

Identifying the concepts in outcome measures of clinical trials on osteogenesis imperfecta using the International Classification of Functioning, Disability and Health - version for children and youth

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ABSTRACT

The biopsychosocial model from the International Classification of Functioning, Disability, and Health (ICF) has been used as a reference in clinical practice to identify and analyze the functioning components in outcome measures. **Objective:** The objectives of this study were to identify the concepts contained in outcome measures of clinical trials on Osteogenesis Imperfecta, to analyze how these concepts are linked with the ICF - Children and Youth version (ICF-CY) and describe what the functioning components are that are assessed in these studies. **Method:** Randomized controlled trials on children with diagnoses of Osteogenesis Imperfecta carried out between 2000 and 2013 were selected using MedLine and Cochrane. The outcome measures were extracted and the concepts contained in the outcome measures were linked to the ICF-CY. **Results:** Fourteen trials were included. The concepts of clinical and technical measures and of one health assessment instrument (Pediatric Evaluation of Disability Inventory - PEDI) were identified. The concepts of clinical and technical measures were linked to the ICF-CY Body Functions and Structures component. The PEDI concepts were linked to the Body Functions and especially to Activity and Participation. **Conclusion:** Using the linking of the concepts of outcome measures to the ICF-CY it was possible to verify that clinical trials on Osteogenesis Imperfecta assessed mainly the Body Functions and Body Structures component. Assessments of Activity and Participation and contextual factors are scarce on these studies. More research is necessary on the effects of interventions on these components.

Keywords: International Classification of Functioning, Disability and Health, Osteogenesis Imperfecta, Outcome Assessment (Health Care)

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INTRODUCTION

Osteogenesis Imperfecta (OI) is a rare genetic collagen disease characterized by bone frailty and, in most cases, caused by mutations in the genes that produce type I collagen. It affects approximately 1: 5,000-10,000 individuals.¹ Among its main clinical manifestations are frequent bone fractures, deformities, ligament laxity, muscle weakness, hearing loss, low stature, blue sclerae, and imperfect dentinogenesis. These manifestations affect functionality in many ways and result in the disabilities of individuals with OI.

Many outcome measures have been used in clinical trials to evaluate interventions in children and adolescents with OI, however, there is a lack of understanding of the functional areas covered by these outcomes. This lack of understanding may widely affect the evaluation of the response to treatment and also make it difficult to choose the appropriate instruments for the intervention. The International Classification of Functioning, Disability, and Health (ICF)² has been used in studies as a model to understand the relationship between the outcome measures and the components of functionality.^{3,4}

The ICF represents a new approach to understanding functionality and disability. Previously, through the International Classification of Impairments, Disabilities, and Handicaps (ICIDH), biomedical logic was used to explain a negative linear model in which the body with impairment would create disabilities that consequently would determine social handicaps. The ICF presents a biopsychosocial and multidirectional model for functionality describing the health condition in its biological, individual, and social dimensions and also the relationships between those dimensions. Disability is not seen anymore as a limitation created by an injury to the body, but it is now seen from the interaction of this injured body with the environment. The functionality of children and adolescents is considered by the International Classification of Functioning, Disability, and Health - Children and Youth version (ICF-CY)⁵ published by the World Health Organization in 2007.

In the clinical context, the ICF can be used to evaluate needs, to plan interventions, for rehabilitation, and to evaluate results.⁶ In the evaluation of changes that occur as a response to treatment, outcome measures are a way to describe the state of the patient in relation to the manifestations of a specific pathology. Cieza et al.⁷ initially proposed a set of rules that

allowed evaluation instruments in the health field to be related to the ICF. These rules were later reviewed to be also applied to clinical outcome measures and techniques which resulted in the eight linking rules.⁸ The technical outcome measures include, for example, laboratory and imaging exams, and the clinical measures include physical and cognitive tests, and the analysis of activities such as gait.⁸

The correct use of the proposed rules and the understanding of which components of functionality are considered in the outcome measures is of great importance in the choice of which instrument/measure is the most appropriate for a specific question in the research and to better interpret and compare the results between different studies.⁸

OBJECTIVE

This work seeks to identify the concepts for the outcomes of clinical trials in Osteogenesis Imperfecta, and to analyze how these concepts relate with the International Classification of Functioning, Disability, and Health, in the children and youth version (ICF-CY), and to describe which components of functionality are most evaluated in these studies.

METHODS

Functionality, according to the ICF, refers to the positive aspects of the components Structures (s) and Functions of the body (b), Activity and Participation (d) and their interactions with the Environmental Factors (e) represented by environmental and personal factors. Functions of the body is understood as the physiological functions of the organic systems, and structures of the body as its anatomical parts. Activity is understood as the execution of a task by the individual and participation, as the involvement in a life situation, encompassing the social perspective of functionality. The contextual factors can act as facilitators or barriers to the individual.

In the ICF encoding, the letters b (Functions of the Body), s (Structures of the Body), d (Activity and Participation), and e (Environmental Factors) are followed by a numerical code beginning with the number of the chapter (first digit) followed by a second, third, or fourth level code. The higher the level, the more detailed would be the code.

A literature review was made of clinical trials involving children and youth with OI to

select the outcome measures used in those articles. After that, the concepts identified in the outcome measures were correlated with the second level classification codes of the ICF-CY. Finally, the functionality areas most evaluated in those studies were described.

For the selection of the articles, a search was made in the Medline and Cochrane electronic databases, in the period between 2000 and 2013, with the term "osteogenesis imperfecta". Only published randomized clinical trials or systematic reviews about children (from 0 to 18 years-old) diagnosed with OI based on clinical and/or laboratorial criteria were included. All the types of OI were included in this study and any intervention in OI was considered. The articles that included children with other pathologies in addition to OI were excluded.

The clinical and technical outcome measures were extracted from the selection of articles including, for example, strength tests, X-rays, bone densitometry, blood and urine exams, and measures directed to the patients such as standardized health evaluation questionnaires.

Following the linking rules of the ICF with the outcome measures proposed by Cieza et al.,⁸ the significant concepts of the outcome measures were extracted and a list of them was made using the second level classification categories of the ICF-CY. The concepts that could not be related to the ICF-CY codes were classified in two ways: "not-definable" when they did not reveal enough to choose the most precise code to be related with, such as the "quality of life" concept, for example. The term "not-covered" applied when a concept not present in the ICF was suggested-for example, "bone metabolism" was a concept not present in the ICF. According to Cieza et al.,⁸ if the outcome measure concept is not explicitly in the ICF, additional information could be used to characterize it. In this study "bone pain" was related with the code "b280 - pain sensation" with the additional information "bone".

The concepts that refer to the same ICF-CY category were analyzed by the same code. (For example: the contents of PEDI "ability to recognize the meaning of the words" and "ability to recognize spoken messages" were related with the same category "b167 - mental functions of language").

Two independent researchers with knowledge of the ICF content and of the linking rules did the linking procedure. The consensus between both researchers was used to choose a second level category for each concept and,

in case they disagreed, a third researcher trained in the linking rules was consulted. The researchers involved in the process were two physiotherapists and a physician.

Descriptive analyses were used to determine the frequency of ICF-CY categories related with the concepts of outcome measures. When a category appeared many times in the same study, it was counted only once.

The categories used were of second level by the understanding that the codes are organized hierarchically and that the second level categories address aspects from the third and fourth level categories.⁵

The agreement between the researchers in the choice of the component and of each category was analyzed based on the *Kappa* index using the SPSS software, version 17.

RESULTS

Initially, 39 articles were found. After reading them completely and applying the eligibility criteria, a total of 14 studies were selected.

From all the articles selected, 13 (93%) were related to interventions with medication for OI, including the use of oral or intravenous bisphosphonates and growth hormone. Only one study (7%) showed a physical treatment as an intervention.⁹

When outcome measures were being examined, it turned out that 13 studies (93%) had used clinical outcomes and techniques (dynamometry, bone densitometry, X-rays, blood exams), and 6 studies (43%) had used standardized evaluation questionnaires (Chart 1).

In the analyses of clinical outcomes and techniques, nine concepts were extracted and related only to the components *Functions* and *Structures of the Body*. Five concepts were related with the function of the body (56%), two concepts, with the structure of the body (22%), and two concepts were classified as "not-covered" by the ICF-CY (22%) (Chart 2).

In the component *Functions of the Body*, the concepts were related with categories in chapter 2 (Sensory functions and pain), chapter 4 (functions of the cardiovascular, hematological, immunological, and respiratory systems), chapter 5 (functions of the digestive, metabolic, and endocrine systems), chapter 6 (genitourinary and reproductive functions), and chapter 7 (neuromusculoskeletal functions related to movement), as a category of each chapter being chosen, totaling 5 codes (Chart 2).

In the component *Structures of the Body*, the concepts were related with a category in

Chart 1. Outcome measures used in Osteogenesis Imperfecta clinical trials

Clinical And Technical	Standardized Instruments
Maximum work capacity ⁹	Health Utility Index-mark III (HUII) ¹²
Peak VO ₂ ⁹	Self Perception Profile for children (SPPC) ^{9,12}
Bone desintometry ^{13,17,19,21-24}	Child Health Questionnaire (CHQ) ⁹
Weight ^{16,17,18}	Pediatric Evaluation of Disability Inventory (PEDI) ^{16,17,19}
Height ^{14,16,18,23,24}	Bleck Score ¹⁶
Head circumference ¹⁶	Gross Motor Function Measure (GMFM) ¹⁹
X-ray ^{13,21,23,24}	The Brief Assessment of Motor Function (BAMF) ²³
Blood exam ^{13,14,15,17,18,20-24}	
Urine exam ^{13,15,16,17,18,20,21,24}	
Pain scale ^{15,23}	
Pain report ¹⁸	
Dynamometer ^{15,17}	
Manual strength test ^{16,23}	

Chart 2. Relationship of the clinical and technical outcomes from OI clinical trials with the ICF-CY categories

Outcome measure concept	ICF-CY Code	ICF-CY Category	Additional Information
Bone pain	b280	Pain sensation	Bone
Functions of the body	Physical capacity	b455	Functions of tolerance to exercising
Growth	b560	Functions of maintaining growth	
Urinary excretion of medication	b610	Functions related to the urinary excretion	
Muscle strength	b730	Functions related to muscle strength	
Bone density	s770	Additional musculoskeletal structures related to movement	
Structures of the body	Bone Structure	s770	Additional musculoskeletal structures related to movement
Not covered	Bone metabolism		
	Adverse effects of medication		

chapter 7 (structures related to movement) with the same code being chosen for the two concepts (Chart 2).

The most frequently used evaluation instrument (21% of the studies) was the Pediatric Evaluation of Disability Inventory (PEDI),¹⁰ which was, for this reason, chosen to be related with the ICF-CY. It is a standardized test made through a structured interview with the parents or caregivers on the functional aspects of the child. The instrument evaluates functional abilities in the areas of self-care, mobility, and social function; it quantifies the assistance given by the caregiver to perform functional activities and lists the changes necessary to the environment so that the child may perform tasks.

From the 197 PEDI items analyzed, 81 were selected to be correlated with the ICF-CY. Eleven concepts (14%) were correlated with codes of the *Functions of the Body*, 63

concepts (78%) were correlated with the *Activity and Participation*, one concept (1%) was correlated with *Environmental Factors*, and six concepts (7%) were classified as "not-covered" by the ICF-CY. The not-covered concepts referred to the ability to go down stairs and ramps, to use safety belts, to use turnstiles in buses, and to do transferences in and out of a car or bus. A PEDI version validated in Portuguese was used for this analysis.¹¹

In the *Functions of the Body* component, the concepts were correlated with the four categories in chapter 1 (global mental functions), with one category in chapter 2 (sensory functions and pain), one category in chapter 5 (functions of the digestive, metabolic, and endocrine systems), and two categories in chapter 7 (neuromusculoskeletal and movement related functions) of the ICF-CY, totaling eight codes (Chart 3).

Chart 3. ICF-CY categories that were related to the PEDI concepts

	ICF-CY Code	ICF-CY Category
Functions of the body	b167	Mental functions of language
	b180	Functions of personal experience and of time
	b114	Functions of orientation
	b164	Higher cognitive functions
	b230	Auditory functions
	b510	Functions of ingestion
	b710	Functions related to joint mobility
	b740	Functions of muscle strength
	d132	Acquiring information
	d130	Imitating
Activity and Participation	d163	Thinking
	d175	Solving problems
	d230	Performing daily routine
	d440	Fine hand use
	d430	Lifting and carrying objects
	d415	Maintaining body position
	d410	Changing body position
	d445	Hands and arms
	d455	Transferring
	d450	Walking
	d460	Transferring to different places
	d465	Transferring using some type of equipment
	d430	Lifting and carrying objects
	d560	Drinking
	d520	Caring for body parts
	d570	Looking after one's health
	d510	Washing oneself
	d540	Dressing
	d530	Toileting
	d571	Looking after one's own safety
Activity and Participation	d650	Caring for house objects
	d640	Household tasks
	d720	Complex interpersonal relationships
	d750	Informal social relationships
	d880	Recreation and leisure
Environmental factors	e115	Products and technology for personal daily use

In the Activity and Participation component, the concepts were correlated with the four categories in chapter 1 (learning and applying knowledge), with one category in chapter 2 (general tasks and demands), with ten categories in chapter 4 (mobility), seven categories in chapter 5 (personal care), two categories in chapter 6 (domestic life), two categories in chapter 7 (interpersonal interactions and relationships), and one category in chapter 8 (major life areas), totaling 27 codes (Chart 3).

In the Environmental Factors component, the concept was correlated with one category

of chapter 1 (products and technology), totaling one code (Chart 3).

Through analyses, it was verified that the clinical measures and techniques were the most used and that they only measured outcomes related to the Structures and Functions of the Body components, which were, consequently, the most frequently evaluated components in OI clinical trials. The categories chosen for Functions of the Body were related to pain sensation, tolerance to exercising, maintenance of growth, urination, and muscle strength. For Structures of the Body, the

category was related to musculoskeletal structures involving movement.

The PEDI analysis correlated its concepts with categories pertaining to Functions of the Body and especially with the Activity and Participation component. The first component was more related to the chapter for "Global mental functions" that included functions of language, personal experience and time, orientation, and higher cognitive functions. As for the Activity and Participation component, the PEDI concepts were mostly related to the chapters for "Mobility" and "Personal Care". In the chapter for mobility, the categories chosen were related to the transferences of position, going in and out of the residence, and the use of upper limbs. In the personal care chapter, the categories were related to hygiene care, dressing, and ingesting liquids.

Environmental factors were not satisfactorily evaluated in the studies. The PEDI showed only one concept related to one category that discusses the use of assistive technology in the daily life.

An excellent agreement occurred between the researchers, when only the components were analyzed ($Kappa$ 86.90%, IC95%, 84.76%-89.04%). When the agreement between the chosen categories was analyzed, the value was moderate ($Kappa$ 50.9%, IC95%, 50.45%-51.34%). This analysis indicates that the researchers strongly agreed in the choice of the component that related to the concept, but in the choice of the complete category, they disagreed, relating the same concept to different categories within one component. After analyzing the disagreements, it was found that the different categories chosen frequently had similar meanings. For example, the PEDI concept "opens and closes door" was related to the category d440 "fine hand use" by one researcher and d445 "hands and arms" by another, demonstrating that, despite the disagreement, the researchers were very close in the definition of the category while relating the concepts. The fact of the ICF having different categories with very similar definitions may be an explanation for the smaller $Kappa$ value, when comparing the categories chosen by the researchers.

DISCUSSION

The linking rules facilitated a standardized procedure in which outcome measures can be evaluated, based on the model of functionality proposed by the ICF.

Through this study, it was found that OI clinical trials have focused their investigation

on the effects of intervention with medication on the vertebral structure, on the speed of growth, and on the reduction of deformity, among other outcomes.^{11-17,19-22}

While analyzing the outcome measures of these studies through the linking rules, it was found that there is a preference for the use of clinical and technical measures that include the Functions and Structures of the Body components. The literature still lacks studies that investigate whether the benefits of this type of intervention in the structure and function of the body translates into benefits to other areas of functionality such as activity and participation of individuals with OI.²⁵ It is important to investigate these components, because there is no way to presume a direct relationship between a deficiency at the level of function and structure of the body and the limitations of daily life activity and restriction of social participation.

Another point shown in this study is the need for clinical trials that evaluate the effects of other types of intervention in children with OI. Only one study verified the effects of physical training on the improvement of functionality for children with this pathology.⁹ Deficits in muscle strength and physical capacity are a clinical finding present in patients with OI and can be related to the disabilities these individuals experience and need to be better investigated.

The selection of the appropriate outcome measure depends on factors like the research question, type of intervention, content, and the psychometric properties of the instruments in addition to their availability to the population to be studied.²⁶ The OI is a heterogeneous condition with clinical variations and many disabilities. It is necessary that the studies evaluating the interventions on these individuals have research questions that include the various components of functionality.

It was verified that there was low usage of the evaluation questionnaire/instrument in OI clinical trials that could examine other functionality components in addition to the structure and function of the body. This finding may be justified by the need for studies that confirm the psychometric characteristics of instruments to be used in OI, however, it shows the difficulty in looking beyond disabilities in the function and structure of the body, a focus preconized by the medical model in which the International Classification of Diseases (ICD-10) and the ICDID.

In recent years, there was a change of focus on interventions in pediatric rehabilitation. The focus on the structure, function

of the body, and activity gave place to considering the environmental factors in order to improve the participation of the pediatric population that receives the intervention.²⁷ In this new scenario, rehabilitation focused on the family has gained space, with the needs of the family and patient and the aspects of their social context being considered important in determining an intervention.²⁸

The evaluation of the participation component is necessary, for it shows the environmental influence inserting the social perspective of functionality. While bringing information on the performance of an individual in his habitual environment, this component helps to expose the function gap between a habitual environment and a standardized one, supplying data on what can be changed in the context to improve the participation of the individual.⁵

The ICF, based on the biopsychosocial model, broadens the perspective of the medical model, considering the experience of functionality and disability and not just related to the health condition and its effects on the structure and function of the body. For the ICF, functionality and disability result from the interaction of the health condition with a facilitating or restrictive environment. Thus, the instrument provides support to describe bodily impediments and to understand social barriers and how they relate to the limiting and restricting the activity and participation of the individual.

It is important when studying the functionality of disabled individuals that instruments to measure outcomes be chosen to include all the functionality components as well as the contextual ones. The PEDI analysis, for example, has proven to be an instrument that evaluates the functionality of the Functions of the Body components and, especially, the Activity and Participation, with emphasis on tasks related to mobility and personal care. This instrument can help in the evaluation of interventions in OI as a supplement to those clinical and technical measures used.

In order to evaluate Environmental Factors, another instrument must be chosen to supplement the PEDI, for the latter has not included contextual aspects in the evaluation.

The results here must be interpreted considering the limitations of this study. Not all the evaluation instruments described in the studies have been analyzed, only the most frequently used (PEDI). The choice was made after concluding that, due to the little use of the other instruments, they would add little to the discussion in the work.

CONCLUSION

Using the ICF-CY as a reference, it was verified that the concepts of outcome measures in OI clinical trials were related, especially, to the Functions and Structures of the Body components. The Activity and Participation and Contextual Factors components are still little evaluated in these studies. The PEDI, although little used, has shown to be a good instrument to evaluate the Activity and Participation component, being an option as a supplement to the clinical and technical measures in OI clinical trials. More studies are necessary on the effects of other interventions, in addition to medication, in the functionality of children and youth with Osteogenesis Imperfecta.

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