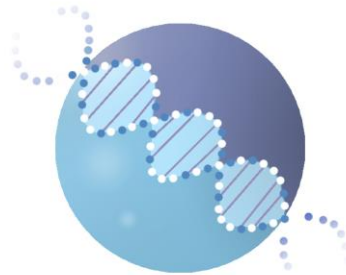


**Workshop SMA Reach UK and the Patient Registry
Stratford-upon-Avon
28th June 2014**

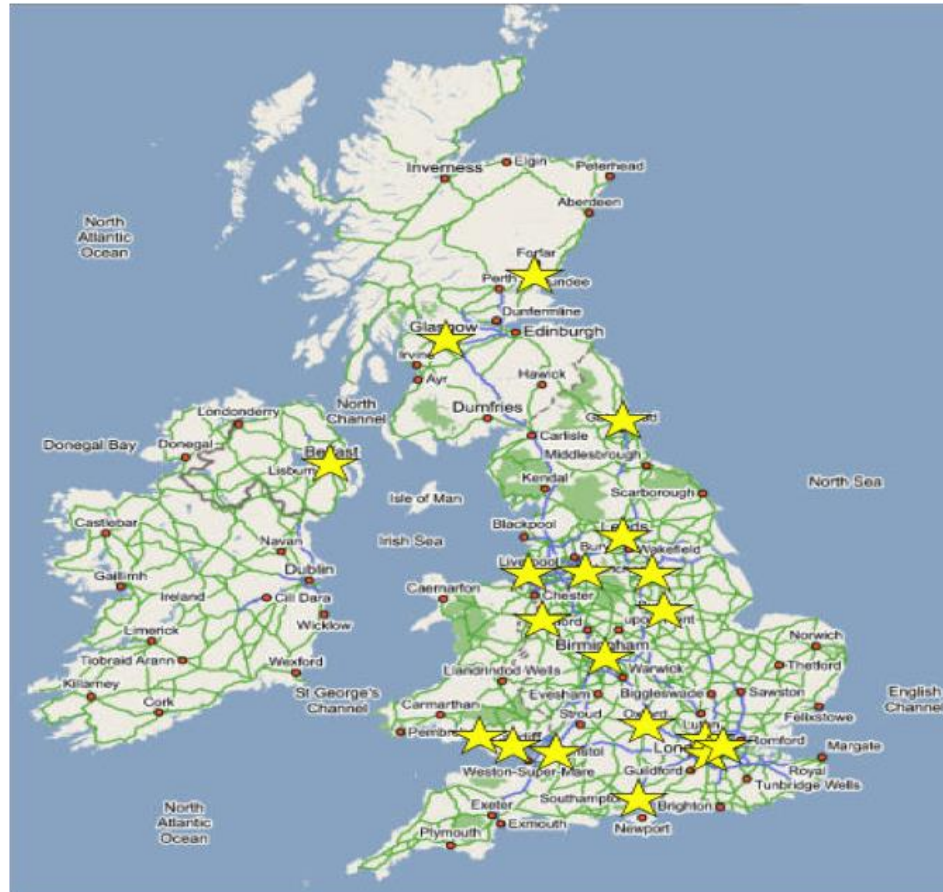
Evolution of SmartNet: SMA REACH UK



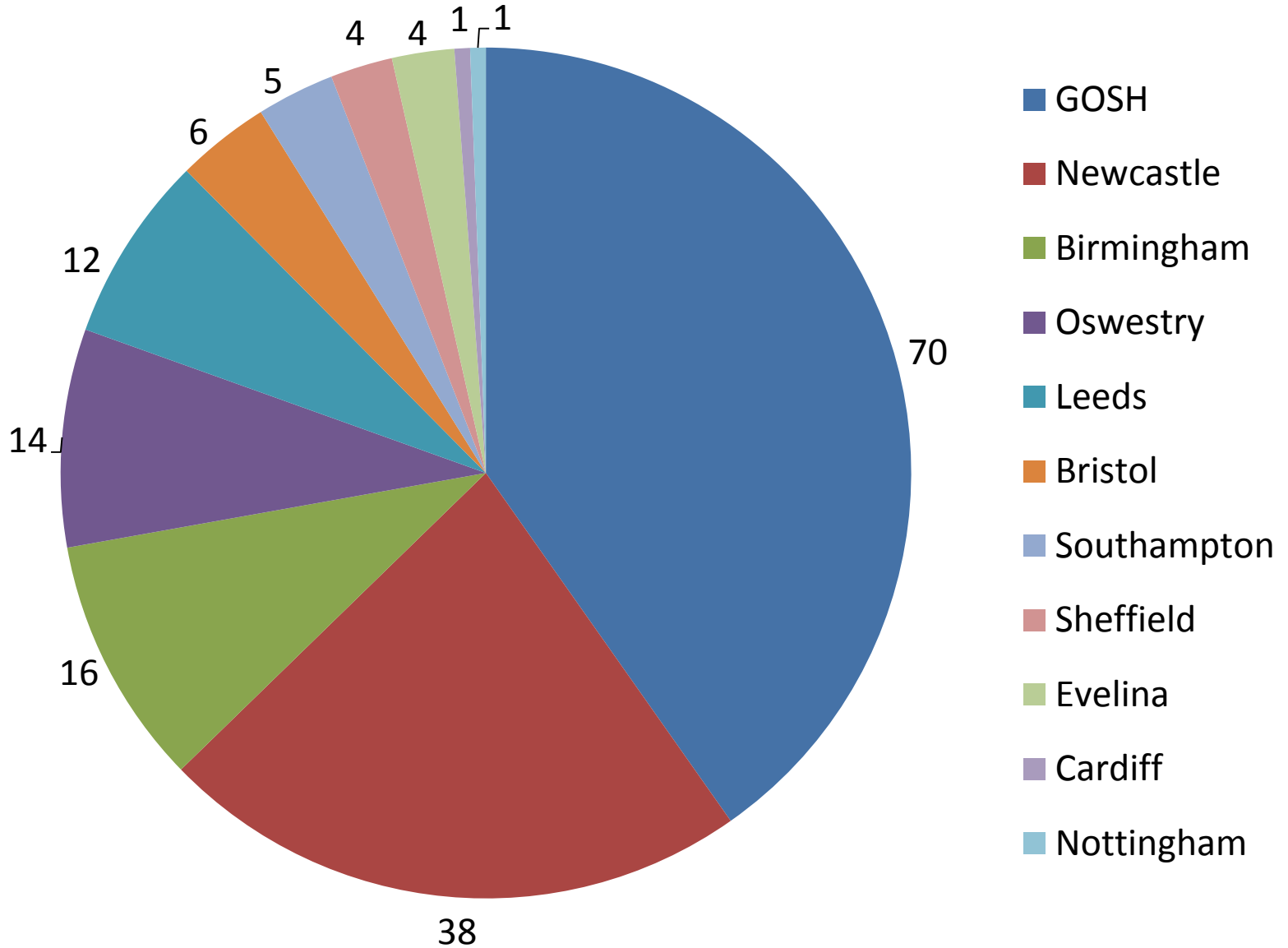
Dr Mariacristina Scoto
Senior Clinical Research Associate
Dubowitz Neuromuscular Centre

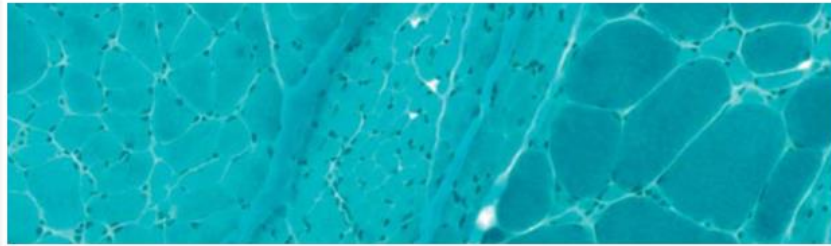
Danielle Ramsey
Research Physiotherapist
Dubowitz Neuromuscular Centre

SMArtNet -11 centres



173 Total SmartNet registered





Spinal Muscular Atrophy Research and Clinical Hub UK

Improving standards of care and translational research
in Spinal Muscular Atrophy

The Scientific Advisory Board

The Scientific Advisory Board consists of a panel of international experts with significant expertise in SMA who provide external advice on the scope and direction of the project.



CHAIR: Richard Finkel
Professor Richard Finkel is a Consultant Paediatric Neurologist and Paediatrician in Orlando, Florida



Helen Roper
Dr Helen Roper is a Paediatric Neuromuscular Consultant at the Birmingham Heartlands Hospital.



Enrico Bertini
Professor Enrico Bertini is a Paediatric Neurologist, Professor in Neurogenetic disorders at the School of Clinical Genetics of the Catholic University of Rome and Contract Professor in Pediatric Neurology, School of Pediatrics of the University of Tor Vergata in Rome.



Helen Dawes
Professor Helen Dawes is the Director of the Movement Science Group, Faculty of Health and Life Sciences at Oxford Brookes University.



Kelvin Talbot
Professor Kevin Talbot is a Consultant Neurologist and Professor of Motor Neuron Biology at the Oxford University Nuffield Department of Clinical Neurosciences

London



Francesco Muntoni
Professor Francesco Muntoni, Principal Investigator, is a Paediatric Neurologist at Great Ormond Street Hospital and Head of the Dubowitz Neuromuscular Centre, Institute of Child Health, UCL



Mariacristina Scoto
Dr Mariacristina Scoto is a Senior Clinical Research Associate at the Dubowitz Neuromuscular Centre, Institute of Child Health, UCL. For all clinical enquiries related to the study contact: m.scoto@ucl.ac.uk



Danielle Ramsey
Danielle Ramsey is the Research Physiotherapist at the Dubowitz Neuromuscular Centre, Institute of Child Health, UCL. For all physio related enquires contact: danielle.ramsey.12@ucl.ac.uk



Isabelle Wilson
Isabelle Wilson is the Study Coordinator at the Dubowitz Neuromuscular Centre, Institute of Child Health, UCL. For all general enquiries relating to the study contact: isabelle.wilson@ucl.ac.uk

Marion Main

Marion Main is a Consultant Physiotherapist in Paediatric Neuromuscular Disorders with a special interest in Spinal Muscular Atrophy

Newcastle



Katie Bushby
Professor Katie Bushby is an Honorary Consultant Geneticist, Newcastle upon Tyne Hospitals NHS Foundation Trust and Deputy Director, MRC Centre for Neuromuscular Diseases at London and Newcastle



Anna Mayhew
Dr Anna Mayhew is a Consultant Research Physiotherapist based at the Centre for Life, Newcastle.



Gillian Kenyon
Gillian Kenyon is a Clinical Trials Coordinator at the Centre for Life, Newcastle.

International Collaborators

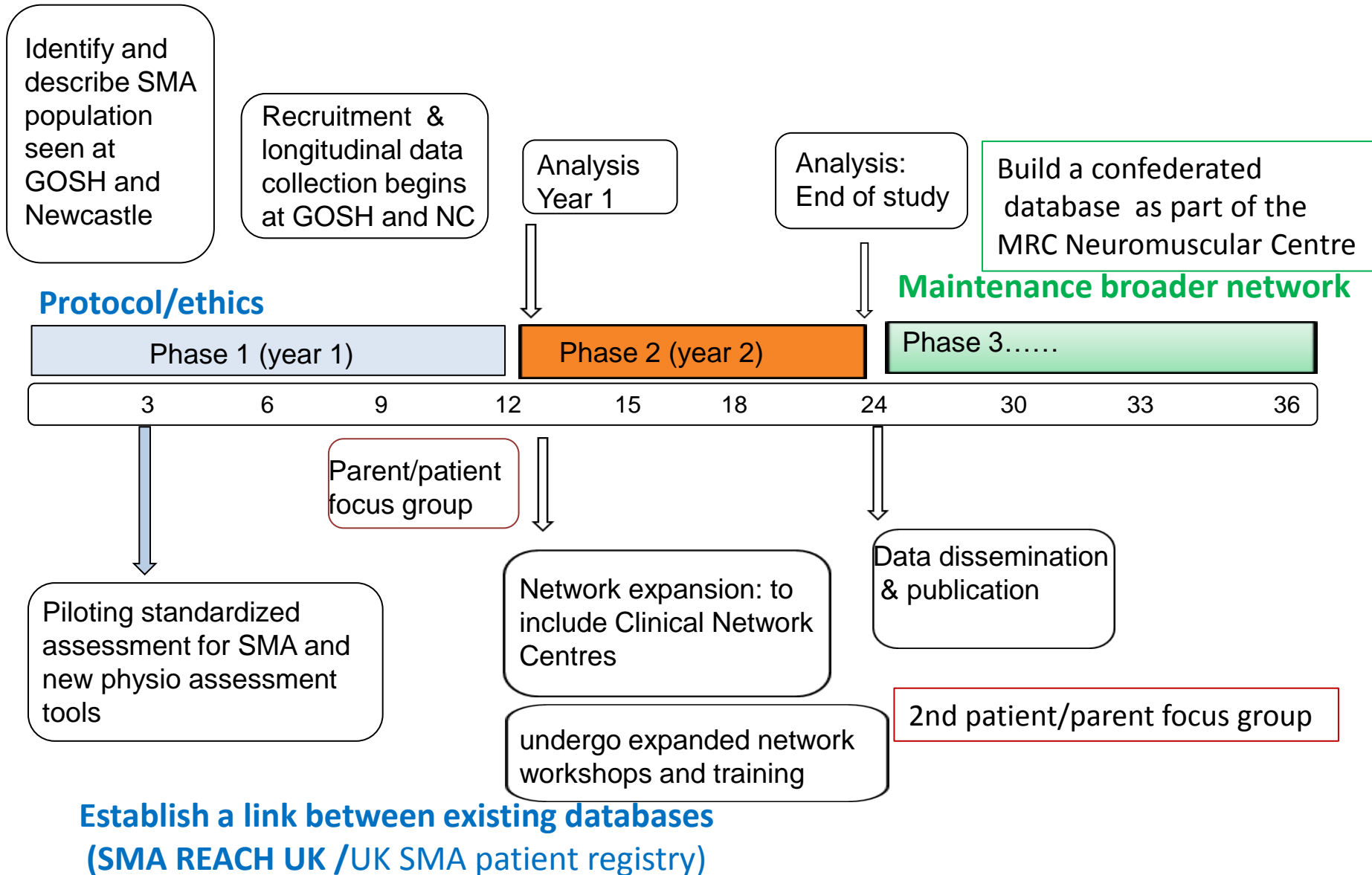
Co-Investigator Professor Eugenio Mercuri and Research Physiotherapist Elena Mazzone from the Catholic University Rome are International Collaborators for this project with significant clinical and research experience in SMA.



Eugenio Mercuri
Professor Eugenio Mercuri is a Paediatric Neurologist at the Pediatric Neurology Unit, Catholic University, Rome

Elena Mazzone
Elena Mazzone is a physiotherapist at the Pediatric Neurology Unit, Catholic University, Rome

Study design (2 years)



Medical Assessment- Schedule of events

Months	0 -baseline	6	12	18	24
Consent/assent	x				
Medical history	x				
Height, weight	x	x	x	x	x
vital signs	x	x	x	x	x
Concomitant medic.	x	x	x	x	x
Physical exam	x	x	x	x	x
FVC	x	x	x	x	x
ECG*	x		x		x
Spine x-ray*					
DEXA*					
Bloods	x		x		x
Physio assessment	x	x	x	x	x

ECG*- additional ECG or Holter ECG can be performed if clinically indicated

Spine x-ray°- first will be performed following a clinical indication; repeated as clinically

DEXA* -currently not regularly performed, lumbar spine could be regularly performed, total body following clinical indication

Bloods* -for electrolytes (salbutamol) vitamin D and ask separate consent for Biobank

SLT and dietician- available in clinic

SMA REACH UK: Physiotherapy Protocol

- Standardised Physiotherapy Assessment in keeping with Standards of Care for SMA
 - SMArtNet Physiotherapy Assessment
 - Functional Scales
 - Parent/Patient Reported Outcome Measures
- Piloting novel outcome measures

Current Outcome Measures in SMA

	Clinically Reported Outcome Measures									Patient Reported Outcome Measures	
Outcome Measures used in SMA	CHOP	TIMPSI	NSAA for SMA	HFMS	6MWT	HFMSE	Pulmonary Function Tests	ULM for SMA	PUL	PODCI	EK Measure
Clinical subgroups	SMA1	SMA1	Ambulant	Non-ambulant	Ambulant	Type2, 3	Type2, 3	Type2, 3	Type2, 3	?	Non-ambulant
Supports mechanism of action	✓ Specific to the therapeutic agent under investigation										
Conceptual framework fits SMA	✓	✓	✓	✓	✓	✓	✓	✓	✓	Needs testing in SMA	✓
Reliability	✓	✓	?	✓	✓	✓	✓	✓	✓		✓
Validation with other measures	✓	✓	?	✓	✓	✓	✓	✓	✓		?
Normative ranges	✓	✓	?	✓	✓		In progress	✓	In progress		
Ongoing natural history studies	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓
Multicenter studies	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Responsiveness to treatment	?	?	?	✓	✓	?	?	?	?		?
Clinical meaningfulness	?	?	?	?	✓	?	?	?	?	?	
SMA REACH UK	✓	✓	✓		✓	✓	✓	✓		✓	✓





Current Outcome Measures in SMA

	Clinically Reported Outcome Measures									Patient Reported Outcome Measures	
Outcome Measures used in SMA	CHOP	TIMPSI	NSAA for SMA	HFMS	6MWT	HFMSE	Pulmonary Function Tests	ULM for SMA	PUL	PODCI	EK Measure
Clinical subgroups	SMA1	SMA1	Ambulant	Non-ambulant	Ambulant	Type2, 3	Type2, 3	Type2, 3	Type2, 3	?	Non-ambulant
Supports mechanism of action	✓ Specific to the therapeutic agent under investigation										
Conceptual framework fits SMA	✓	✓	✓	✓	✓	✓	✓	✓	✓	Needs testing in SMA	✓
Reliability	✓	✓	?	✓	✓	✓	✓	✓	✓		✓
Validation with other measures	✓	✓	?	✓	✓	✓	✓	✓	✓		?
Normative ranges	✓	✓	?	✓	✓		In progress	✓	In progress		
Ongoing natural history studies	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓
Multicenter studies	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Responsiveness to treatment	?	?	?	✓	✓	?	?	?	?		
Clinical meaningfulness	?	?	?	?	✓	?	?	?	?		?
SMA REACH UK	✓	✓	✓		✓	✓	✓	✓		✓	✓

Why do we need to improve the scales?

- Ensure they are robust for research in anticipation of clinical trials
 - Need to be psychometrically sound
 - Clinically meaningful
 - Sensitive to detect change
 - Have the ability to demonstrate improvement not seen previously
- Reflect meaningful changes to people with SMA
- Some aspects have been missing
 - Measurements of the arms
 - Self-reported scales

Development of New Scales in SMA

Scales	Scale Readiness	Currently being piloted by	Which type of SMA	SMA REACH UK
Revised Hammersmith for SMA (Draft)	In development & being piloted <ul style="list-style-type: none"> - Initial pilot (Jan – May 2014) - Revised June 2014, sites expanded to include US 	<ul style="list-style-type: none"> - SMA REACH UK - Italian SMA Network - PNCR, US 	2 & 3	
Upper Limb Module 2	In development	<ul style="list-style-type: none"> - SMA REACH UK - Italian SMA Network - PNCR, US 	2 & 3	
Patient/Parent reported outcome measures <ul style="list-style-type: none"> - PODCI - PEDI CAT 	PODCI – has been piloted, unlikely to adopt PEDI-CAT – work has been done in US to modify for SMA	<ul style="list-style-type: none"> - SMA REACH UK - PNCR, US - SMA REACH UK 	2 & 3	 
SMA 1 Outcomes	To be addressed as part of future work with SMA REACH UK			

RHS (Draft) Method of Development

1st International SMA REACH UK Workshop

Dec 2013

EXPERT PANEL

Each item of HFMSE discussed regarding:

Clinical meaningfulness
Available Rasch analysis
Experience of use in current clinical trials

January 2014
Exploratory HFMSE
27 items

Piloted in:

- UK (London & Newcastle)
- Italy (Rome)

Feb 2014

Preliminary Analysis

Psychometric Properties via Rasch analysis

Promising early signs

– continue pilot with larger sample

2nd International SMA REACH UK Workshop

May 2014

EXPERT PANEL

Each item of Expl. HFMSE discussed regarding:

Clinical meaningfulness
Rasch analysis of pilot data
Potential for change in clinical trials

June 2014

Revised Hammersmith for SMA (RHS) Draft*

30 items

Sites prospectively piloting RHS Draft:

- UK (London & Newcastle)
- Italy (Rome)
- USA (PNCR Sites)

Why is piloting a scale important?

- Have we got the scale right?
- Does it work well, is it measuring what we want?
- Do we trust the score?
- Are we certain what the score means?
- Is it able to detect meaningful change for the person with SMA, clinicians or researchers?
- We need to have a good representation of the condition
- Is it easy to do and repeat?