

The DMD Hub in Clinical Practice

The Changing Landscape in Leeds

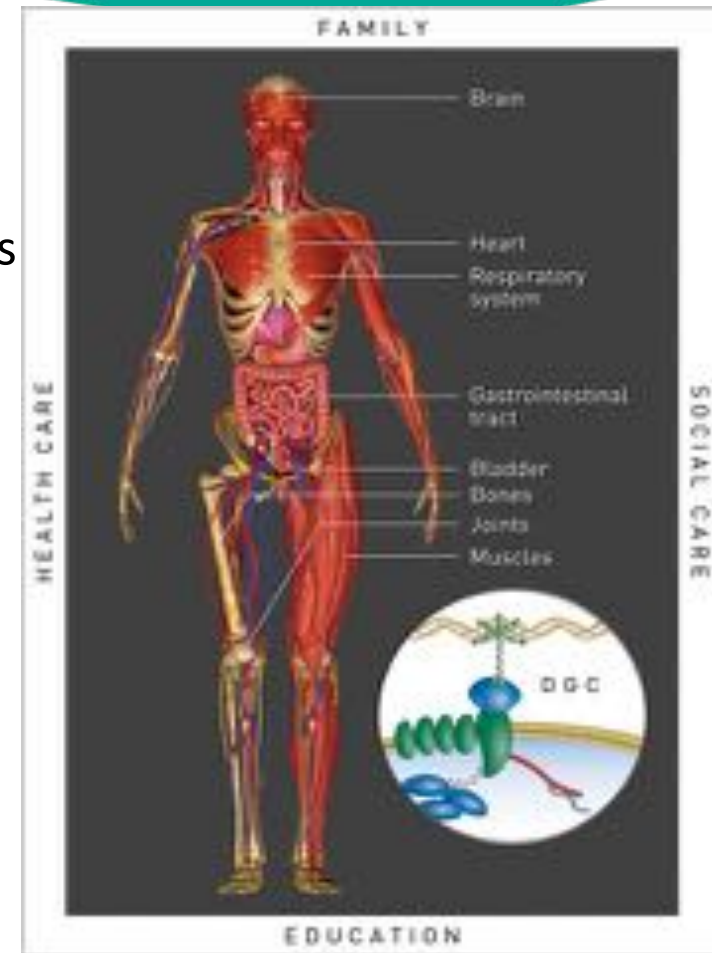
Overview

- Consider drivers for change:
 - DMD care
 - ‘Explosion’ in Research Activity
- How NM Centres can Develop Research Capacity?
 - Role of the DMD Hub
 - How it supported our Service in Leeds
- Future Challenges
 - Sustaining and Developing Services in Future



Exciting times in DMD

- Improvements in care
 - Greater understanding of natural history thanks to National Registries and Databases
 - Northstar
 - CINRG
 - More effective management of complications
 - Role of Glucocorticoids (Steroids)
 - More intervention and monitoring
 - Updated and Revised Standards of care DMD 2018
- Huge increase in Research activity
 - 1st Licensed therapies in DMD
 - Translarna for nonsense Mutations
 - Eteplersen (USA only)
 - Many potential drugs in phase 2/3 trials
 - Initiatives to 'speed' up Access to effective therapy



Recent advances in the management of Duchenne muscular dystrophy

Eugen-Matthias Strehle, Volker Straub *Arch Dis Child* 2015;100:1173–1177

Challenges:

- More Resources Needed to Optimise Management
 - All UK centres should be working to Standards of Care
 - National audits and initiatives like ‘MDUK Centres of Excellence’
 - Reduce delays in diagnosis
 - Mean age in UK 4.3 yrs (1st symptoms 2.7 yrs)*
 - Developing Services for “Unexpected adults”
 - Adult Networks



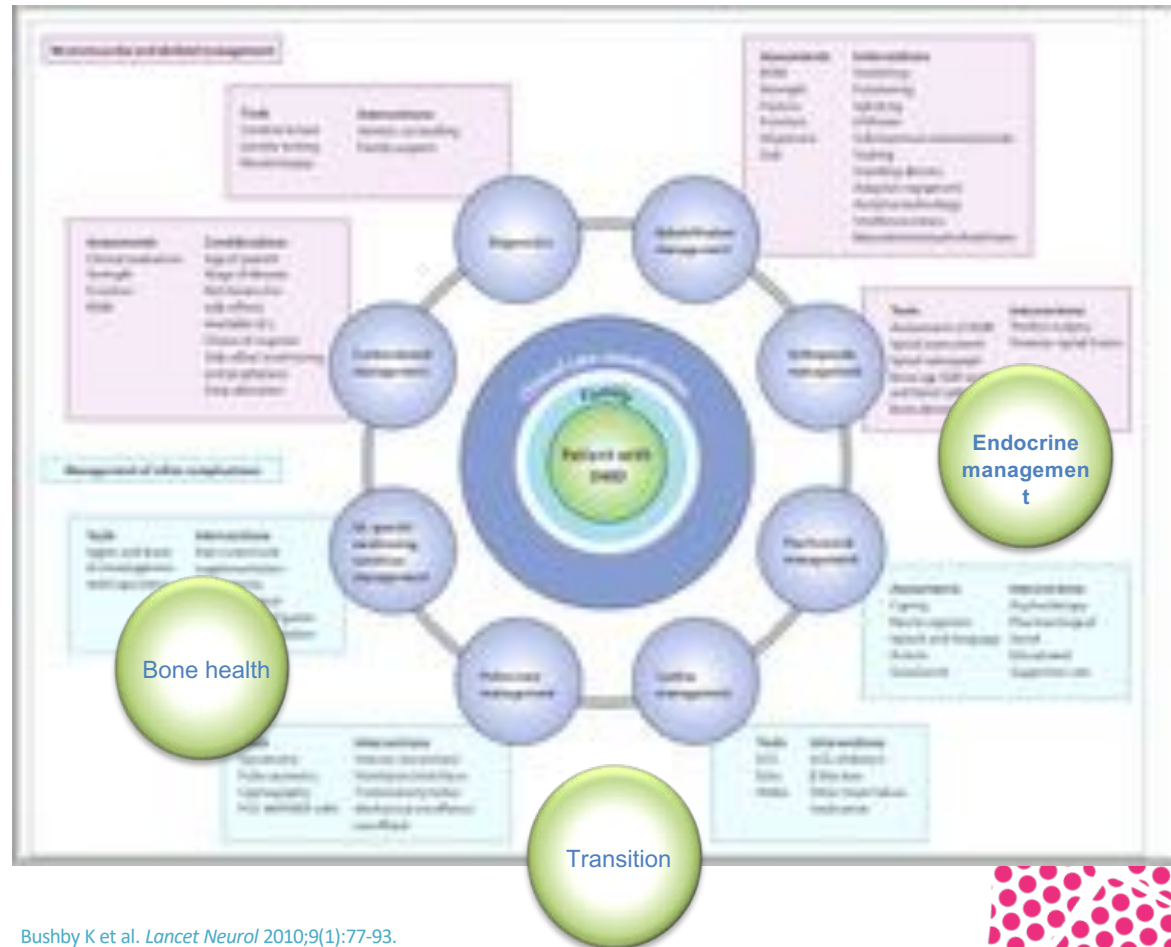
DMD care considerations

Bushby et al Lancet Neurology 2010

5 disease 'phases'

1. Pre-symptomatic
2. Early ambulatory
3. Late ambulatory
4. Early non ambulatory
5. Late non ambulatory

Updated in 2018, Birnkrant et al



Bushby K et al. *Lancet Neurol* 2010;9(1):77-93.

Different Priorities/Challenges at Each Phase

1. Pre-symptomatic
2. Early ambulatory
3. Late ambulatory
4. Early non ambulatory
5. Late non ambulatory



Different Priorities/Challenges at Each Phase

1. Pre-symptomatic (Diagnosis)
2. Early ambulatory (Steroids, MDT care)
3. Late ambulatory (Trial Target Cohort)
4. Early non ambulatory (Transition)
5. Late non ambulatory (Access!)

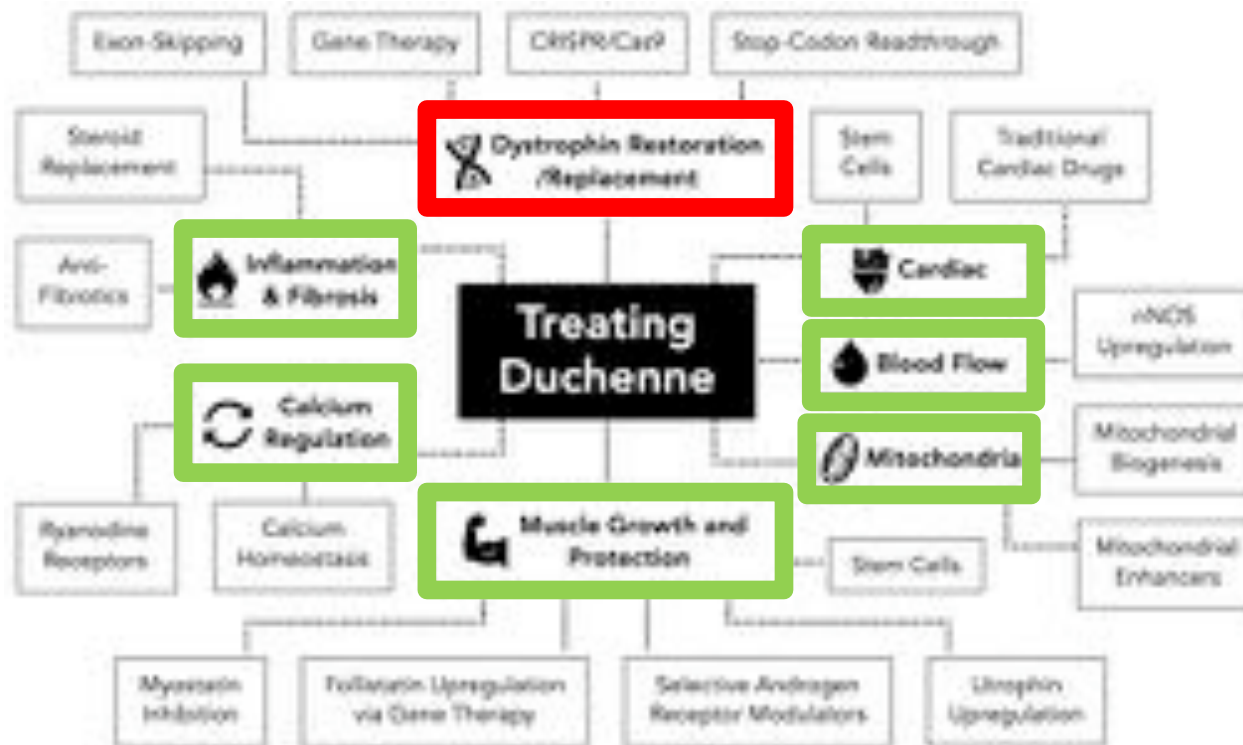


Challenges in DMD Research

- Providing equal access to Clinical trials
 - Need more 'research' centres
 - Most trials targeting at the same 'subgroup' of patients
- Support for families Navigating the System
 - How to access clinical trials near to home?
 - Which trial is right for an individual CYP and their family?
 - Managing 'Expectations': Practical Support for families

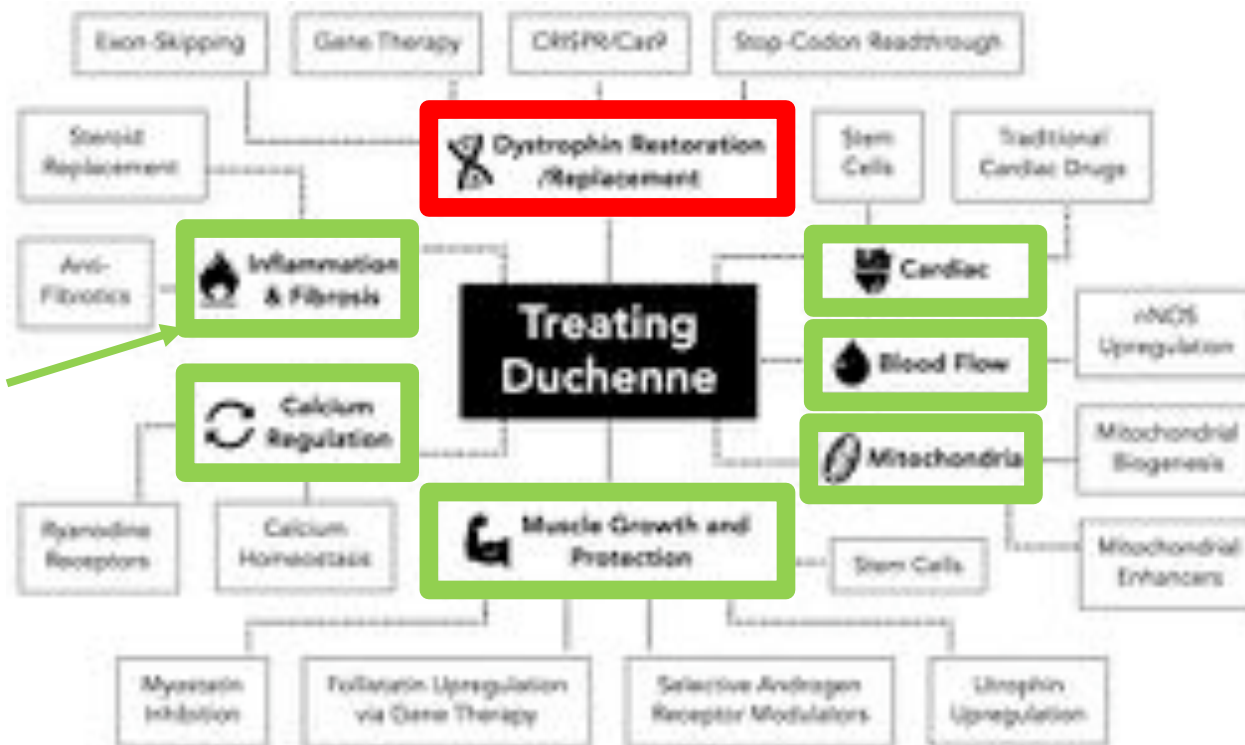


Potential Therapeutic Targets in DMD



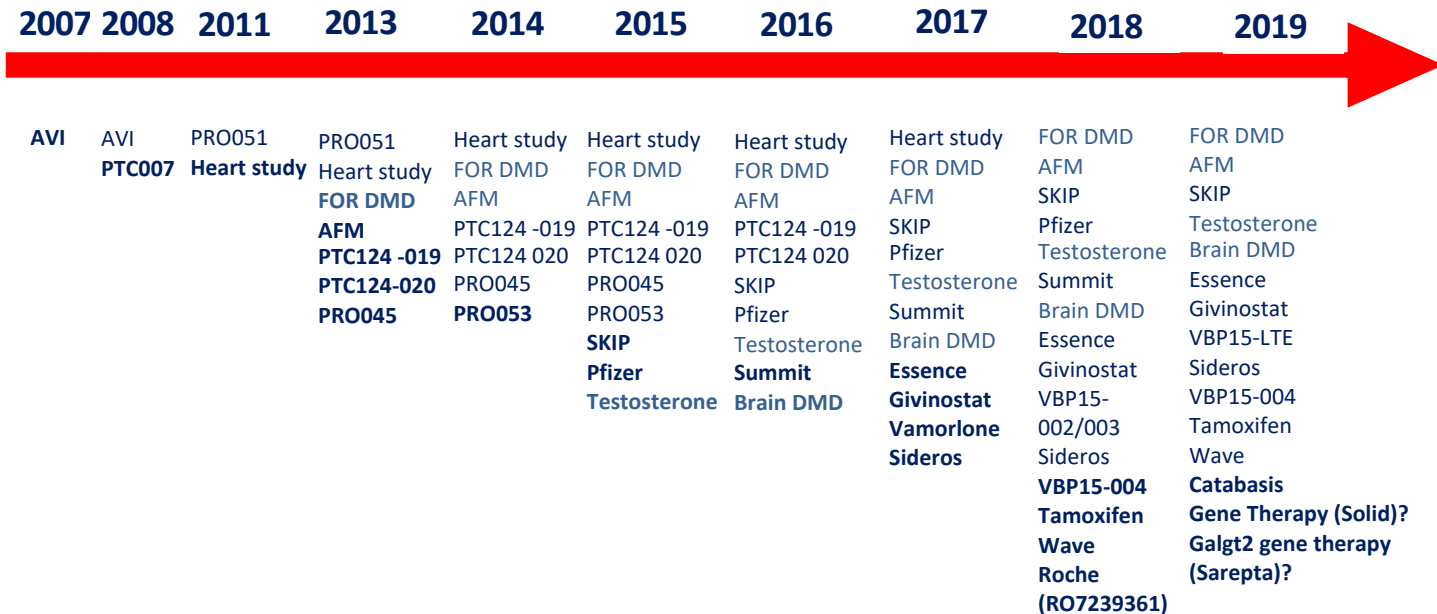
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Potential Therapeutic Targets in DMD

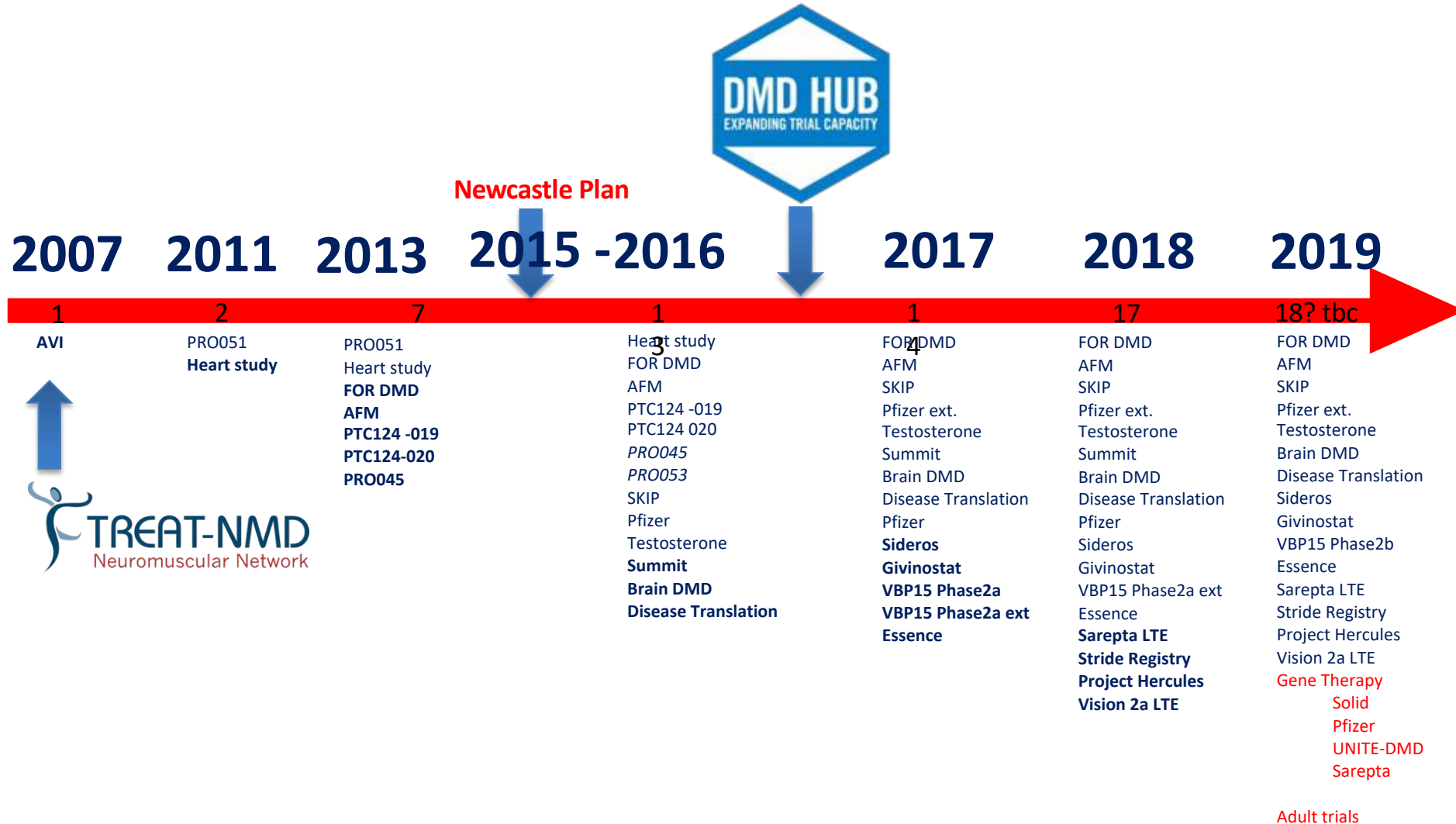


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DMD Trial Evolution



DMD Clinical Trial Landscape





Meanwhile back in Leeds....

- 1992 NM service began
- Cover the old 'Yorkshire Health Authority'
 - 1 million children
- Caseload of 450+ patients
 - 80-100 DMD
 - 30-40 SMA
- NM team 2013
 - 1 → 2 consultants and 1 → 2 specialist care
 - 1 PT band 7 NM physio (+ some band 6 support)
 - 1 PT band 7 NM OT (+ some band 5 support)
- MDUK audit 1 of 7 UK centres of excellence in the management of NMD in children

Leeds NM Research in 2015

- Recruiting to clinical trials in 2 UK study sites
- 2013 Approached to take part in FOR DMD
 - Quite good at it
 - One of best recruiting sites in Europe
 - Retained all 10 patients
- Expanding knowledge/experience in research
 - improvements in clinical care



How to do more research studies in Leeds?

- Positives

- Excellent MDT good links to UK NM networks
- Suitable cohort of patients
- Support from CRN in Leeds and plans for a new CRF
- Aligned with National focus on NM research
- Newcastle Plan and Duchenne UK
- More collaboration with industry

- Negatives

- Limited NHS Resources
 - Clinical, therapy and nursing staff
 - 'Space'
- Lack of experience in certain studies



Strategy to Develop Services in Leeds

- Expand the NM clinical (and research) team
 - Roald Dahl Marvellous Children's Charity
 - Band 7 Clinical Nurse Specialist (2016/7)
 - Band 7 Transition Nurse Specialist (2019)
 - PTC Therapeutics
 - Band 8, Specialist Physiotherapist (2017/8)
 - Duchenne UK with the DMD Hub
 - P/T Clinical Fellow and NM Coordinator (2017/8)
 - Research administrator (2017/8)
 - Wave
 - NM trial administrator (2019)
- Networking
 - Raise awareness of service
 - Develop research profile
- 2017 Recognised as the 2nd Research Hub Site



Impact of the Hub – For Patients and Families

- Website - 2,000 page views per month in 2019 , steadily increased



Info about what it is like to be part of a clinical trial. Updates on trials.

Clinical Trial Finder

- Details 27 trials in 12 sites
- Keeps patients informed in fair and equitable way
 - Eligibility checker
- Provides contact details for trial sites
 - Trial status per site
- Aids recruitment to trials

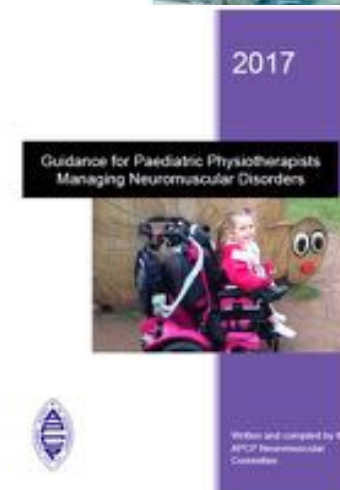
Impact of the Hub on Professionals and NM centres

- Resource for Families, Professionals and Carers
- Funding Posts
 - Help alleviate immediate capacity issue at sites and support development of clinical trial portfolio
 - Tapered funding model implemented (100:70:40)
 - Not all always straight forward : Sustainability and Recruitment
- Promote sites as trial sites to industry
 - Feasibility and capacity enquiries
 - Recruitment (via clinical trial finder and collaboration with TREAT-NMD)
 - No trials being turned away from the UK
- Collaboration
 - Signposting for staff training – TREAT-NMD (e.g. DMD Masterclass) and NIHR resources
- Sharing experiences, agreeing national process
 - Enabled by the DMD-Hub Toolkit e.g ethics / IRAS submission and protocol issues



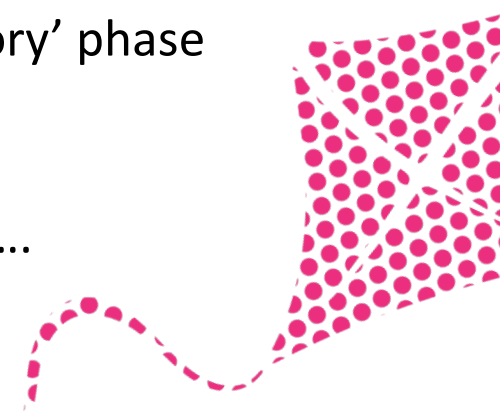
Leeds 2019

- Expanded the NM team with support of charities, industries, LTHT and DMD Hub
- Created a new NM consultant post from tapered Duchenne UK funding
- Have successfully developed DMD Research Portfolio in Leeds
 - 6 DMD interventional studies (FOR DMD, Sideros, Essence, Vision DMD, Tam DMD, Dystance 51)
 - Recruited 26 boys to Clinical Trials of an IMP
 - Recruited further 46 boys to observational studies
- Raised awareness of Leeds as NM centre
 - Engaging with Hub and Industry re Gene Therapy
- Extended clinical expertise and knowledge
- Further proposals to industry for funding
- Engaged with other NM clinical research studies



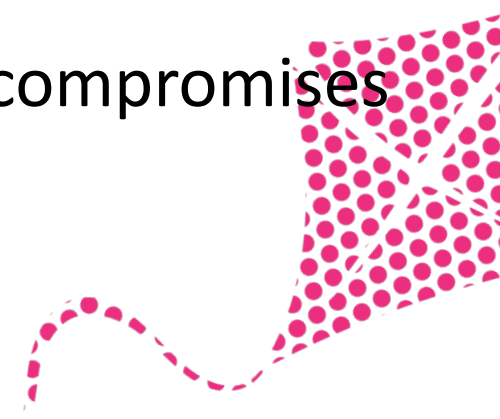
Ongoing Challenges for the Hub and Hub Sites

- Capacity to take on New studies??
- Balancing numbers of trials at specific trials sites
 - Fewer sites recruiting individually greater numbers of patients?
 - Limiting access to individual patients as a result
- How to ensure 'fair' allocation across UK centres?
 - Geographical
 - Social
 - Ethnicity
- Supporting Adults to engage in research?
 - Adult services considerably under-resourced
 - Expanding research in DMD beyond the 'late ambulatory' phase
 - Most Trials are targeting specific disease phase
- Measuring Outcomes
 - Developing meaningful v practical outcome measures....



Translating Research Studies into Therapies?

- Long delays from 1st 'breaking news' to actual treatment if at all
- Extending Approved Use outside the 'Study' Population
- 'Repurposing' a previously licensed drug ie Tamoxifen bypasses some stages
 - Potential access outside clinical trial - compromises validity of the trial data



Thank You

- NM team
- Leeds Clinical Research Team
 - Research Nurses and Administrators
- Children and Young people (and their carers)
- Partners from Charity and Industry

