. Evidence from the literature on this topic is limited and of low quality, also when extending the research to the adult population. All the recommendations are therefore based on the experience of the professionals involved, according to the consensus methodology.

It is stated that a multidisciplinary care team is needed to take care of these patients and their families. The team should include rehabilitation professionals. This is important considering the increase in pediatric oncology survival rates. In many cases, rehabilitation is now required from the time of diagnosis, during adjuvant therapies, and after surgery, and often continued after completion of treatment to improve outcomes and minimize long-term side effects.

It is recommended that the rehabilitation assessment is carried out by considering the patient's collaboration, age, and antineoplastic treatment phase, with a periodicity depending on many factors including type of tumors, phase of treatment, and periodical rehabilitation results. The rehabilitation assessment should be comprehensive and based on appropriate quantitative assessment scales. Validated tools for the specific disease and population are still lacking, therefore, scales validated for the pediatric world and those created for measuring observed phenomenon could be used.

The most limiting factors in this work have been the lack of specific evidence and the variability of HCPs and national health care organizations involved. However, to our knowledge this is the first attempt to create a comprehensive consensus on this topic.

In our opinion, future steps are needed, mainly focused on generating and validating reliable assessment tools and on identifying innovative models of care.

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Ravizzotti, Development Neuro and Psychomotor Therapy Degree Course, Public Health and Pediatric Sciences Department, University of Turin, Italy; Ilaria Ripamonti, Pediatric Onco-Hematology, Blood & Marrow Transplant Program, University of Milano-Bicocca Monza's Hospital-Fondazione MBBM onlus, Monza, Italy; Emma Sarlo, representative Association "Italian Parents Union against Child Cancer ONLUS (UGI); Danila Siravegna, Rehabilitation Service, Public Health and Pediatric Sciences Department, A.O.U. Cittàdella Salute e della Scienza-Regina Margherita Children's Hospital, Turin, Italy; Marco Spinelli, Department of Pediatrics, Fondazione, MBBM/Ospedale San Gerardo, Monza, Italy; Sandro Stefanin, Federated Library of Medicine «Fernando Rossi», University of Turin, Italy; Giulia Zucchetti, Pediatric Oncohematology, Stem Cell Transplantation and Cell Therapy Division, A.O.U. Città della Salute e della Scienza-Regina Margherita Children's Hospital, Turin, Italy.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ORCID

Francesca Rossi  <https://orcid.org/0000-0002-1335-5121>

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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**APPENDIX****Participant members of the AIEOP Rehabilitation Working Group**

Roberta Gasparini PT, Rehabilitation Department of Pediatric Orthopedics Unit, A.O.U. Cittàdella Salute e della Scienza - Regina Margherita Children's Hospital, Turin, Italy; Daniele Panzeri PT, Scientific Institute, IRCCS E. Medea, Neuro-oncological Rehabilitation Unit, Bosisio Parini, Lecco, Italy; Chiara Pellegrini TNPEE, Palliative Care, Pain Therapy and Rehabilitation Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Michela Peranzoni PT, Health Trust, Department of Physiotherapy, Hospital of Bolzano, Italy; Antonella Perna PT, Medical Department of Continuity of Care and Disability, Physical Medicine and Rehabilitation University Hospital St. Orsola-Malpighi, Bologna, Italy; Nadine Petit TNPEE, Pediatric Hematology Department, A.O.U. Policlinico Umberto I-Rome, Italy; Fabiola Picone PT, Functional Rehabilitation Unit - A.O.U. Meyer, Florence, Italy;

Gianna Pittorru PT16, Medical Department of Continuity of Care and Disability, Physical Medicine and Rehabilitation University Hospital St. Orsola-Malpighi, Bologna, Italy; Debora Raffa PT, IRCCS Rizzoli Orthopedic Institute, Nursing, Technical and Rehabilitation Assistance Service, Bologna, Italy; Veronica Recchiuti TNPEE, Physical Therapy Neuroscience Department and Functional Rehabilitation Children's Hospital Bambino Gesù, Rome, Italy; Lucia Rizzato PT, Complex Operative Unit of Orthopaedic Rehabilitation, AO of Padua, Italy; Marina Sarzana PT, Pediatric Immunohematology Unit and Stem Cell Program, IRCCS San Raffaele Scientific Institute, Milan, Italy; Raffaella Sensi PT, Palliative Care, Pain Therapy and Rehabilitation Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Daniela Vigna PT, IRCCS Rizzoli Orthopedic Institute, Nursing, Technical and Rehabilitation Assistance Service, Bologna, Italy.