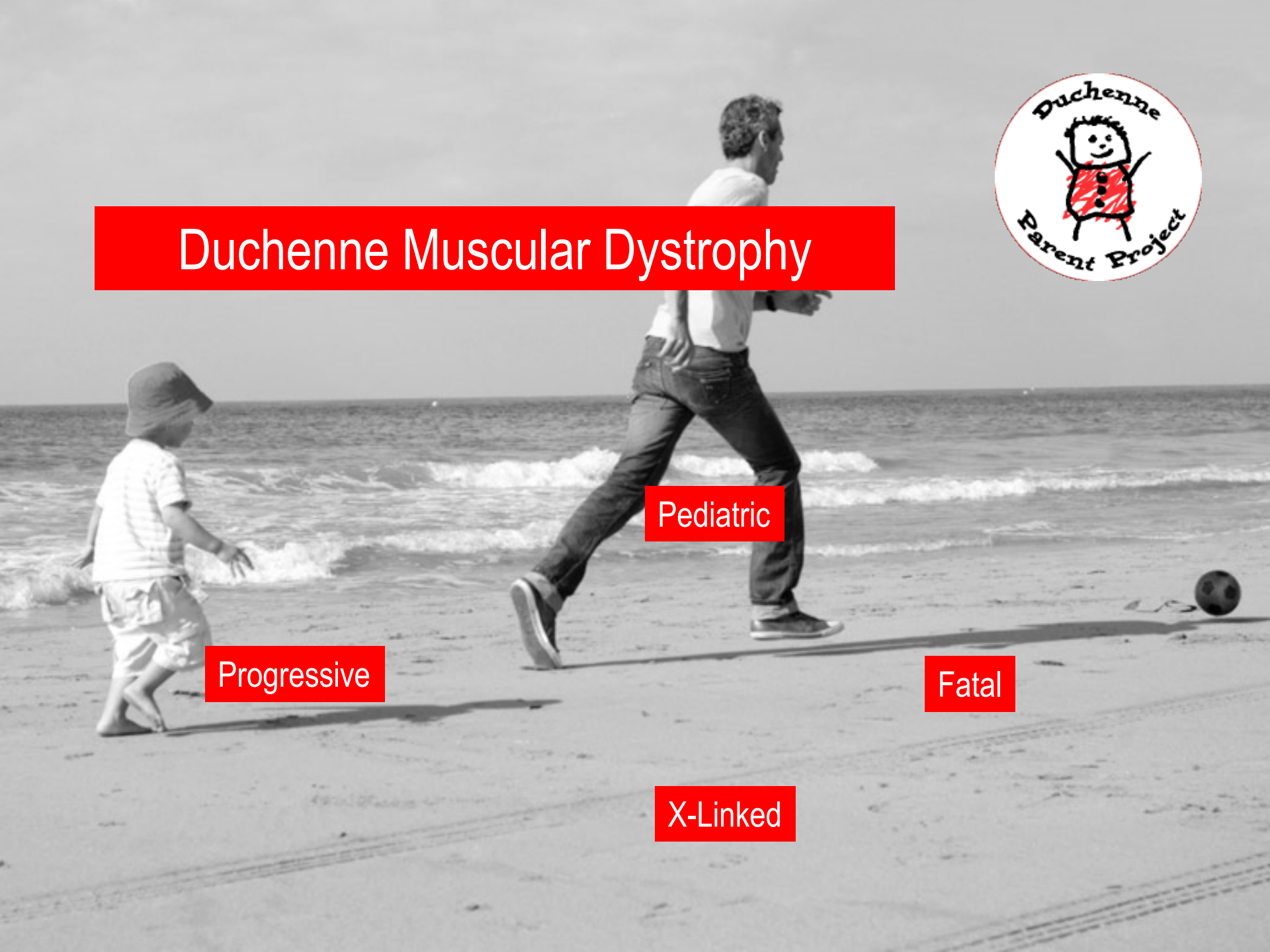
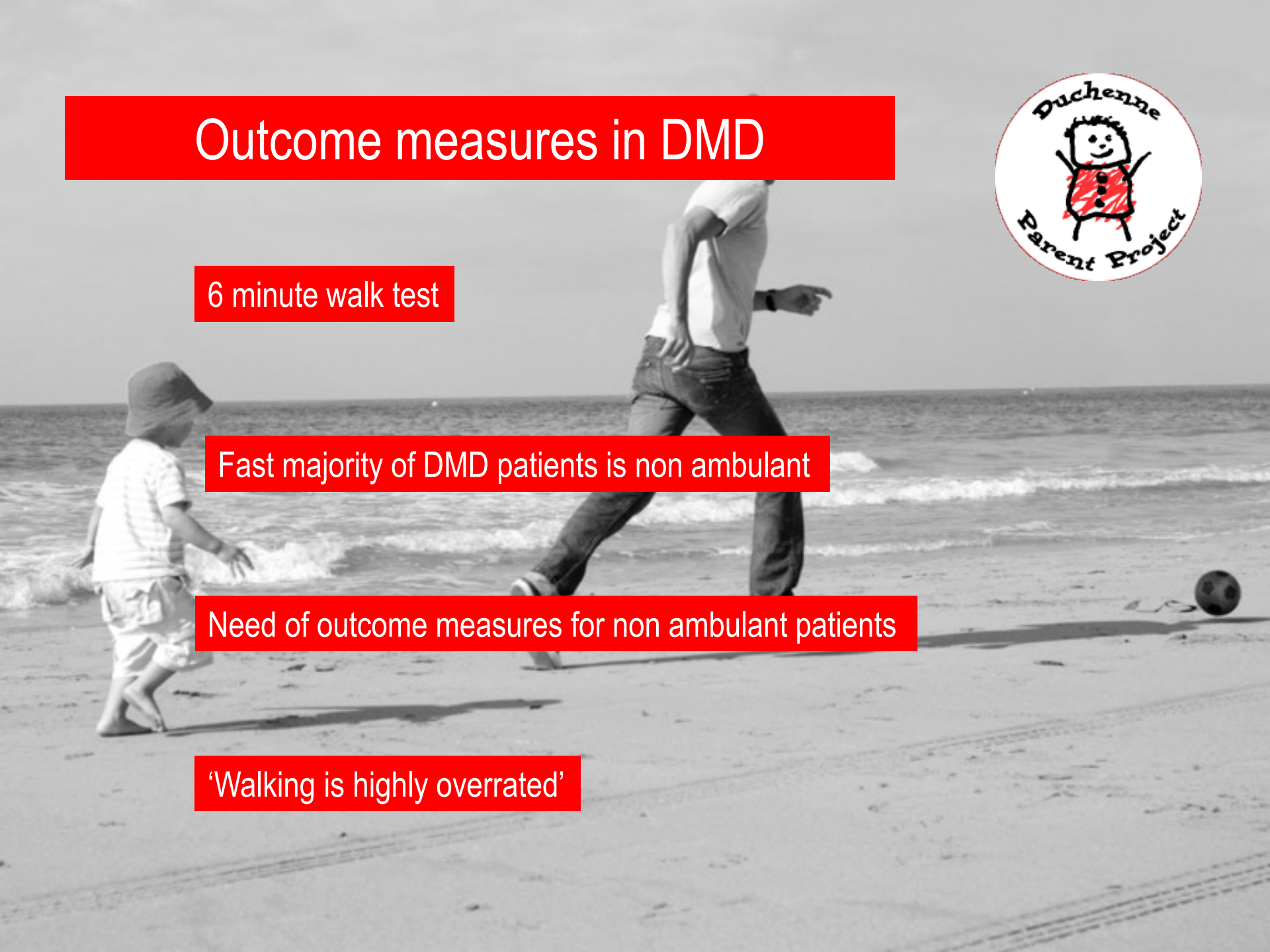
Development PROM Performance of Upper Limb

EMA 17-18 April 2023

Elizabeth Vroom, World Duchenne Organization


Duchenne Muscular Dystrophy
Pediatric
Progressive
Fatal
X-Linked
Duchenne
Parent Project

Outcome measures in DMD



6 minute walk test

Fast majority of DMD patients is non ambulant

Need of outcome measures for non ambulant patients

‘Walking is highly overrated’

Interviewed patients

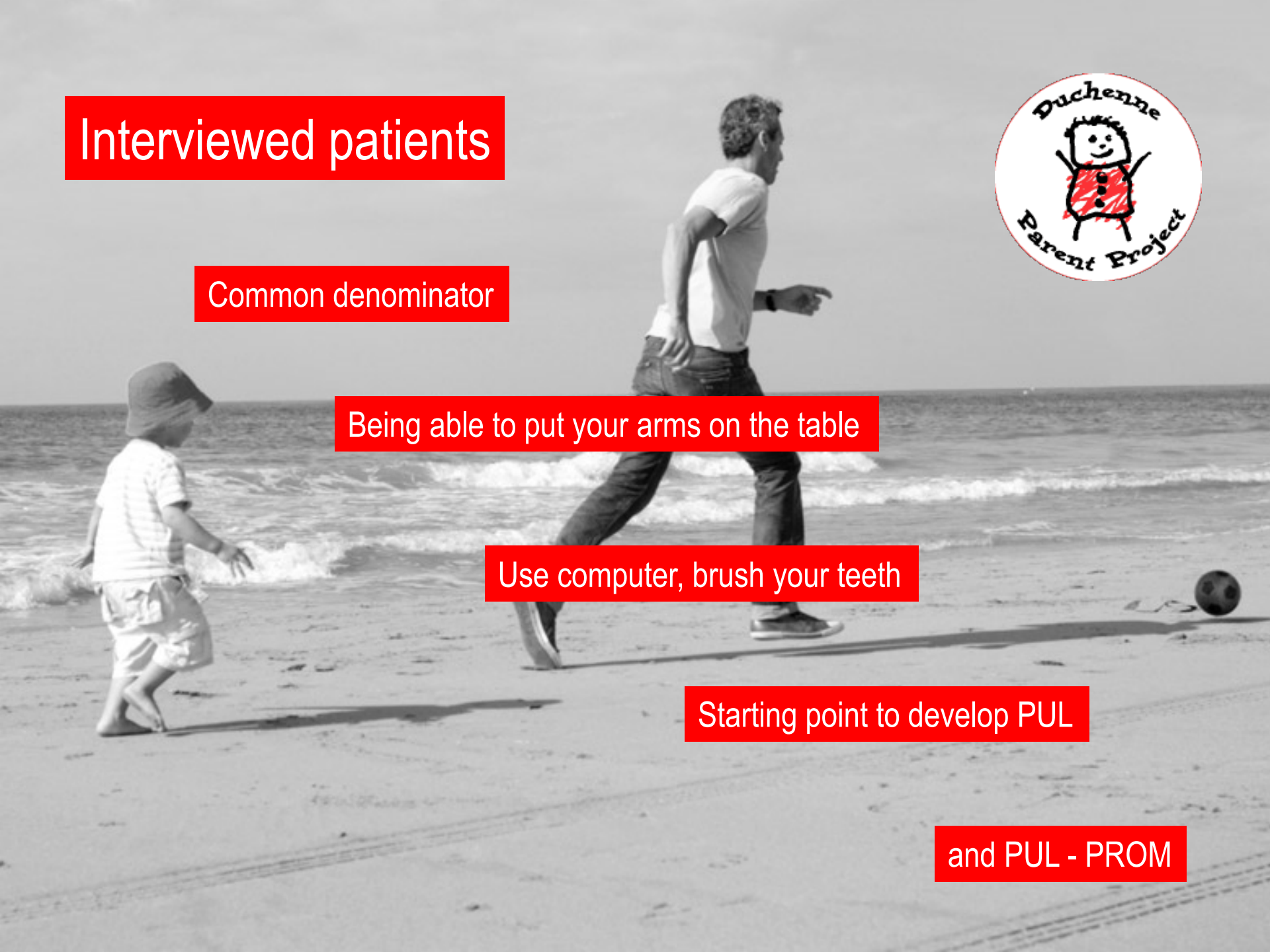
Common denominator

Being able to put your arms on the table

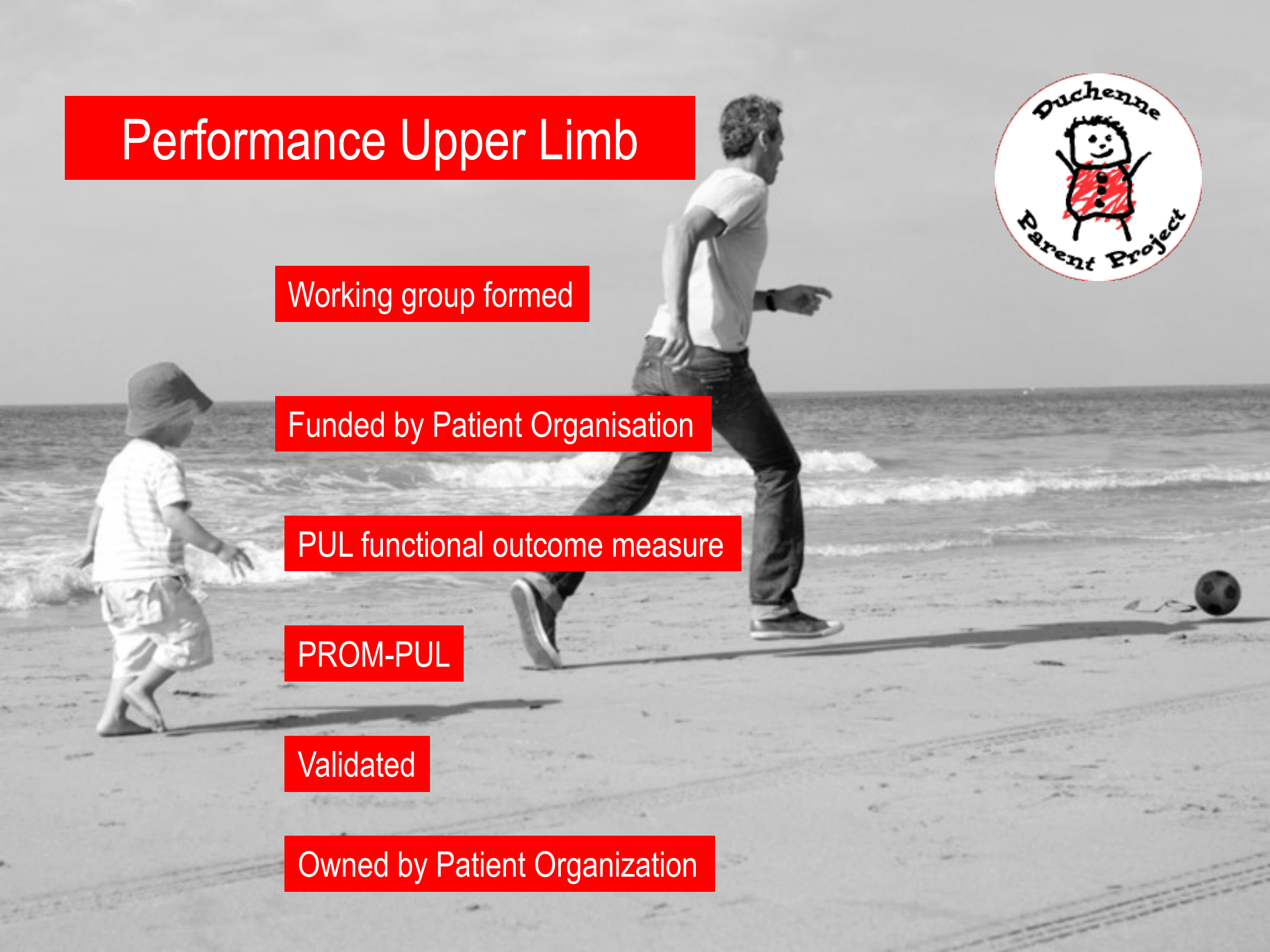
Use computer, brush your teeth

Starting point to develop PUL

and PUL - PROM



Performance Upper Limb



Working group formed

Funded by Patient Organisation

PUL functional outcome measure

PROM-PUL

Validated

Owned by Patient Organization


Co-Creation
Duchenne
Parent Project
patagonia

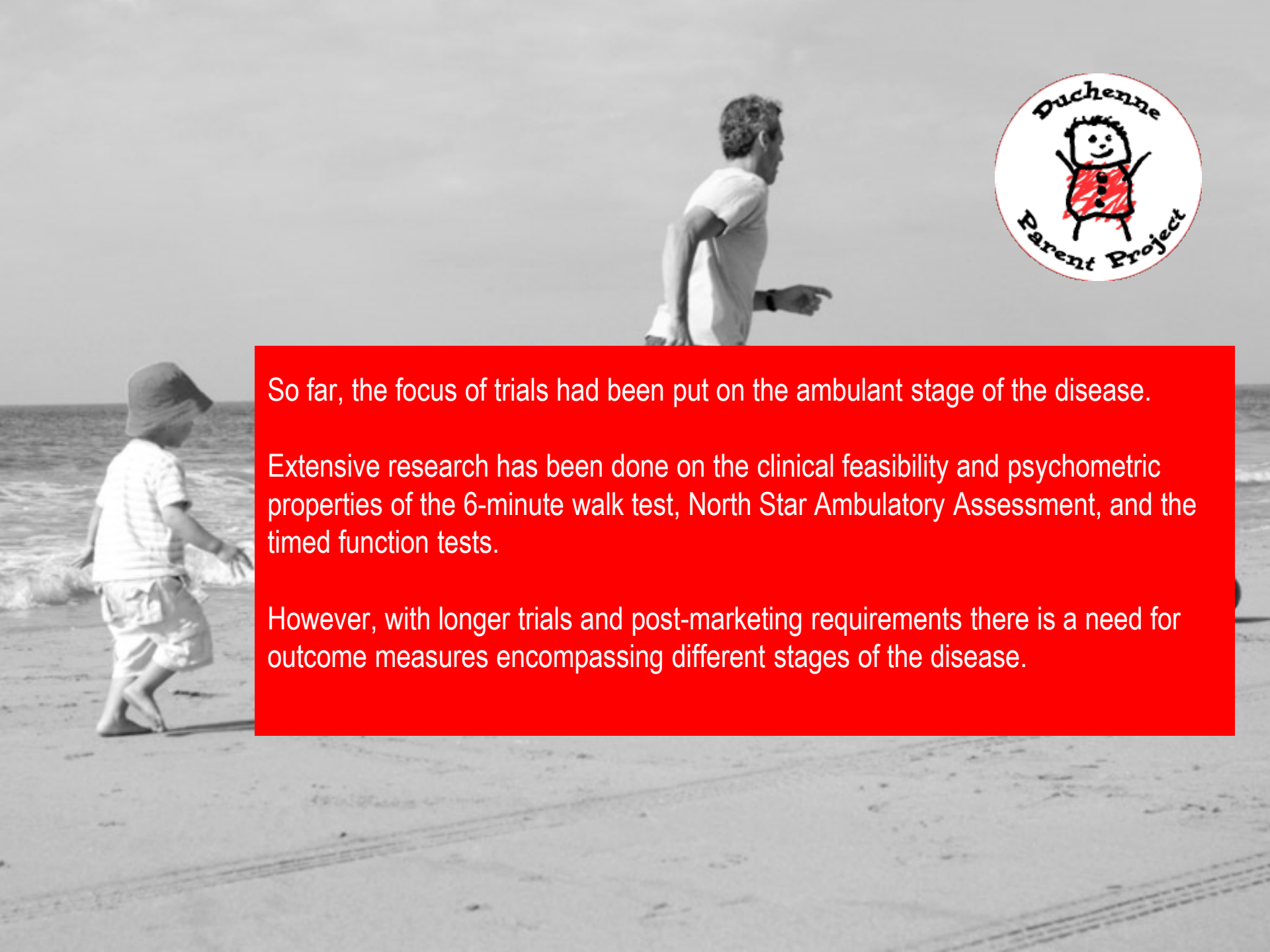
Dev Med Child Neurol. 2013 Nov;55(11):1038-45. Development of the Performance of the Upper Limb module for Duchenne muscular dystrophy

Mayhew A1, 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.

Development of a patient-reported outcome measure for upper limb function in Duchenne muscular dystrophy: DMD Upper Limb PROM

Klingels K, Mayhew AG, Mazzone ES, Duong T, Decostre V, Werlauff U, **Vroom E**, Mercuri E, Goemans NM; Upper Limb Clinical Outcome Group.

Dev Med Child Neurol. 2016 Sep 26



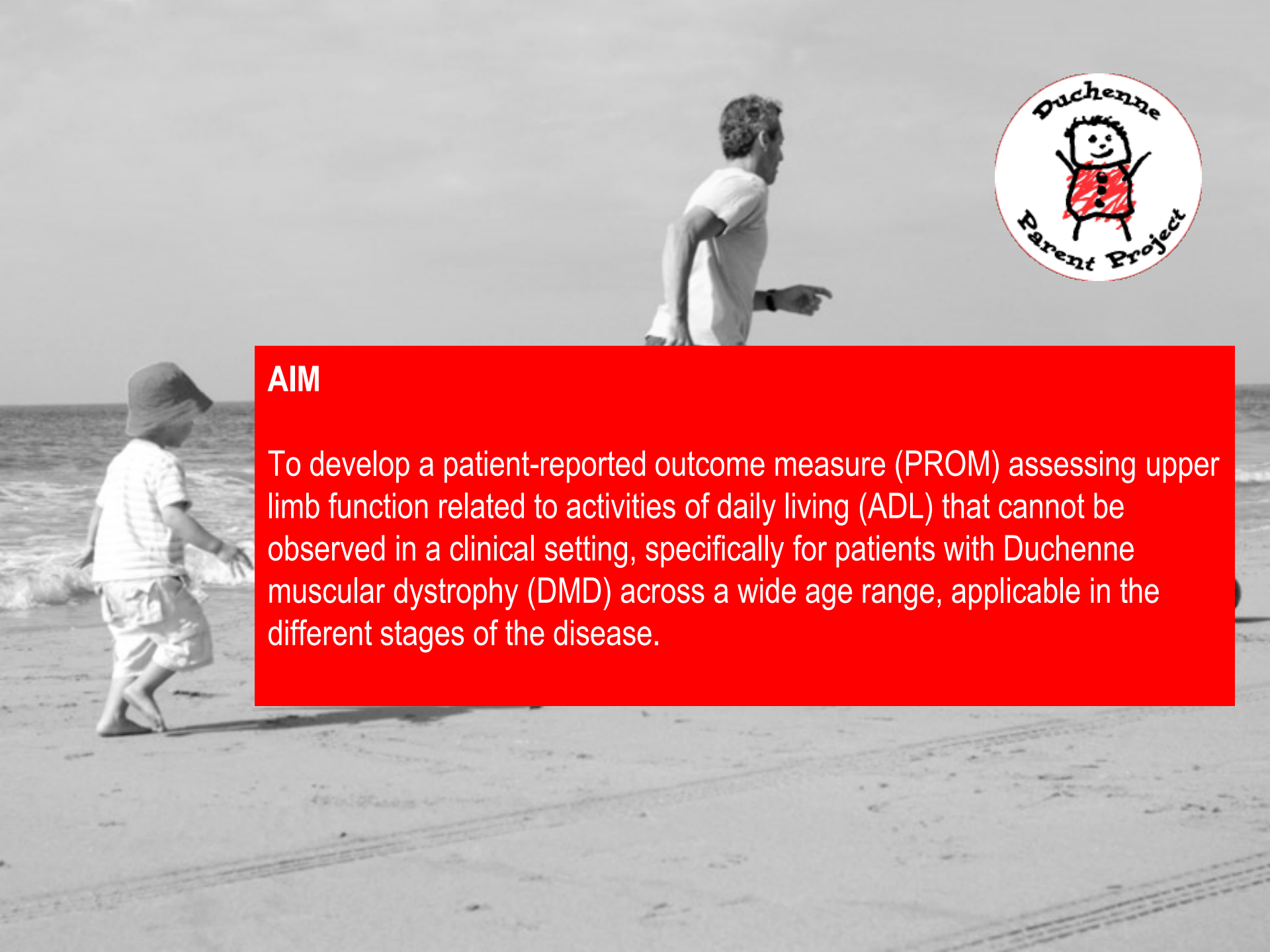
So far, the focus of trials had been put on the ambulant stage of the disease.

Extensive research has been done on the clinical feasibility and psychometric properties of the 6-minute walk test, North Star Ambulatory Assessment, and the timed function tests.

However, with longer trials and post-marketing requirements there is a need for outcome measures encompassing different stages of the disease.

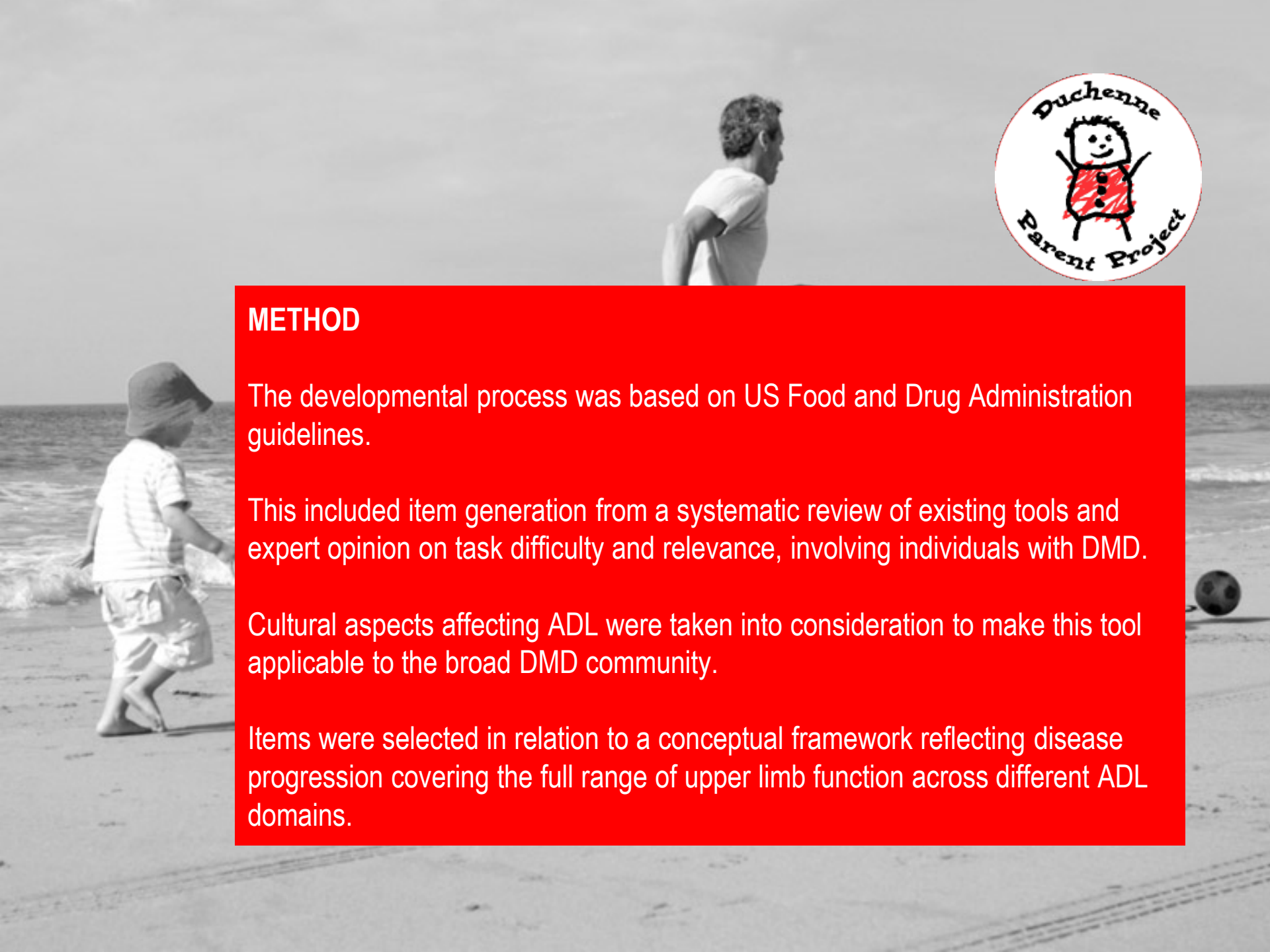
The next step therefore is to invest in developing outcome measures that describe disease progression in the upper limbs from early ambulant stages over transition stages to non-ambulant stages.

These would allow a better understanding of disease evolution and efficacy of interventions throughout the lifespan.
Upper limb weakness manifests



AIM

To develop a patient-reported outcome measure (PROM) assessing upper limb function related to activities of daily living (ADL) that cannot be observed in a clinical setting, specifically for patients with Duchenne muscular dystrophy (DMD) across a wide age range, applicable in the different stages of the disease.



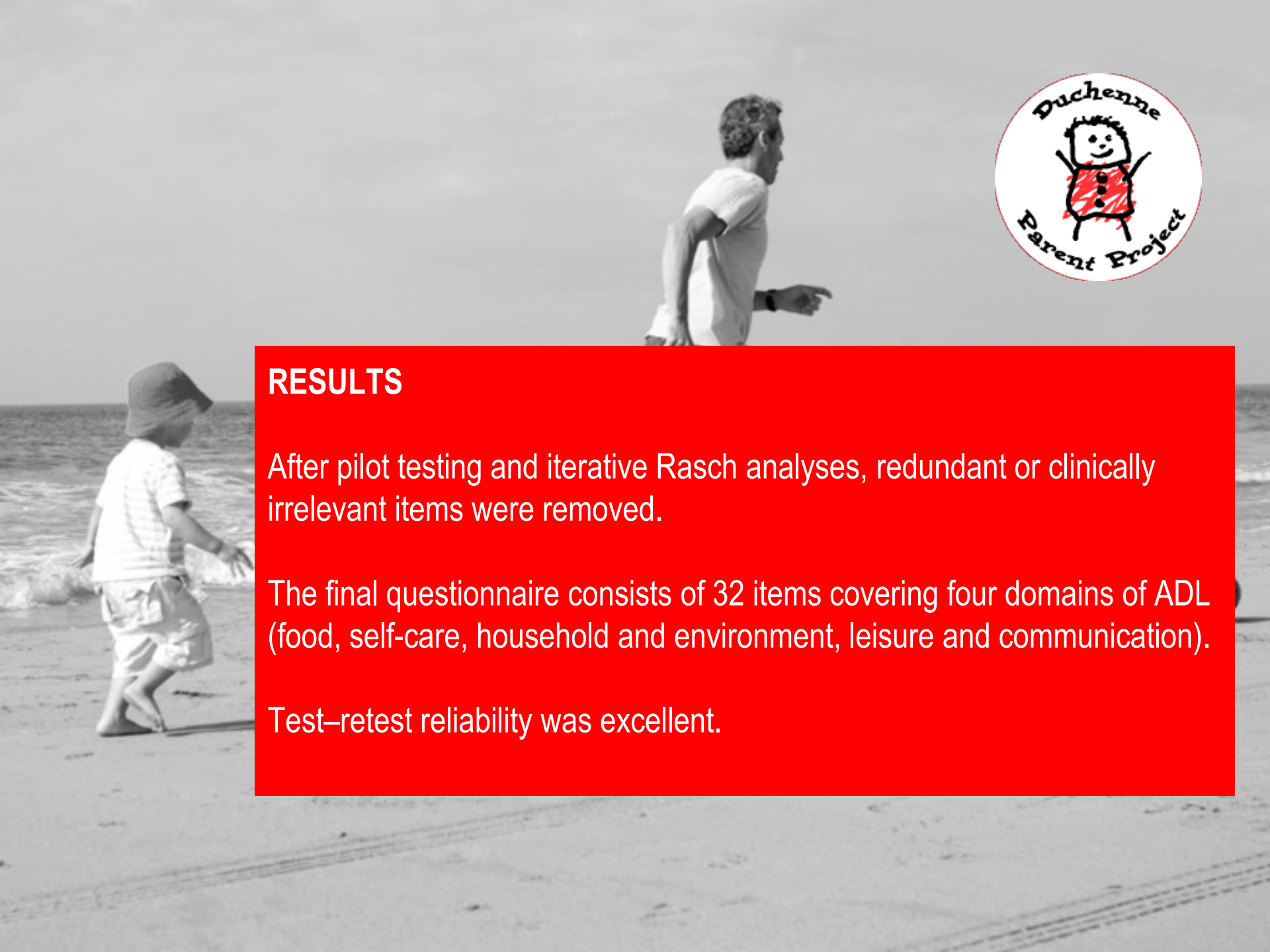
METHOD

The developmental process was based on US Food and Drug Administration guidelines.

This included item generation from a systematic review of existing tools and expert opinion on task difficulty and relevance, involving individuals with DMD.

Cultural aspects affecting ADL were taken into consideration to make this tool applicable to the broad DMD community.

Items were selected in relation to a conceptual framework reflecting disease progression covering the full range of upper limb function across different ADL domains.



RESULTS

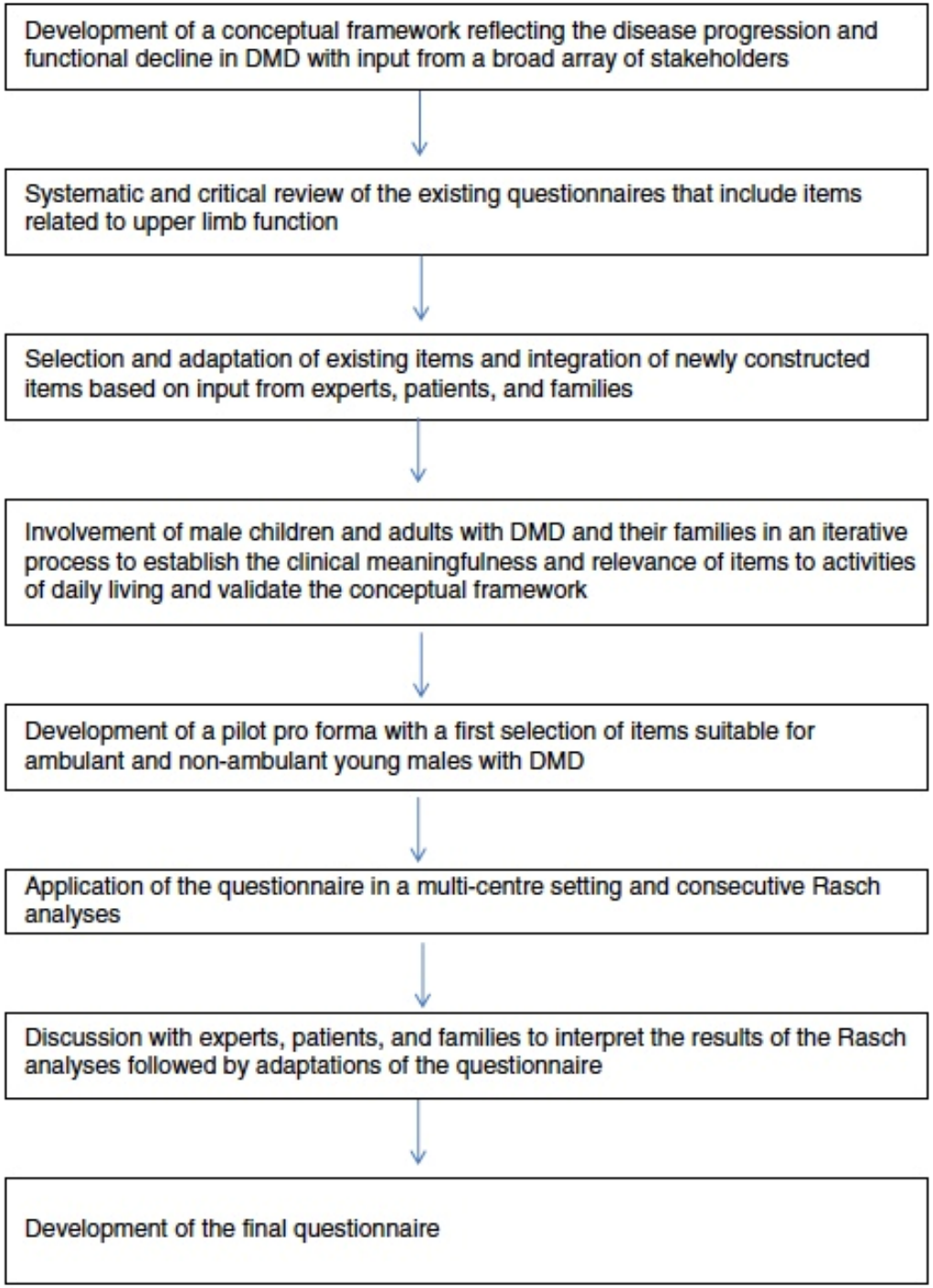
After pilot testing and iterative Rasch analyses, redundant or clinically irrelevant items were removed.

The final questionnaire consists of 32 items covering four domains of ADL (food, self-care, household and environment, leisure and communication).

Test–retest reliability was excellent.

INTERPRETATION

A DMD-specific upper limb PROM was developed on the basis of clinical relevance and psychometric robustness. Its main purpose is to document the patient selfreported natural history of DMD and assess the efficacy of interventions.


Development of a conceptual framework reflecting the disease progression and functional decline in DMD with input from a broad array of stakeholders
Systematic and critical review of the existing questionnaires that include items related to upper limb function
Selection and adaptation of existing items and integration of newly constructed items based on input from experts, patients, and families
Involvement of male children and adults with DMD and their families in an iterative process to establish the clinical meaningfulness and relevance of items to activities of daily living and validate the conceptual framework
Development of a pilot pro forma with a first selection of items suitable for ambulant and non-ambulant young males with DMD
Application of the questionnaire in a multi-centre setting and consecutive Rasch analyses
Discussion with experts, patients, and families to interpret the results of the Rasch analyses followed by adaptations of the questionnaire
Development of the final questionnaire

A new patient-reported outcome measure (PROM) for Duchenne muscular dystrophy (DMD) has been developed.

The DMD Upper Limb PROM targets upper limb function in daily life.

Psychometric techniques confirmed its unidimensionality, internal consistency, and test–retest reliability.

Involvement of different stakeholders guaranteed the clinical relevance of the tool.

Participants
- medical doctors
- researchers
- physiotherapists
- clinicians working with patients with DMD

representatives from
- patients
- advocacy groups
- industries.

The questionnaire is recommended from 7 years of age onwards.

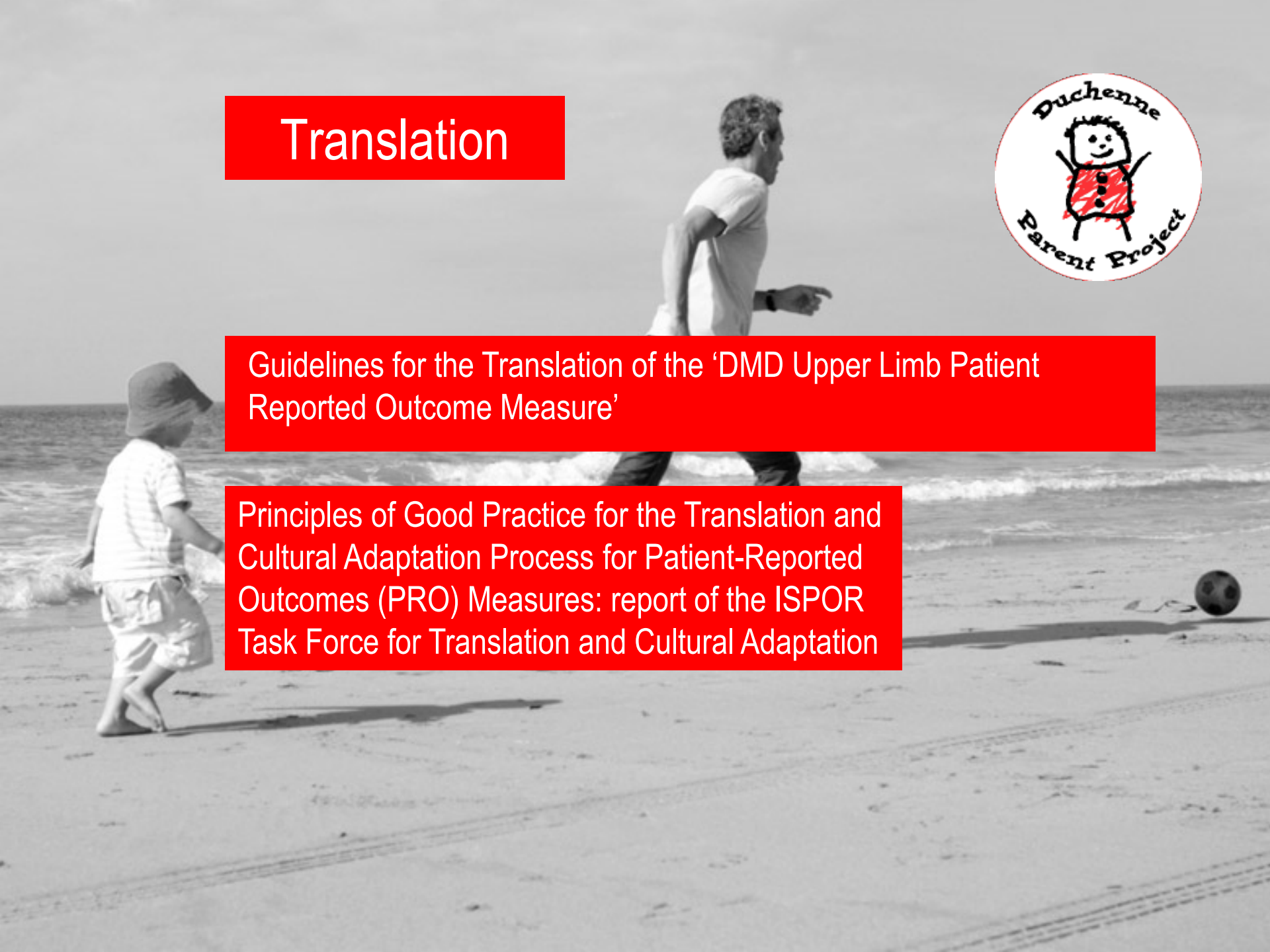
Total of 33 items

It can be completed by the individual himself or his parent/caregiver.

Used in clinical trials (exploratory & secondary outcome measure), Natural History studies Academic research and Care

Correlation outcomes PUL-PROM and PUL

Paper will be submitted shortly



Translation

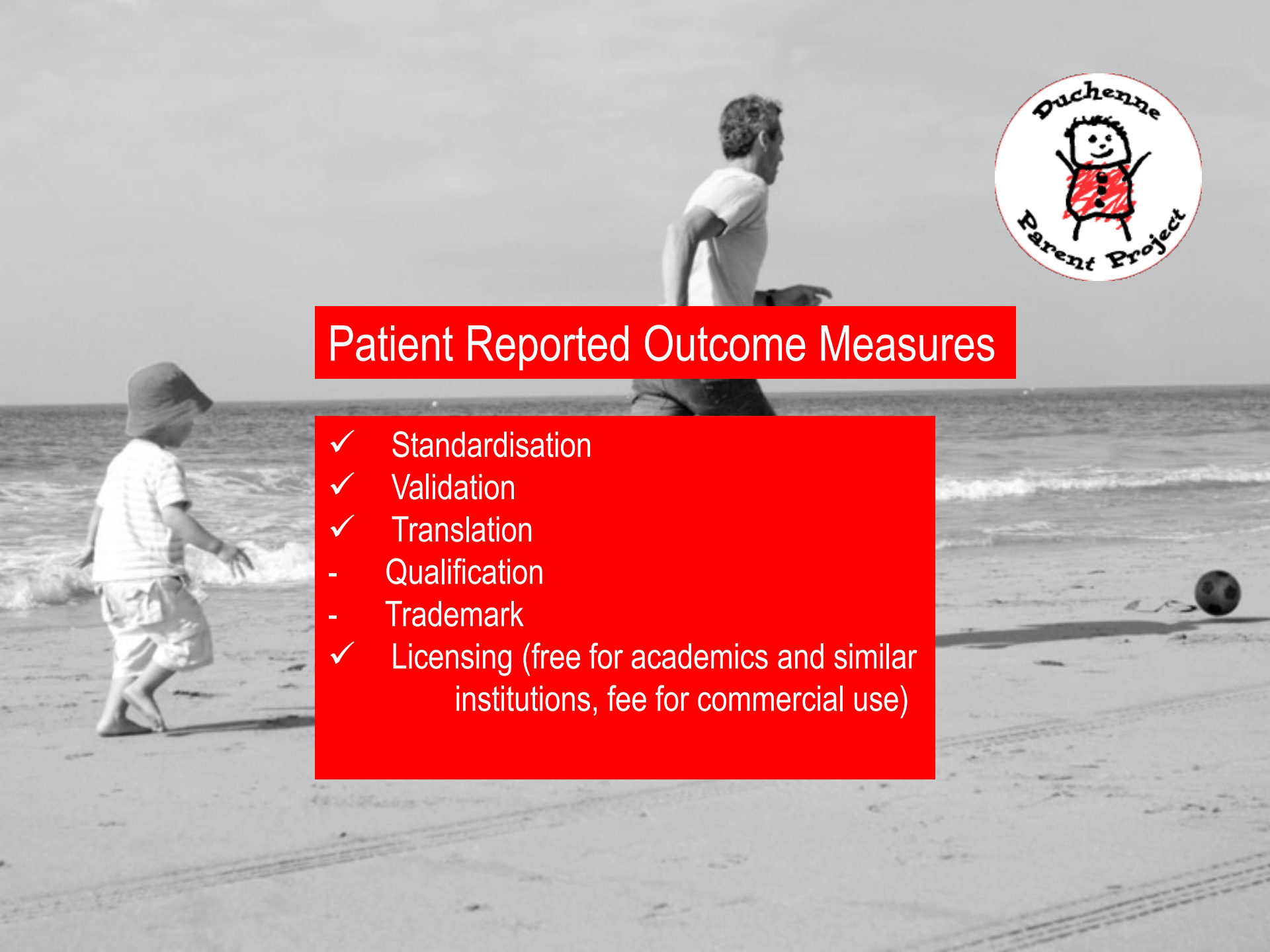
Guidelines for the Translation of the ‘DMD Upper Limb Patient Reported Outcome Measure’

Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes (PRO) Measures: report of the ISPOR Task Force for Translation and Cultural Adaptation

Ther Innov Regul Science. 2022 Jul;56(4):572-586.
Unmet Therapeutic Needs of Non-Ambulatory Patients with Duchenne Muscular Dystrophy: A Mixed-Method Analysis

Anne L R Schuster 1, Norah L Crossnohere 2, Ryan Fischer 3, Patricia Furlong 3, John F P Bridges 2

Non-ambulatory Duchenne patients want new treatments that improve upper limb functioning and body system functioning, and not exclusively regaining ambulation. The PUL-PROM can be used as a patient-centric measure that accounts for the needs of later-stage Duchenne patients.



Patient Reported Outcome Measures

- ✓ Standardisation
- ✓ Validation
- ✓ Translation
- \- Qualification
- \- Trademark
- ✓ Licensing (free for academics and similar institutions, fee for commercial use)

For discussion

What is the added value of qualification of a PROM?

Is the current qualification process ‘fit for purpose’ for PROMs?
Lenghty process. Resources. Context of Use?

Or should a ‘lighter’ procedure be considered?
Comparable to the Letter of Support?

Is patient relevance and input ‘qualified’ in the qualification process?


Thank you!