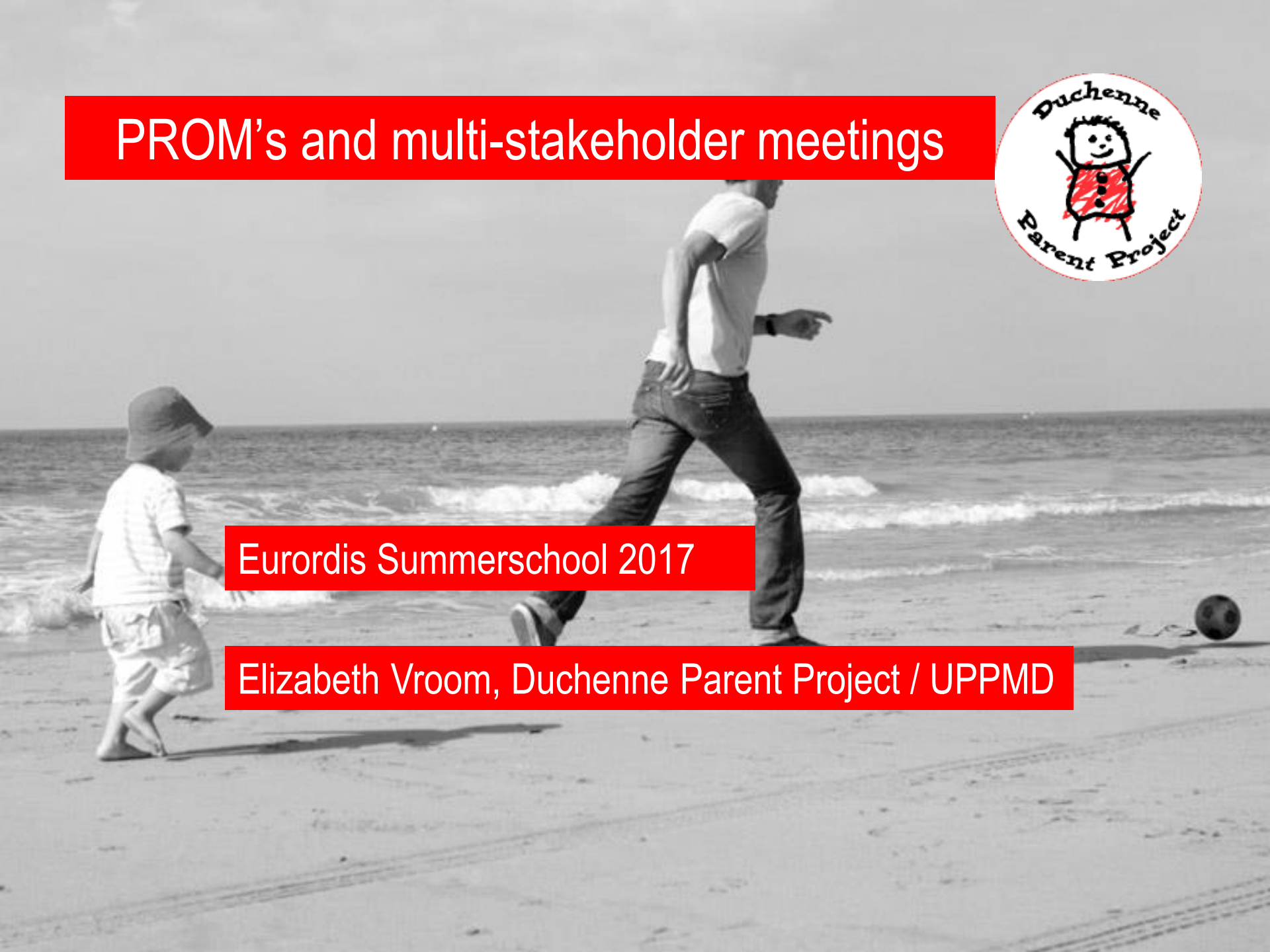
PROM's and multi-stakeholder meetings



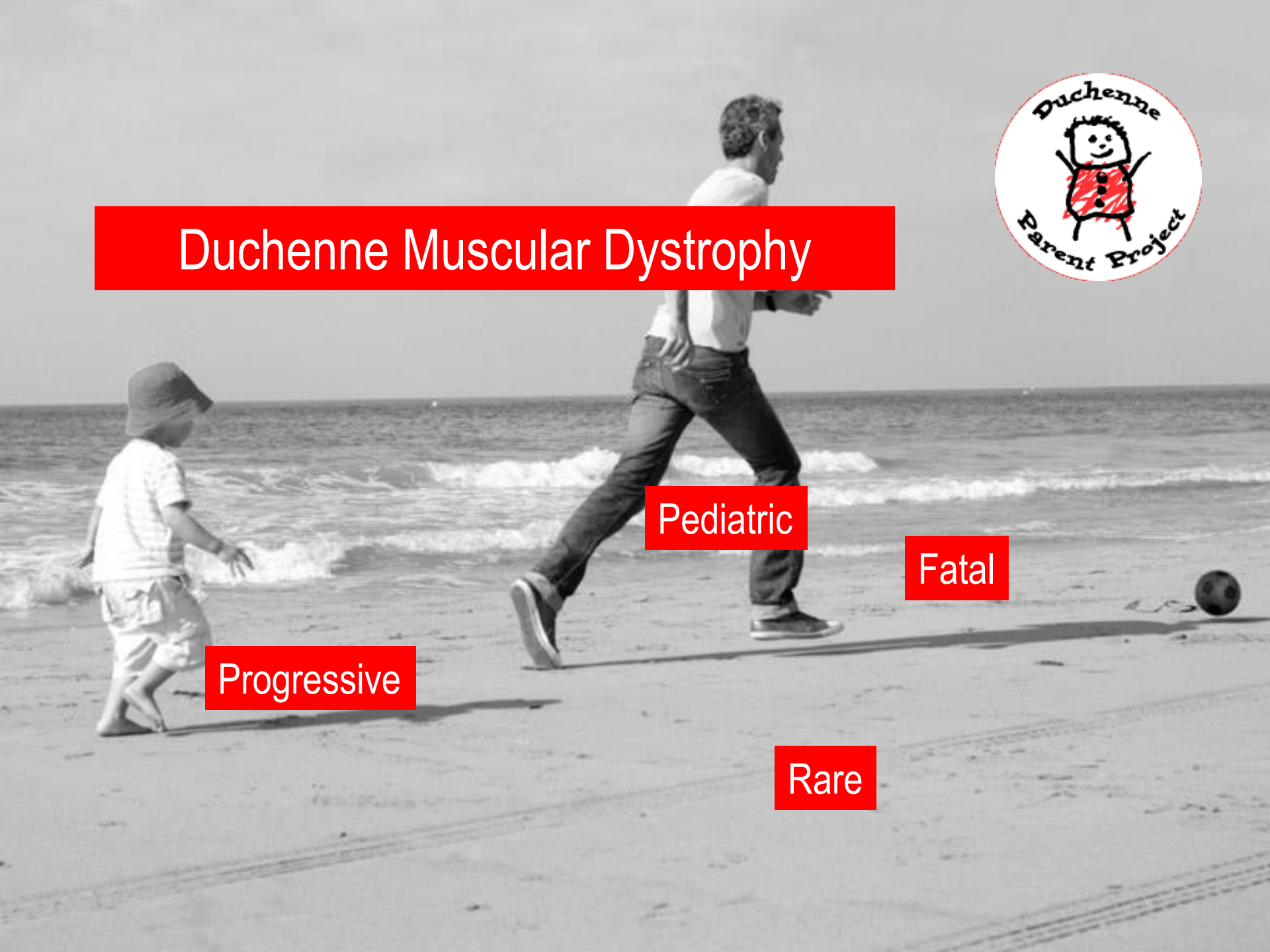
Eurordis Summerschool 2017

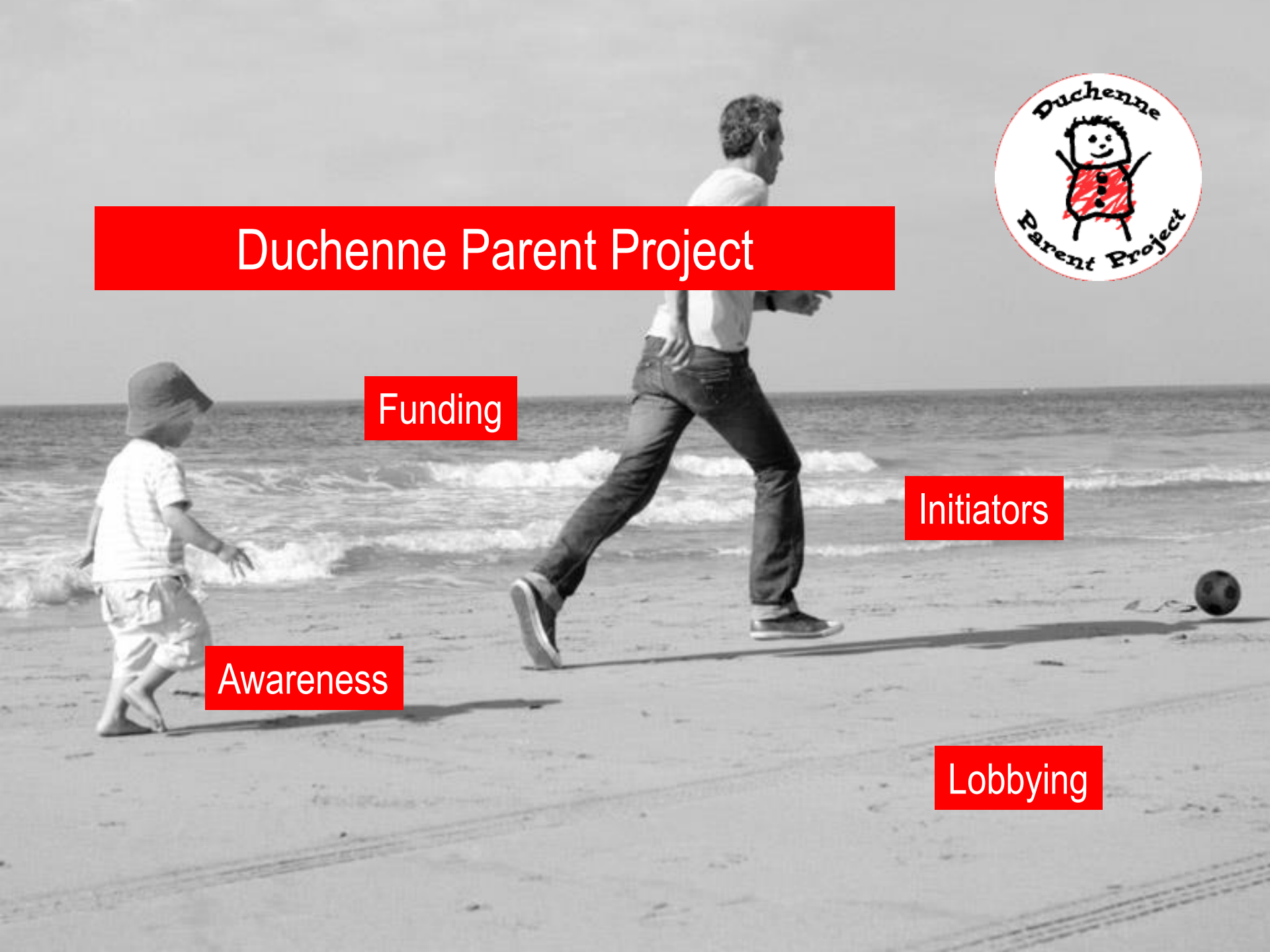
Elizabeth Vroom, Duchenne Parent Project / UPPMD

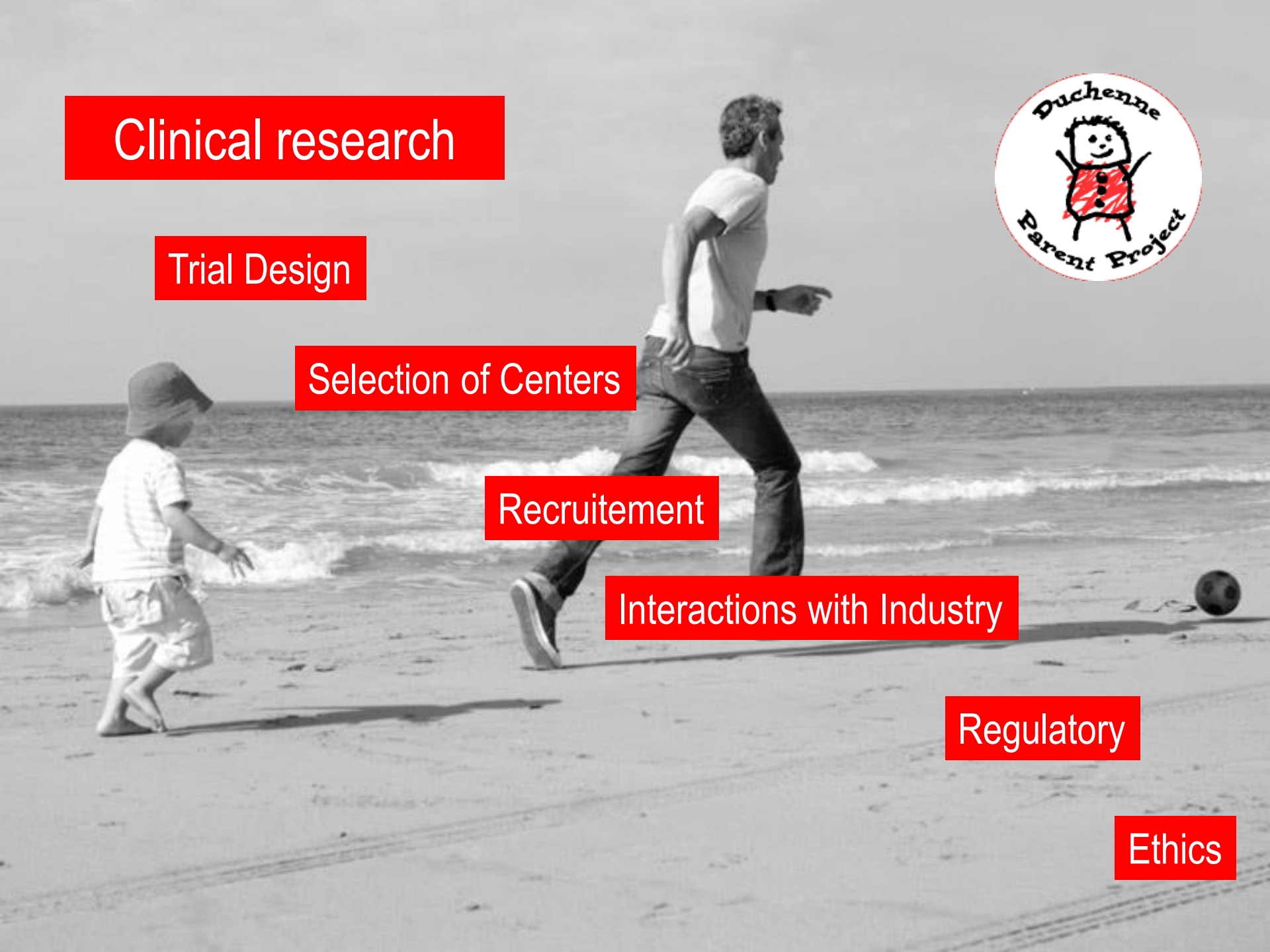
Patient opinions - input in drug development

Prom: effect of a treatment or drug

Multistakeholder meetings: input in policies and guidelines


Duchenne Muscular Dystrophy
Pediatric
Fatal
Progressive
Rare
Duchenne
Parent Project


Duchenne Parent Project
Funding
Initiators
Awareness
Lobbying
Duchenne
Parent Project


Clinical research
Trial Design
Selection of Centers
Recruitement
Interactions with Industry
Regulatory
Ethics
Duchenne
Parent Project

Outcome measures

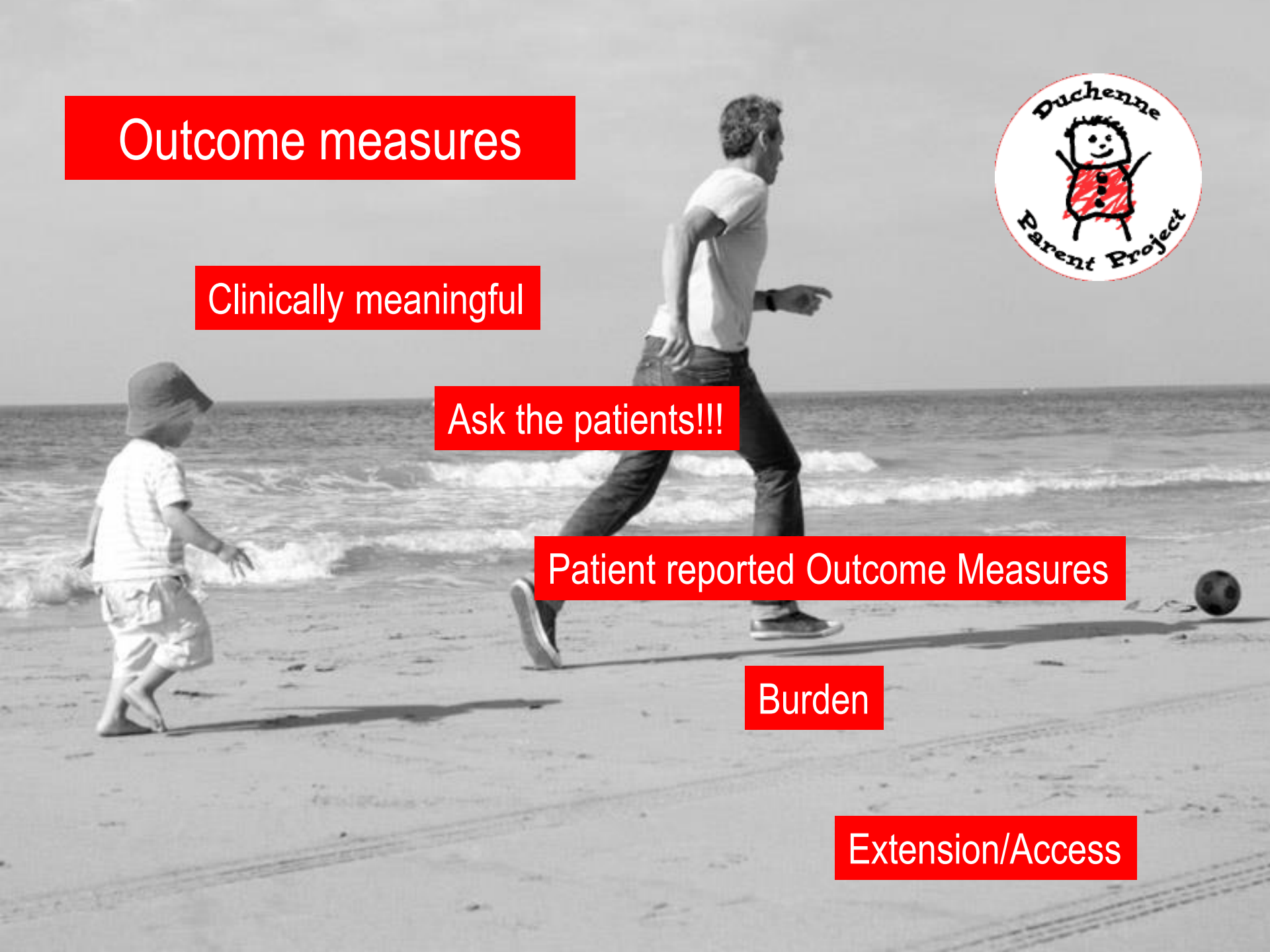
Clinically meaningful

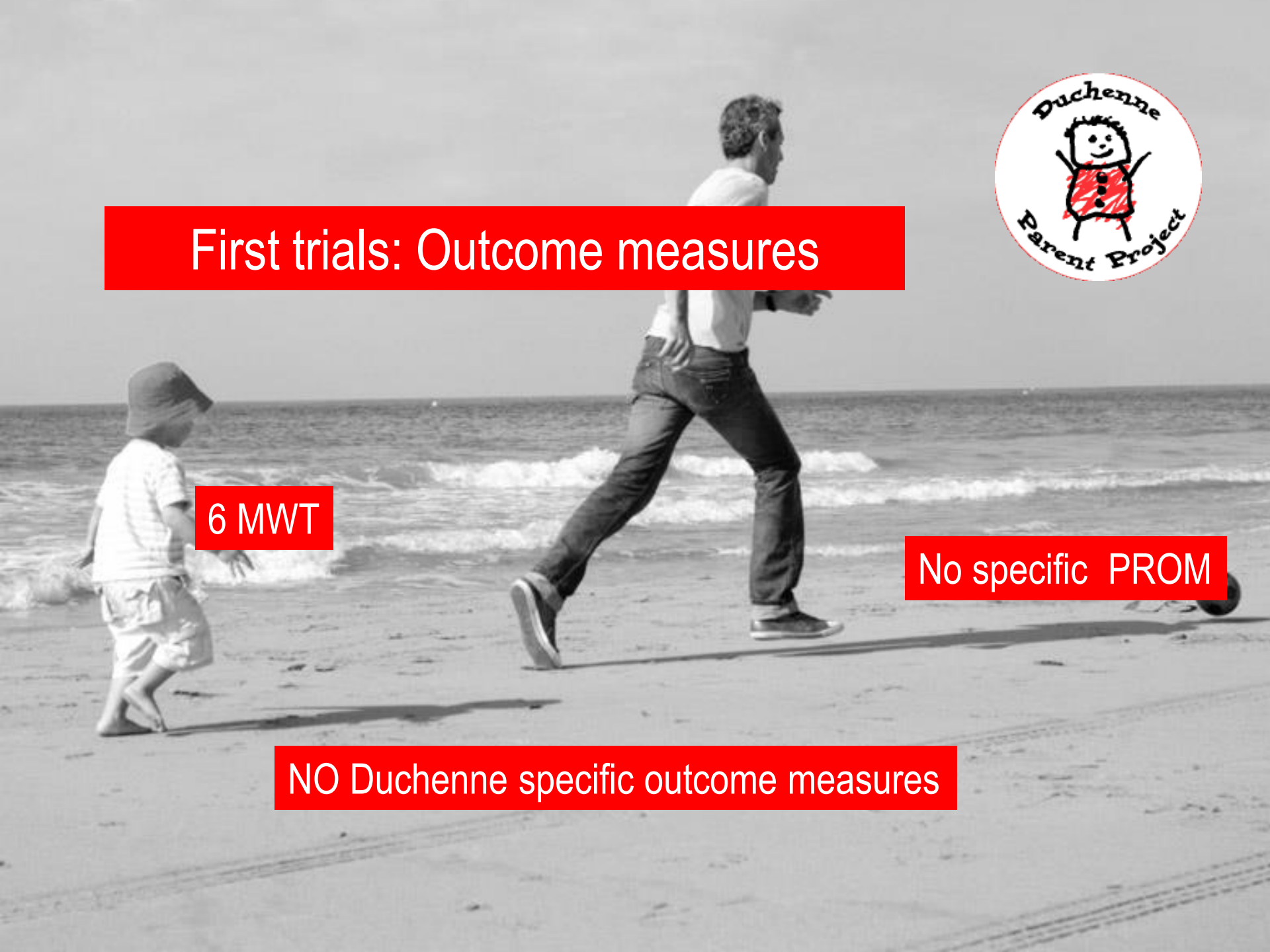
Ask the patients!!!

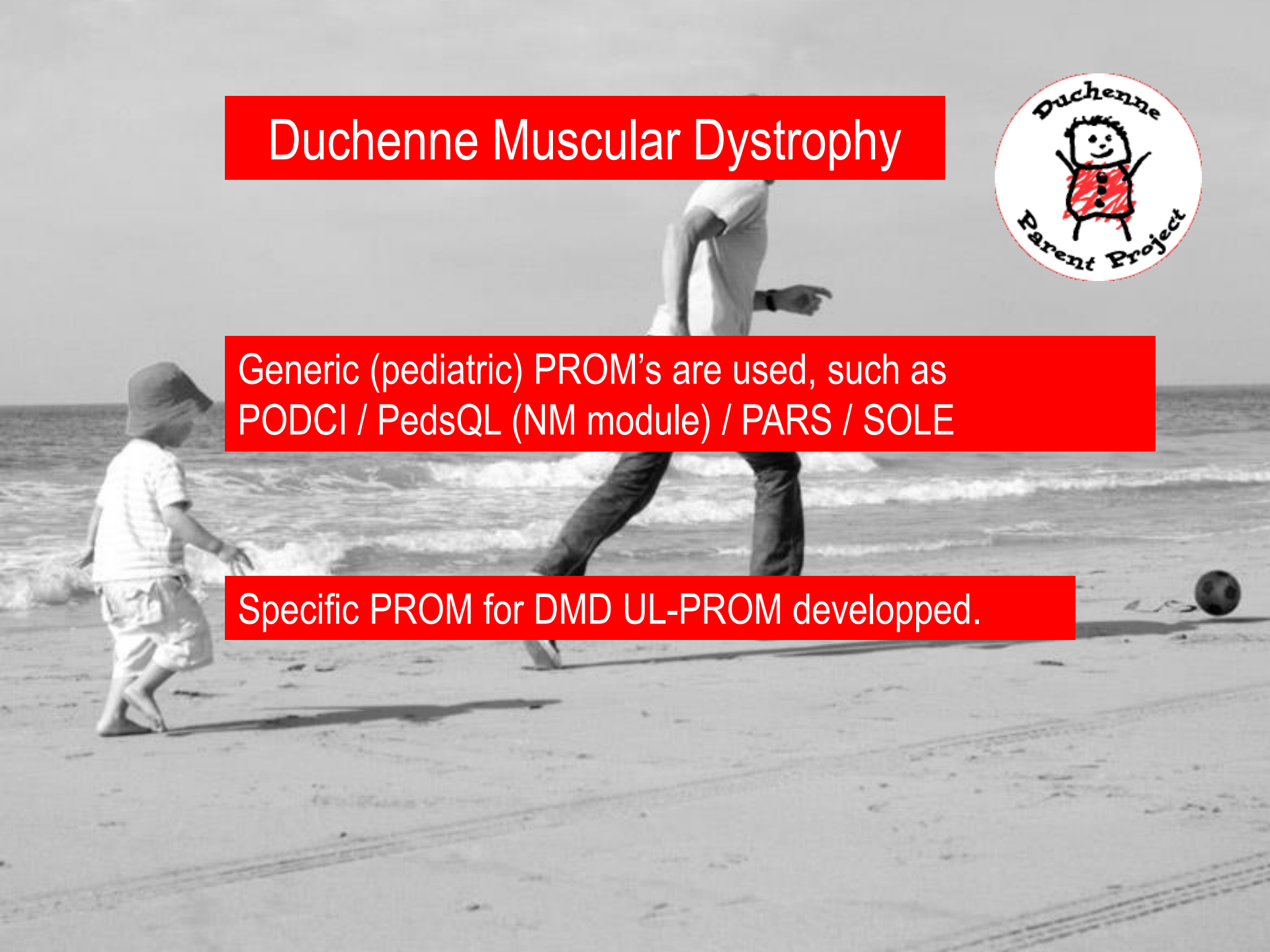
Patient reported Outcome Measures

Burden

Extension/Access




First trials: Outcome measures
6 MWT
No specific PROM
NO Duchenne specific outcome measures
Duchenne
Parent Project

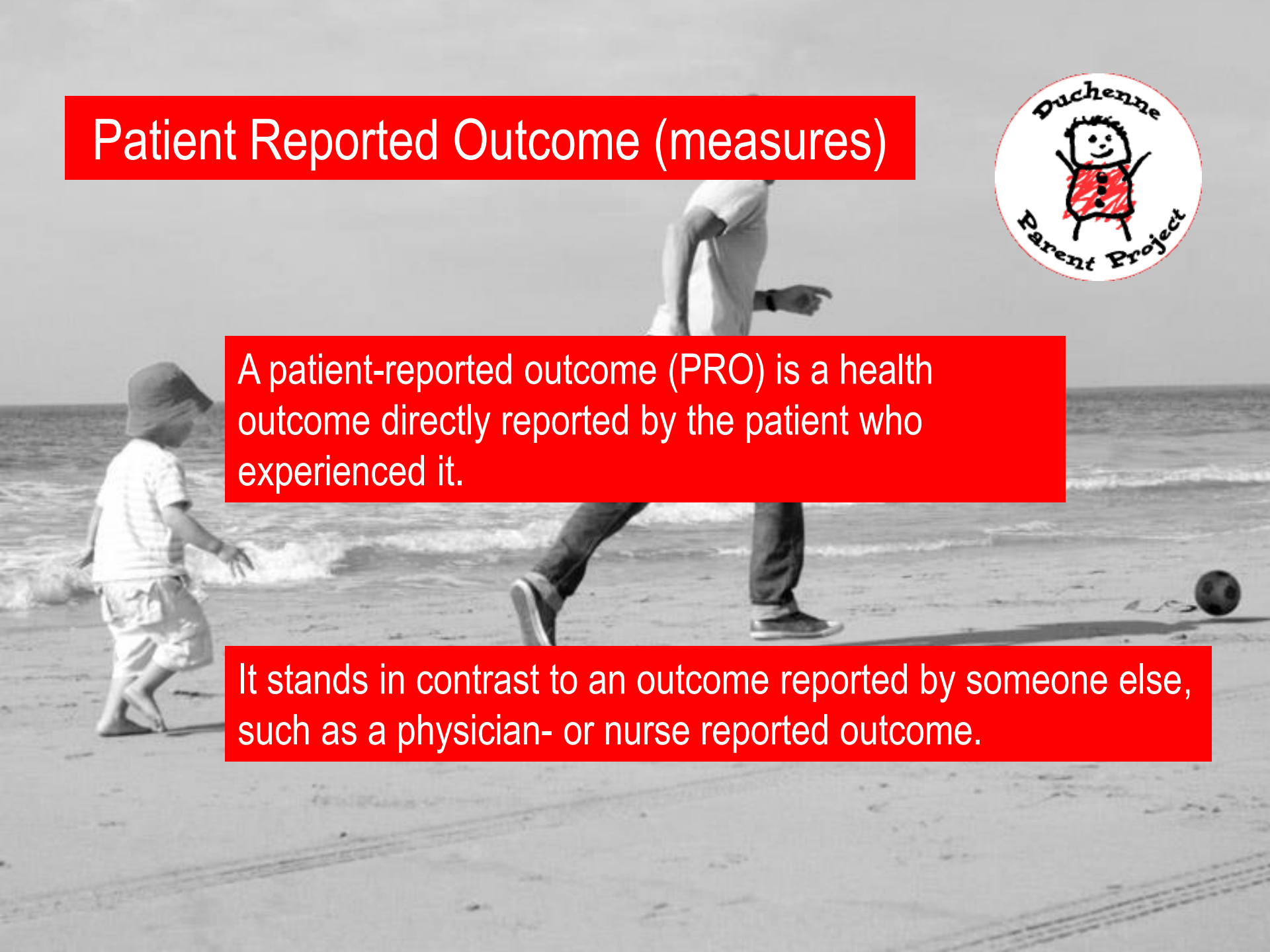

Duchenne Muscular Dystrophy
Generic (pediatric) PROM's are used, such as
PODCI / PedsQL (NM module) / PARS / SOLE
Specific PROM for DMD UL-PROM developped.
Duchenne
Parent Project

Performance of Upper LImb

Development of the Performance of the Upper Limb module for **Duchenne** muscular dystrophy.
Dev Med Child Neurol. 2013 Nov;

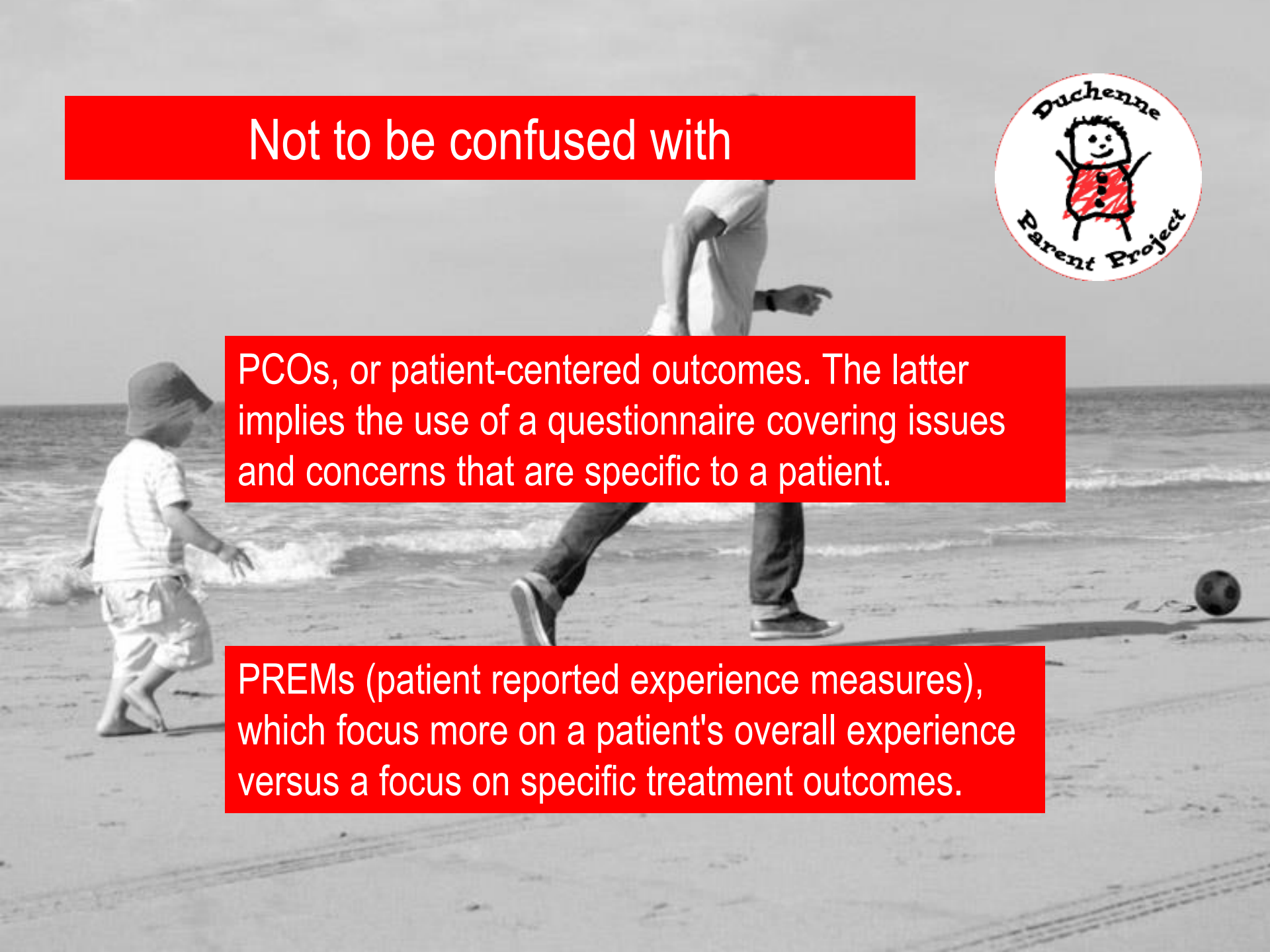
Mayhew A, Mazzone ES, Eagle M, Duong T, Ash M, Decostre V, Vandenhauwe M, Klingels K, Florence J, Main M, Bianco F, Henrikson E, Servais L, Campion G, ***Vroom*** *E, Ricotti V, Goemans N, McDonald C, Mercuri E; Performance of the Upper Limb Working Group..*

Patient Reported Outcome (measures)



A patient-reported outcome (PRO) is a health outcome directly reported by the patient who experienced it.

It stands in contrast to an outcome reported by someone else, such as a physician- or nurse reported outcome.

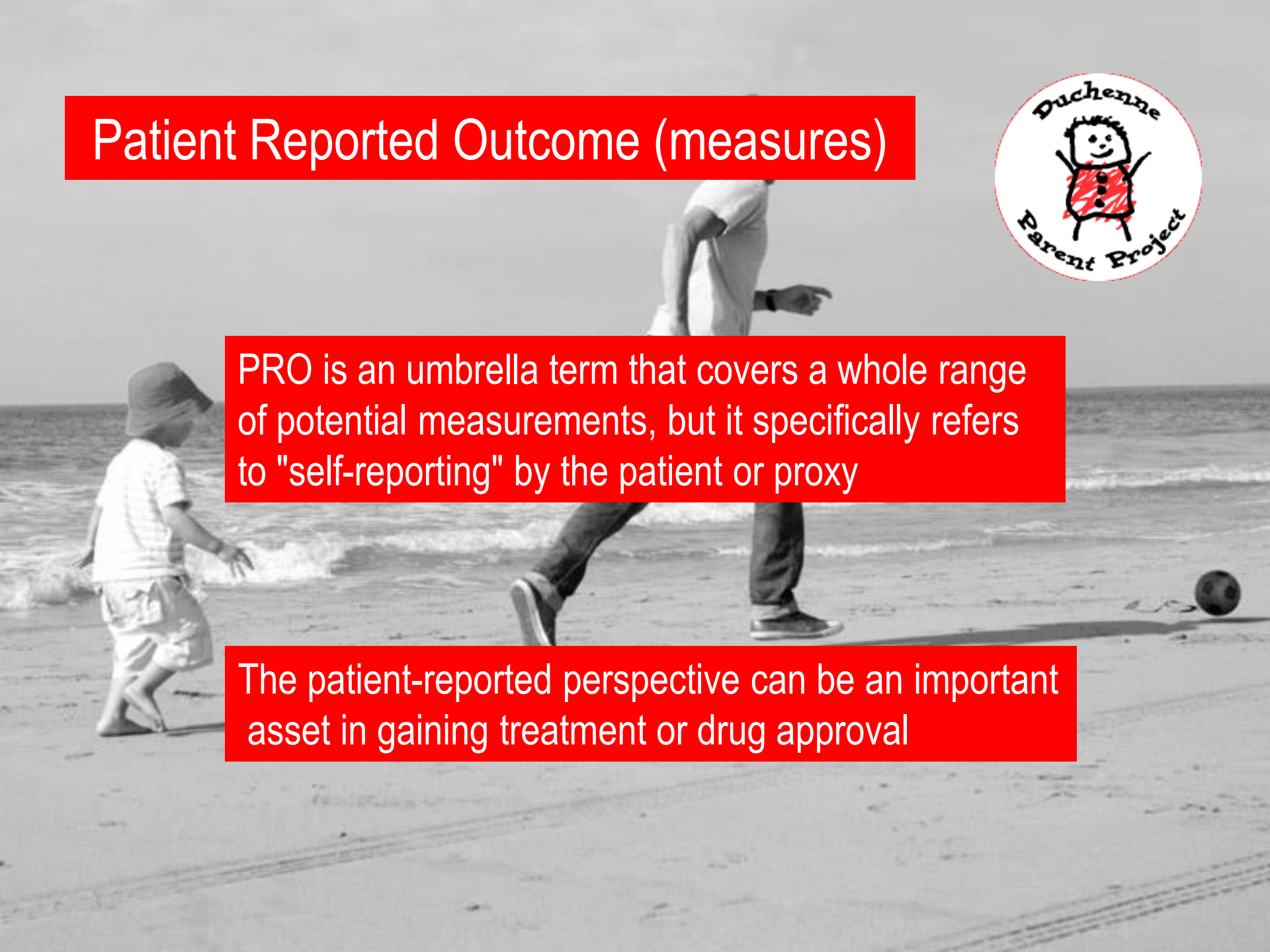


Not to be confused with

PCOs, or patient-centered outcomes. The latter implies the use of a questionnaire covering issues and concerns that are specific to a patient.

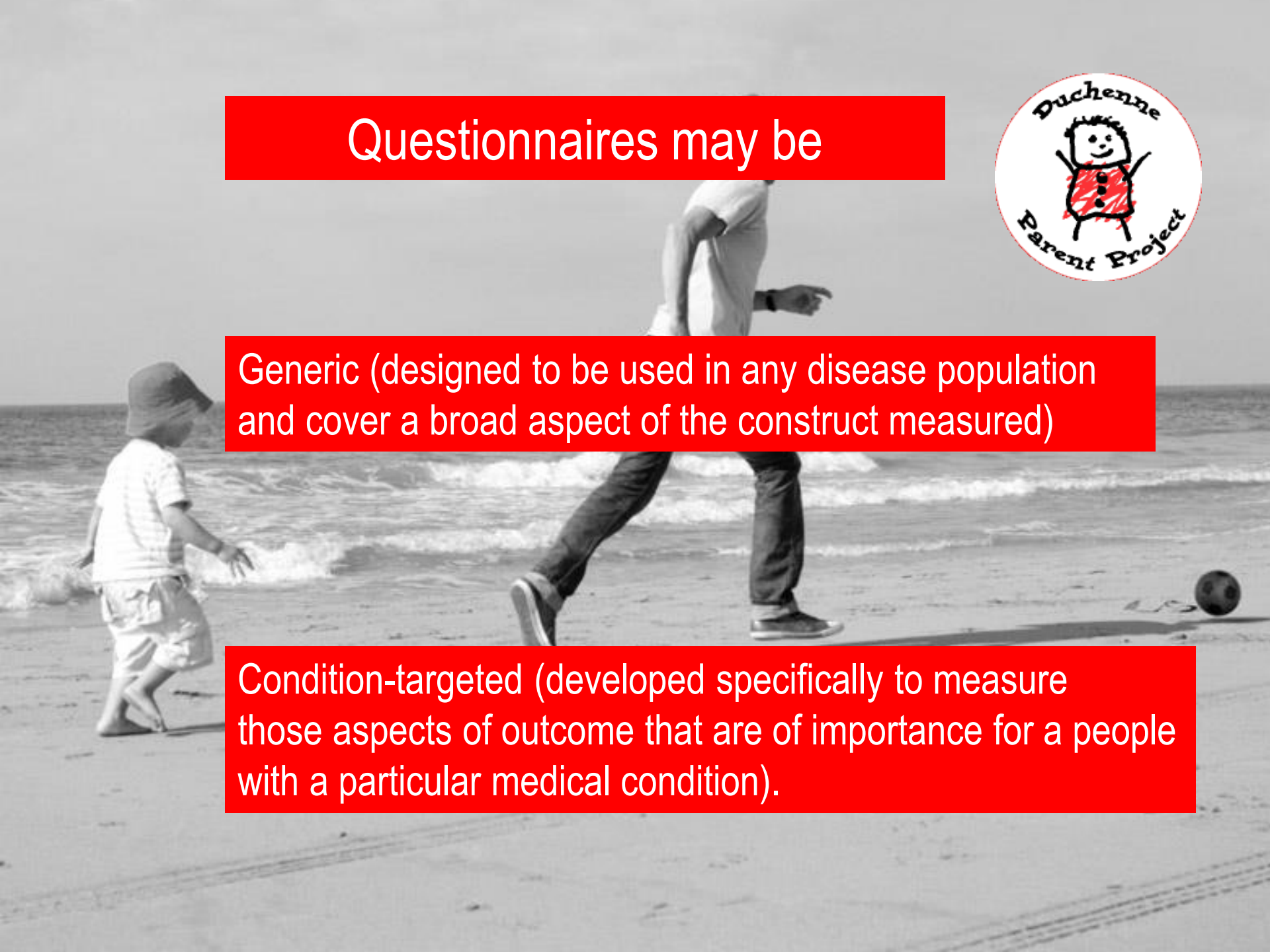
PREMs (patient reported experience measures), which focus more on a patient's overall experience versus a focus on specific treatment outcomes.

Patient Reported Outcome (measures)



PRO is an umbrella term that covers a whole range of potential measurements, but it specifically refers to "self-reporting" by the patient or proxy

The patient-reported perspective can be an important asset in gaining treatment or drug approval

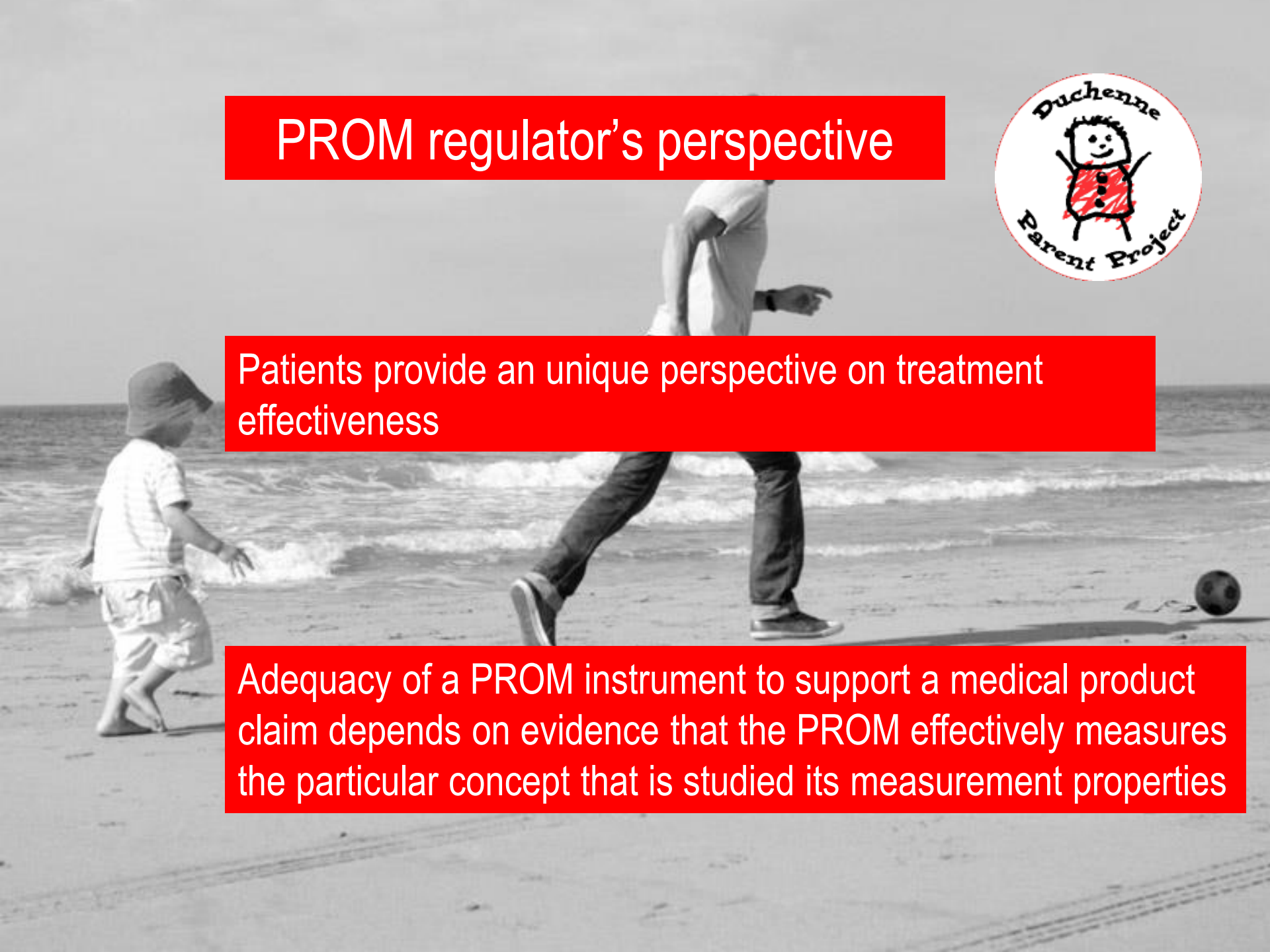


Questionnaires may be

Generic (designed to be used in any disease population and cover a broad aspect of the construct measured)

Condition-targeted (developed specifically to measure those aspects of outcome that are of importance for a people with a particular medical condition).

PROM regulator's perspective



Patients provide an unique perspective on treatment effectiveness

Adequacy of a PROM instrument to support a medical product claim depends on evidence that the PROM effectively measures the particular concept that is studied its measurement properties

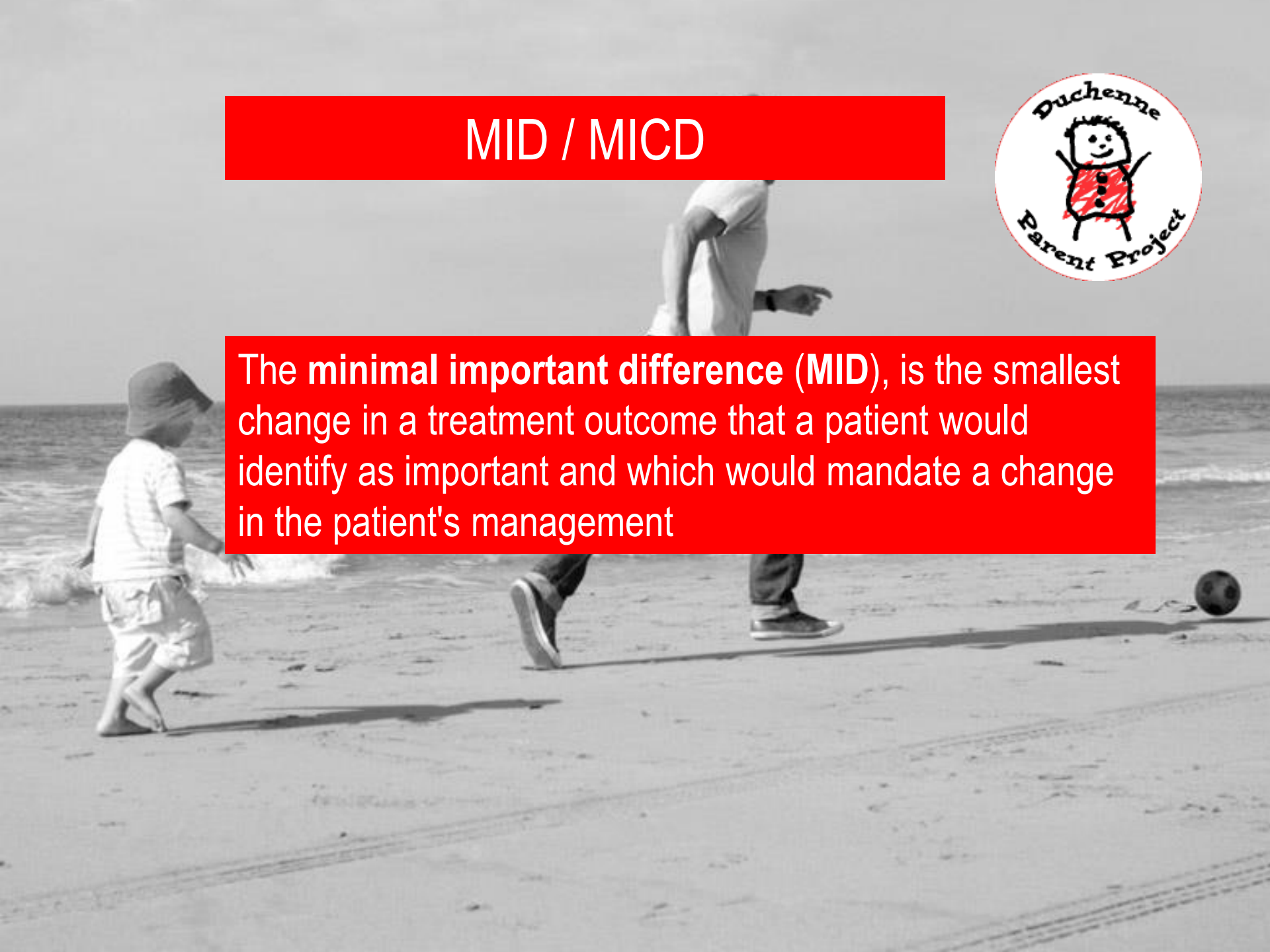
PROM regulator's perspective

Valid measures should be selected based on their 'fit' with a hypothesis led strategy

> Concept and domains to be measured, intended application should be well defined

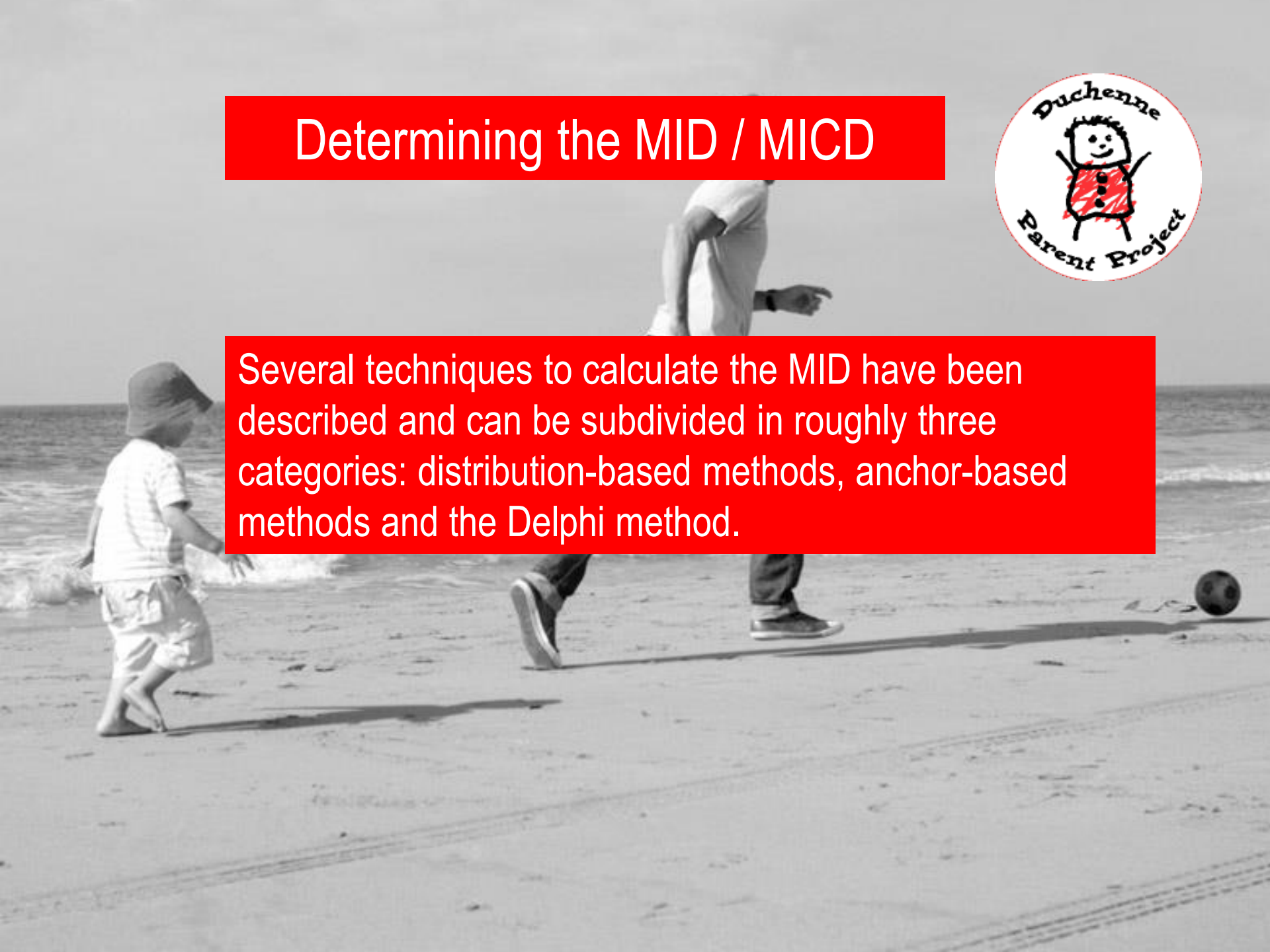
> Reliability, validity, ability to detect changes, definition of MCID and definition of responders should be established

MID / MICD



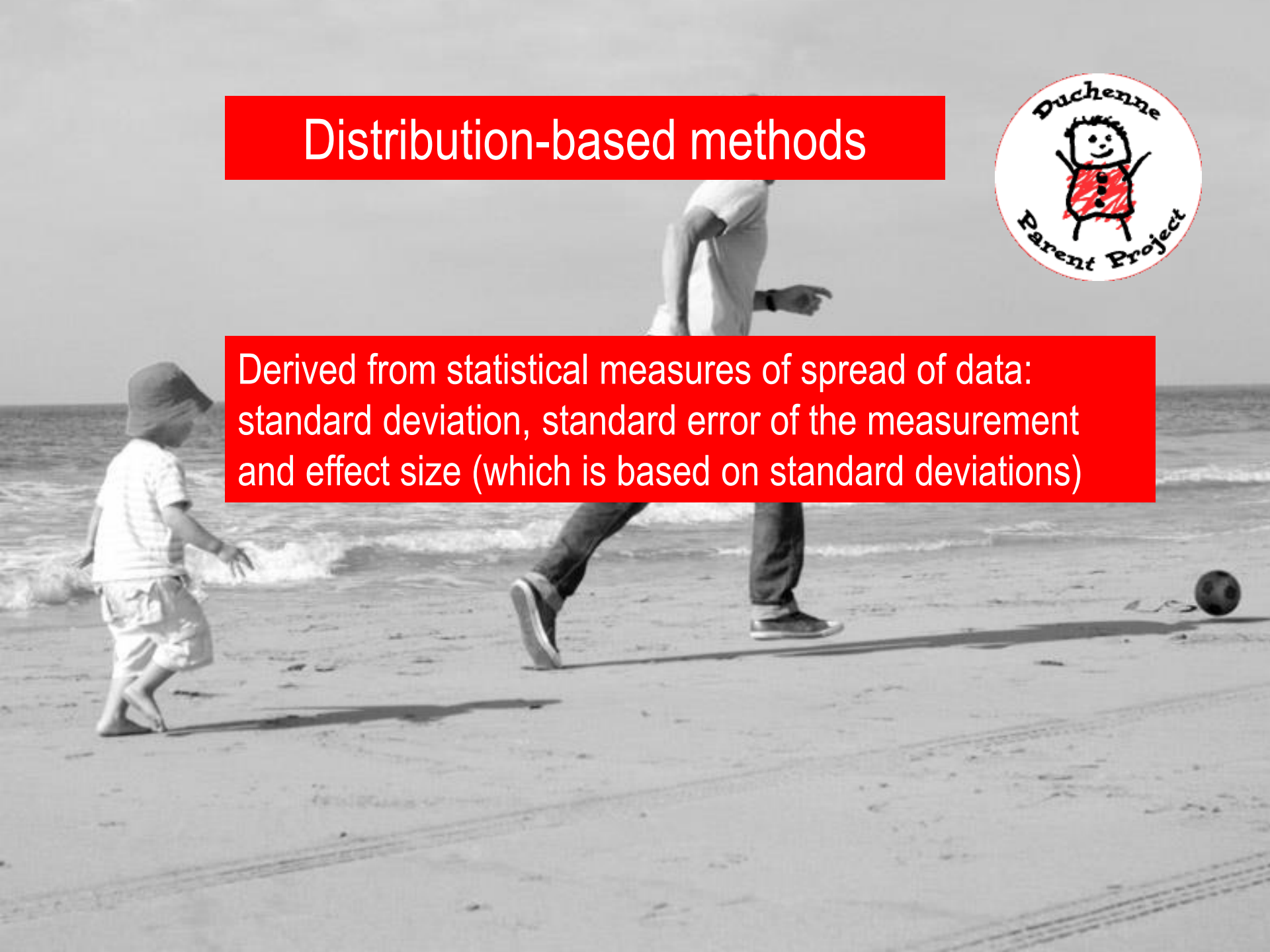
The **minimal important difference** (**MID**), is the smallest change in a treatment outcome that a patient would identify as important and which would mandate a change in the patient's management

Determining the MID / MICD



Several techniques to calculate the MID have been described and can be subdivided in roughly three categories: distribution-based methods, anchor-based methods and the Delphi method.

Distribution-based methods



Derived from statistical measures of spread of data: standard deviation, standard error of the measurement and effect size (which is based on standard deviations)

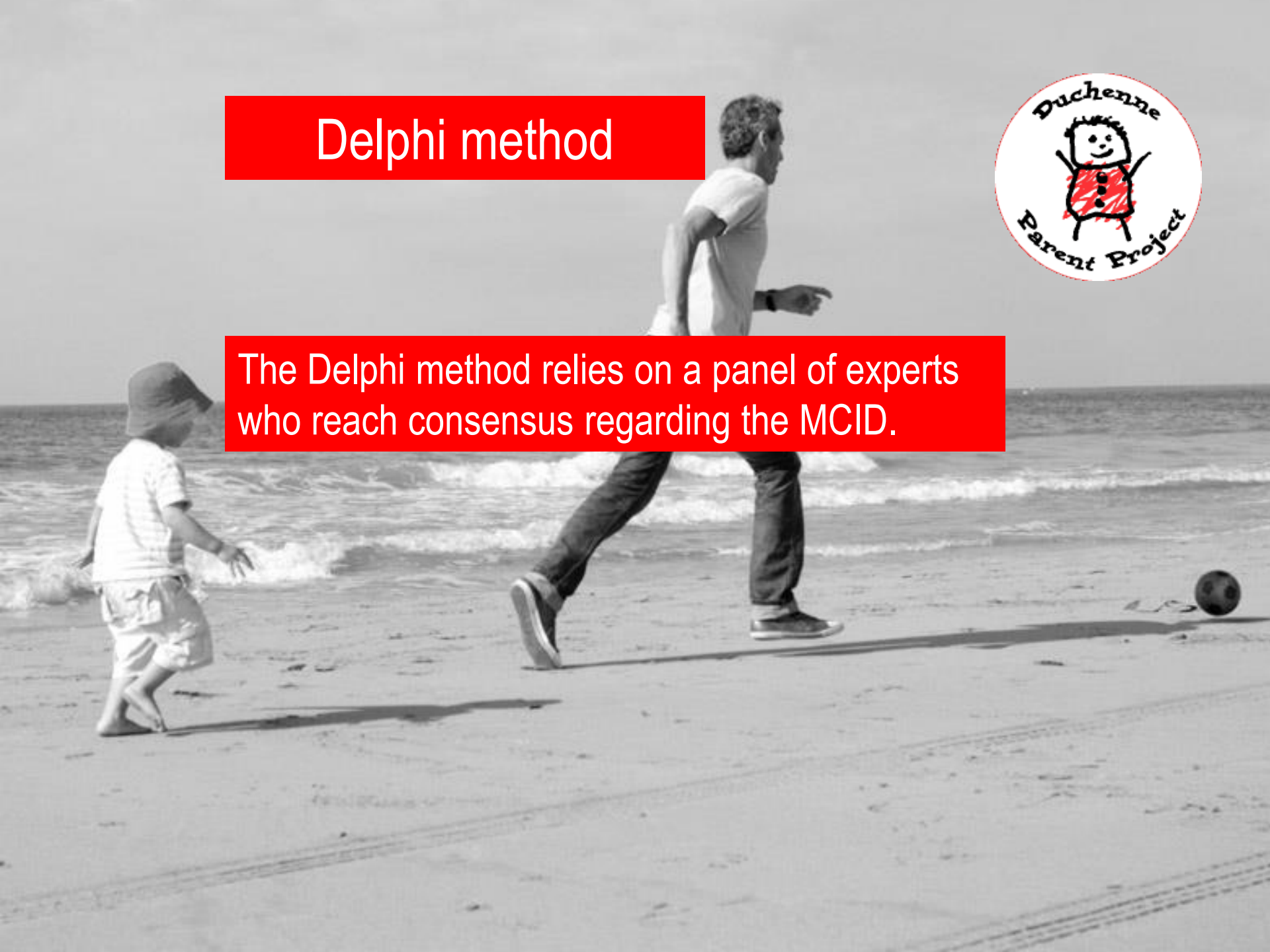
Anchor based

The anchor based method compares changes in scores with an “anchor” as reference. An anchor establishes if the patient is better after treatment compared to baseline according to the patients own experience.

A popular anchor is the anchor question, at a specific point in time after treatment the patient might be asked: “Do you feel that you are improved by your treatment?”

Delphi method

The Delphi method relies on a panel of experts who reach consensus regarding the MCID.

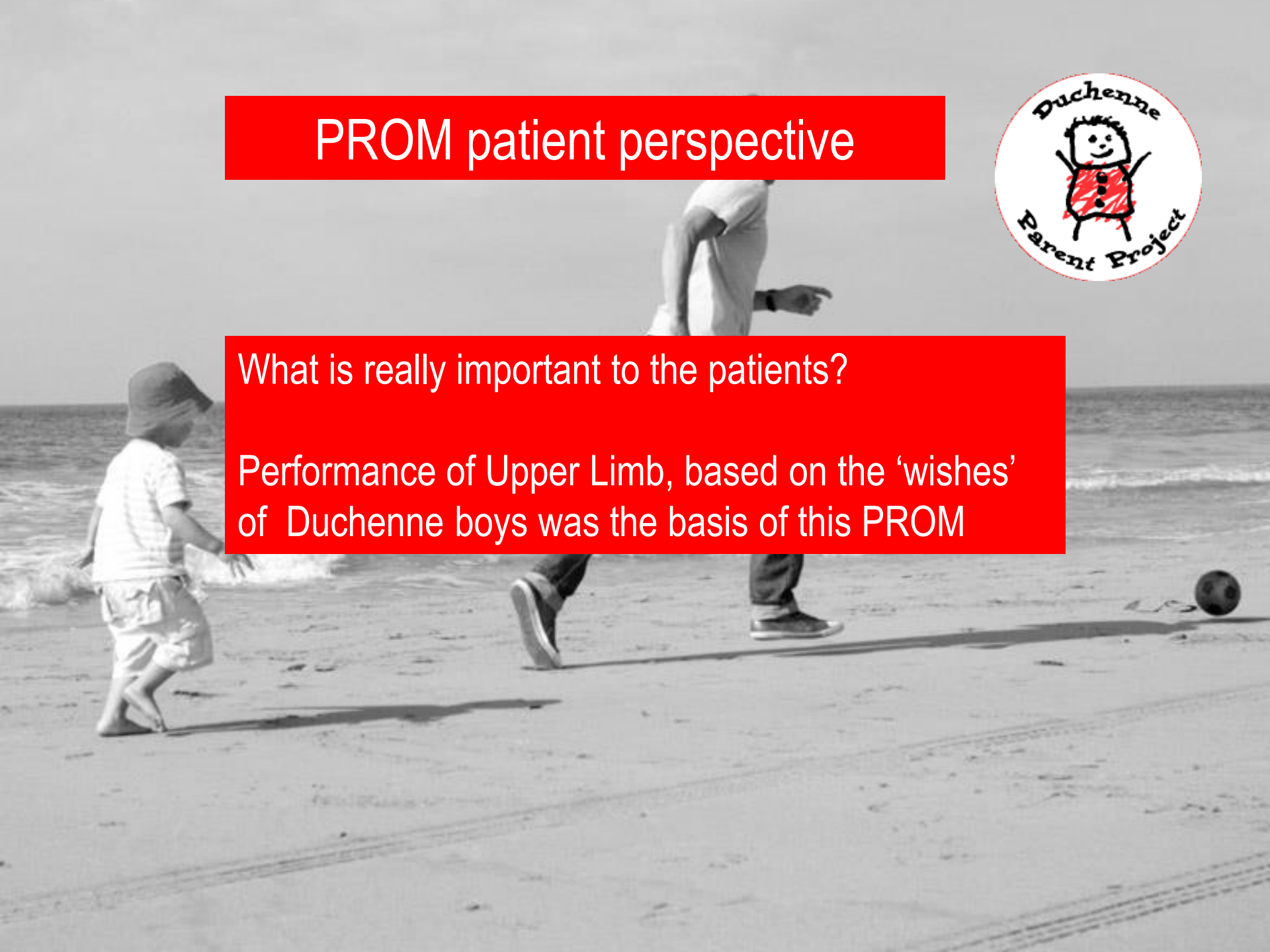


PROM patient/DMD perspective

The concept measured by the instrument should be relevant to the patient, i.e. reflecting their experience at the time of completion.

Parents/caregivers perspective versus the boys and young man with DMD (overall poor agreement between child self-report and parent/proxy report)

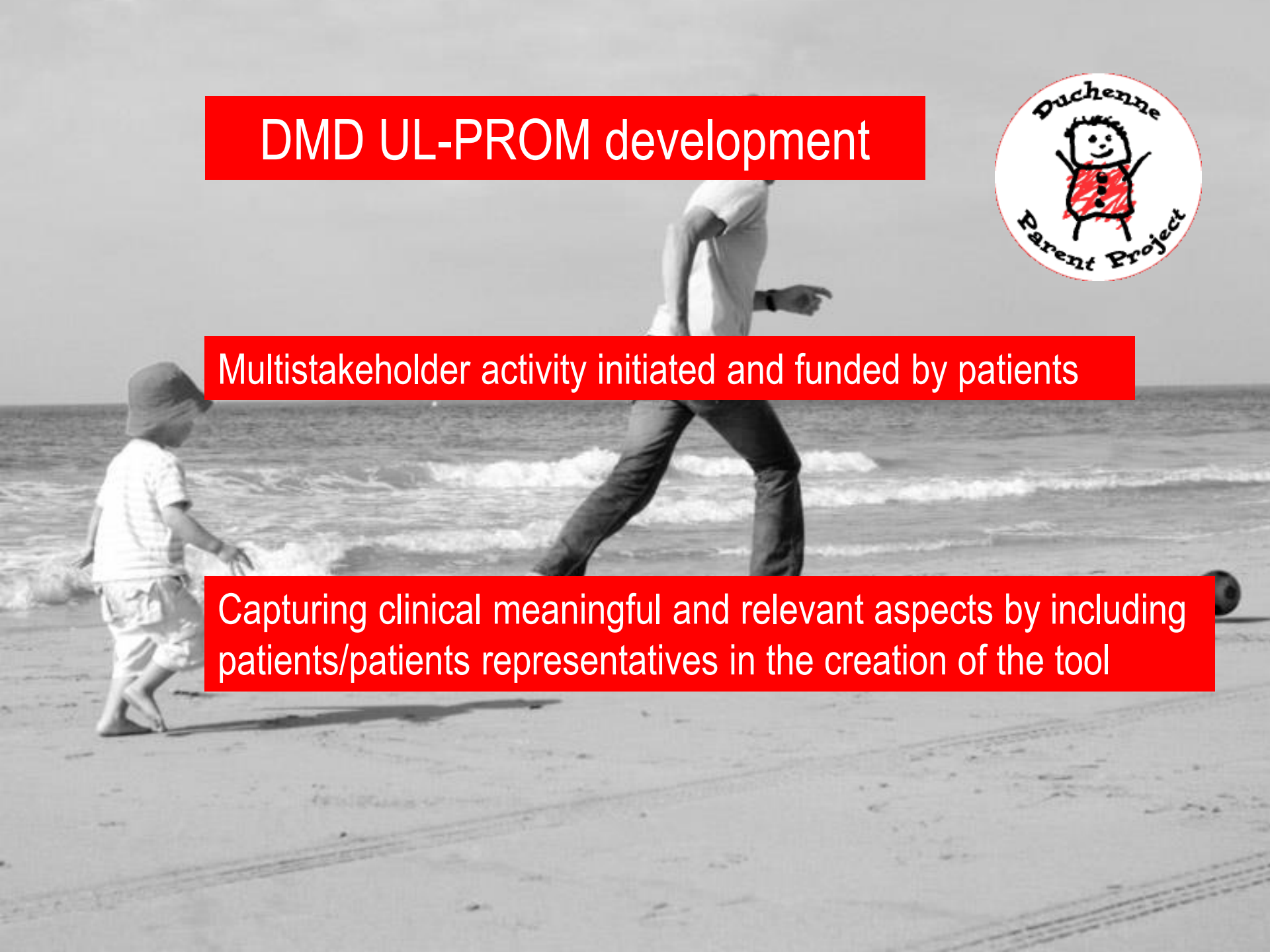
PROM patient perspective



What is really important to the patients?

Performance of Upper Limb, based on the ‘wishes’ of Duchenne boys was the basis of this PROM

DMD UL-PROM development



Multistakeholder activity initiated and funded by patients

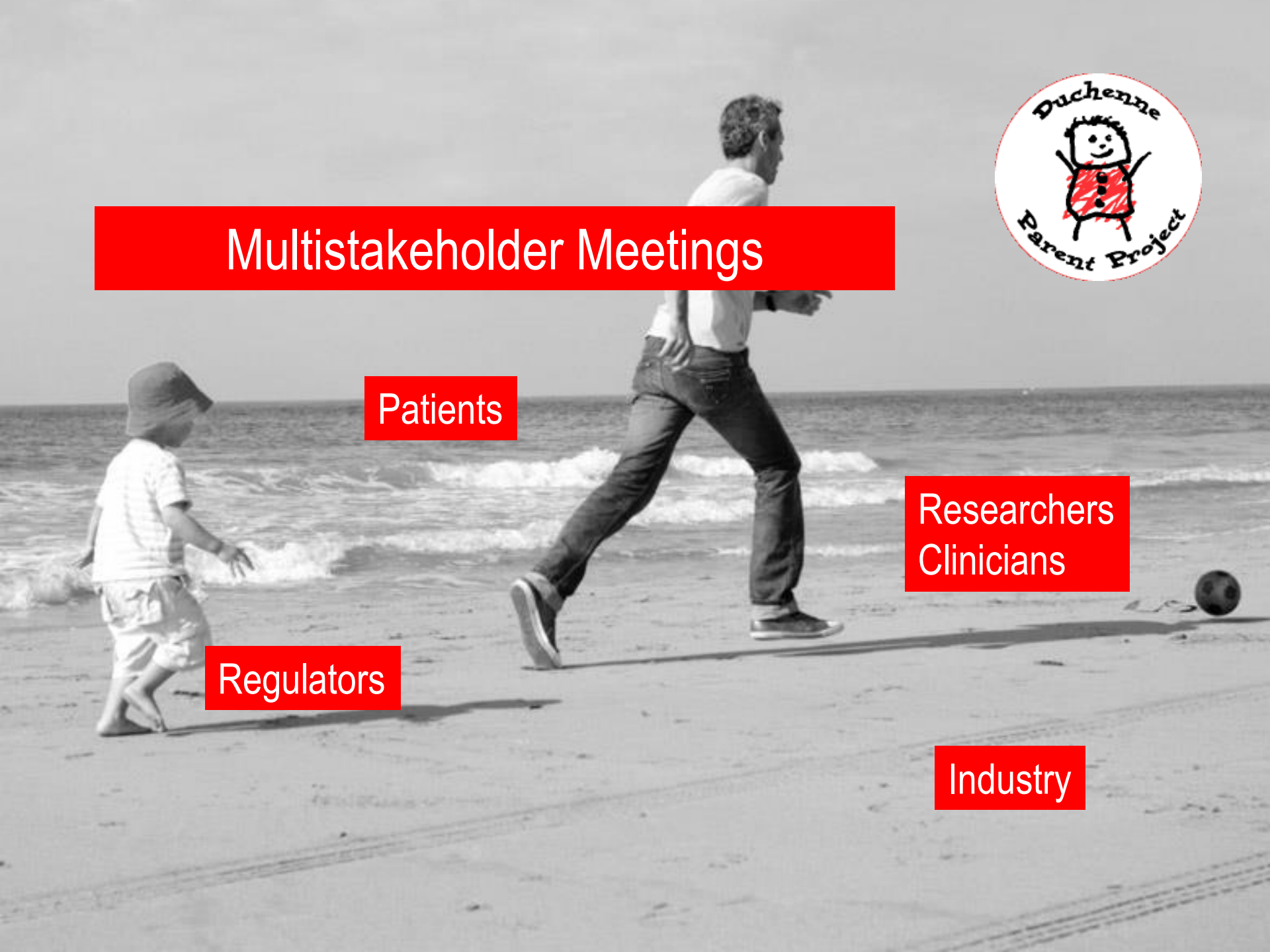
Capturing clinical meaningful and relevant aspects by including patients/patients representatives in the creation of the tool

Publication

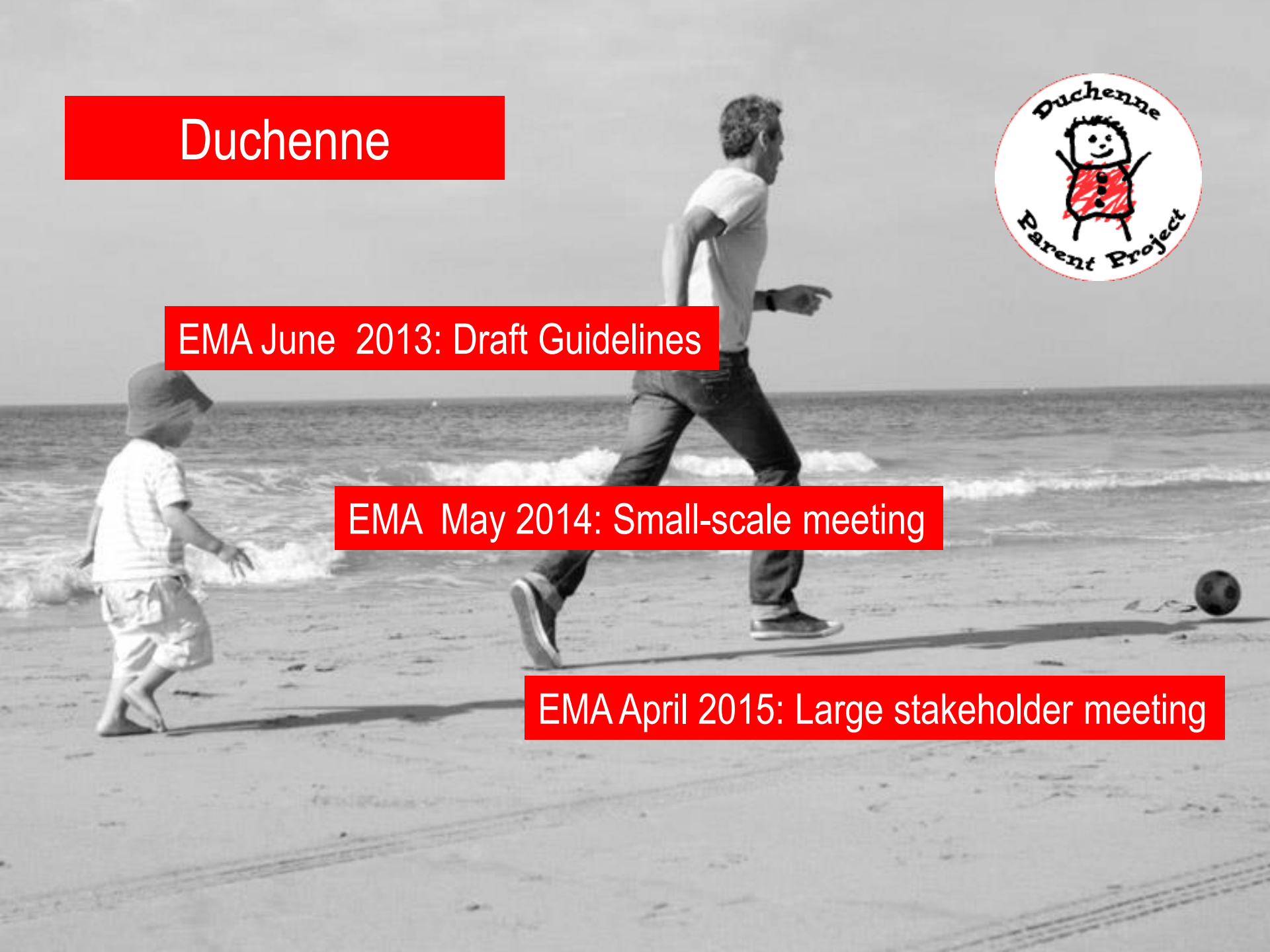
Development of a patient-reported outcome measure for upper limb function in **Duchenne** muscular dystrophy: DMD Upper Limb PROM. Dev Med Child Neurol. 2017
*Klingels K, Mayhew AG, Mazzone ES, Duong T, Decostre V, Werlauff U, **Vroom** E, Mercuri E, Goemans NM; Upper Limb Clinical Outcome Group..*

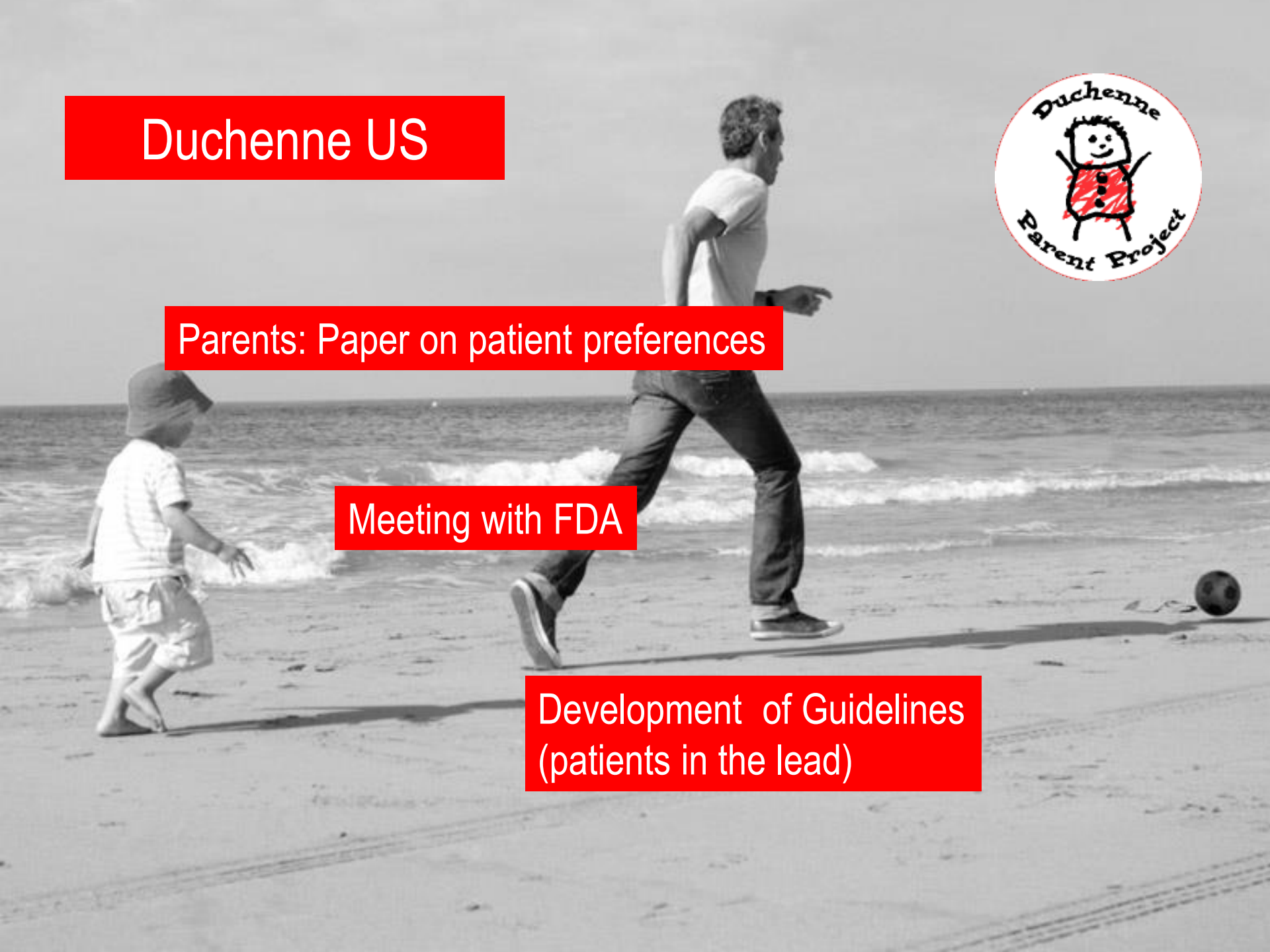
Quality of Life

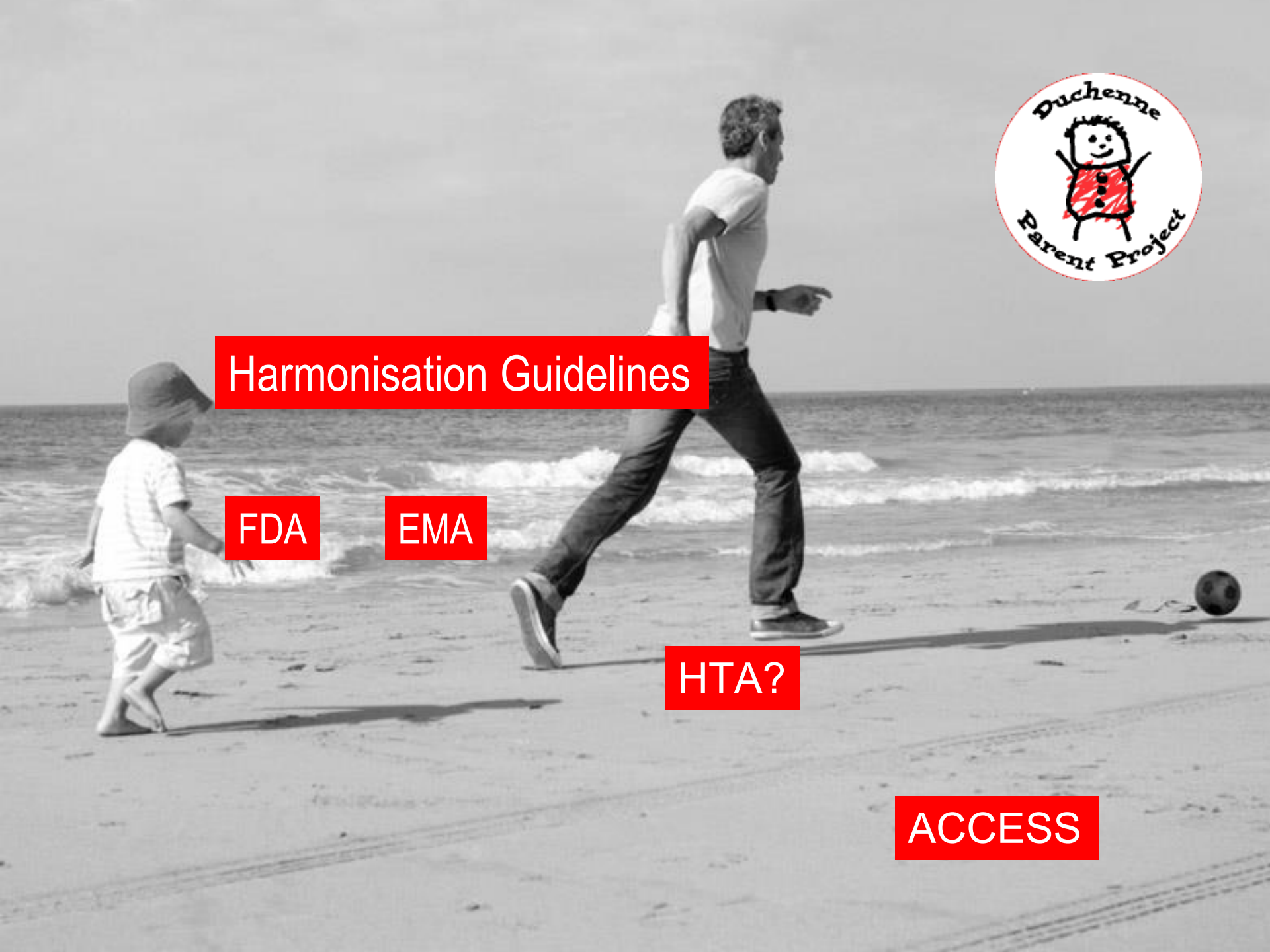
Generally assumed that a reduced physical ability and greater disease severity are the main factor determining impaired quality of life however a whole series of factor personal, cognitive, socialncontextual, relational, environmental, can impact greatly on QoL (subjective and multidimensional concept)


Multistakeholder Meetings
Patients
Researchers
Clinicians
Regulators
Industry
Duchenne
Parent Project


Multi-stakeholder Meetings
Insights
Indentification of gaps
Guidelines
Publications
Duchenne
Parent Project


Duchenne
EMA June 2013: Draft Guidelines
EMA May 2014: Small-scale meeting
EMA April 2015: Large stakeholder meeting
Duchenne
Parent Project


Duchenne US
Parents: Paper on patient preferences
Meeting with FDA
Development of Guidelines
(patients in the lead)
Duchenne
Parent Project


Duchenne
Parent Project
Harmonisation Guidelines
FDA
EMA
HTA?
ACCESS

Patients and PO's should not only be included at an early stage, but also take initiatives and be proactive.


Thank you!

Publications

Stakeholder cooperation to overcome challenges in orphan medicine development: the example of Duchenne muscular dystrophy. Lancet Neurol. 2016 Jul

Straub V, Balabanov P, Bushby K, Ensini M, Goemans N, De Luca A, Pereda A, Hemmings R, Campion G, Kaye E, Arechavala-Gomeza V, Goyenvalle A, Niks E, Veldhuizen O, Furlong P, Stoyanova-Beninska V, Wood MJ, Johnson A, Mercuri E, Muntoni F, Sepodes B, Haas M, Vroom E, Aartsma-Rus A.

Publications

The development of antisense oligonucleotide therapies for **Duchenne** muscular dystrophy: report on a TREAT-NMD workshop hosted by the European Medicines Agency (EMA), on September 25th 2009. Neuromuscul Disord. 2010

Muntoni F; Meeting Steering Committee and TREAT-NMD Network..

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