Evolution of SmartNet: SMA REACH UK

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Dubowitz Neuromuscular Centre

Danielle Ramsey
Research Physiotherapist
Dubowitz Neuromuscular Centre
SMArtNet - 11 centres
Spinal Muscular Atrophy Research and Clinical Hub UK
Improving standards of care and translational research in Spinal Muscular Atrophy

The Scientific Advisory Board

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 Consultant Professor in Pediatric Neurology, School of Pediatrics of the University of Tor Vergata in Rome.

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

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

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

Marialastina Scotho
Dr Marialastina Scotho is a Senior Clinical Research Associate at the Duchenne Neuromuscular Centre, Institute of Child Health, UCL. For all clinical inquiries related to the study contact: m.scotho@ucl.ac.uk

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Isabelle Wilson
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Marlon Main
Marlon Main is a Consultant Physiotherapist in Paediatric Neuromuscular Disorders with a special interest in Spinal Muscular Atrophy.

International Collaborators

Co-Investigator Professor Eugenio Mercuro 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 Mercuro
Professor Eugenio Mercuro 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.
Identify and describe SMA population seen at GOSH and Newcastle

Recruitment & longitudinal data collection begins at GOSH and NC

Analysis: Year 1

Analysis: End of study

Build a confederated database as part of the MRC Neuromuscular Centre

Parent/patient focus group

Piloting standardized assessment for SMA and new physio assessment tools

Network expansion: to include Clinical Network Centres

undergo expanded network workshops and training

Establish a link between existing databases (SMA REACH UK / UK SMA patient registry)
## Medical Assessment - Schedule of events

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

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 indicated
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

<table>
<thead>
<tr>
<th>Outcome Measures used in SMA</th>
<th>Clinically Reported Outcome Measures</th>
<th>Patient Reported Outcome Measures</th>
</tr>
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<tbody>
<tr>
<td>Clinical subgroups</td>
<td>CHOP</td>
<td>TIMPSI</td>
</tr>
<tr>
<td>SMA1</td>
<td>SMA1</td>
<td>Ambulant</td>
</tr>
<tr>
<td>Supports mechanism of action</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Conceptual framework fits SMA</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Reliability</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Validation with other measures</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Normative ranges</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>In progress</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Ongoing natural history studies</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Multicenter studies</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Responsiveness to treatment</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Clinical meaningfulness</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>SMA REACH UK</td>
<td>✓</td>
<td>✓</td>
</tr>
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</table>

- ✓: Present
- ?: Not specified

Specific to the therapeutic agent under investigation.
## Current Outcome Measures in SMA

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<td>✓</td>
<td>✓</td>
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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

<table>
<thead>
<tr>
<th>Scales</th>
<th>Scale Readiness</th>
<th>Currently being piloted by</th>
<th>Which type of SMA</th>
<th>SMA REACH UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revised Hammersmith for SMA (Draft)</td>
<td>In development &amp; being piloted&lt;br&gt;- Initial pilot (Jan – May 2014)&lt;br&gt;- Revised June 2014, sites expanded to include US</td>
<td>- SMA REACH UK&lt;br&gt;- Italian SMA Network&lt;br&gt;- PNCR, US</td>
<td>2 &amp; 3</td>
<td>✓</td>
</tr>
<tr>
<td>Upper Limb Module 2</td>
<td>In development</td>
<td>- SMA REACH UK&lt;br&gt;- Italian SMA Network&lt;br&gt;- PNCR, US</td>
<td>2 &amp; 3</td>
<td>✓</td>
</tr>
<tr>
<td>Patient/Parent reported outcome measures&lt;br&gt;- PODCI&lt;br&gt;- PEDI CAT</td>
<td>PODCI – has been pilotted, unlikely to adopt&lt;br&gt;PEDI-CAT – work has been done in US to modify for SMA</td>
<td>- SMA REACH UK&lt;br&gt;- PNCR, US&lt;br&gt;- SMA REACH UK</td>
<td>2 &amp; 3</td>
<td>✓</td>
</tr>
<tr>
<td>SMA 1 Outcomes</td>
<td>To be addressed as part of future work with SMA REACH UK</td>
<td></td>
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</table>
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)

* RHS (Draft) new name for Expl. HFMSE version 2
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?