Central Manchester University Hospitals NHS
NHS Foundation Trust

Management of neuromuscular disease

EPNS Neuromuscular Course

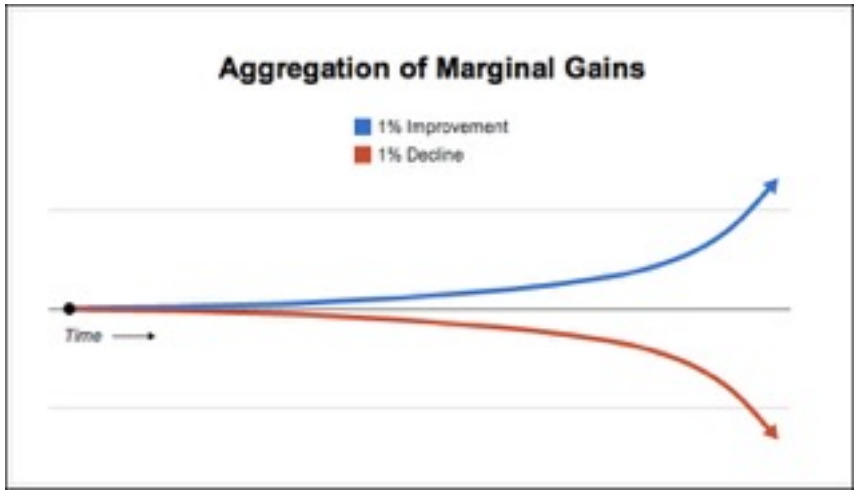
Dr Imelda Hughes
Consultant Paediatric Neurologist
Royal Manchester Children's Hospital

Declarations

- PI in clinical trials for PTC Therapeutics, Summit
- Consultancy for Santhera and Biogen
- Conference fees and travel by PTC therapeutics

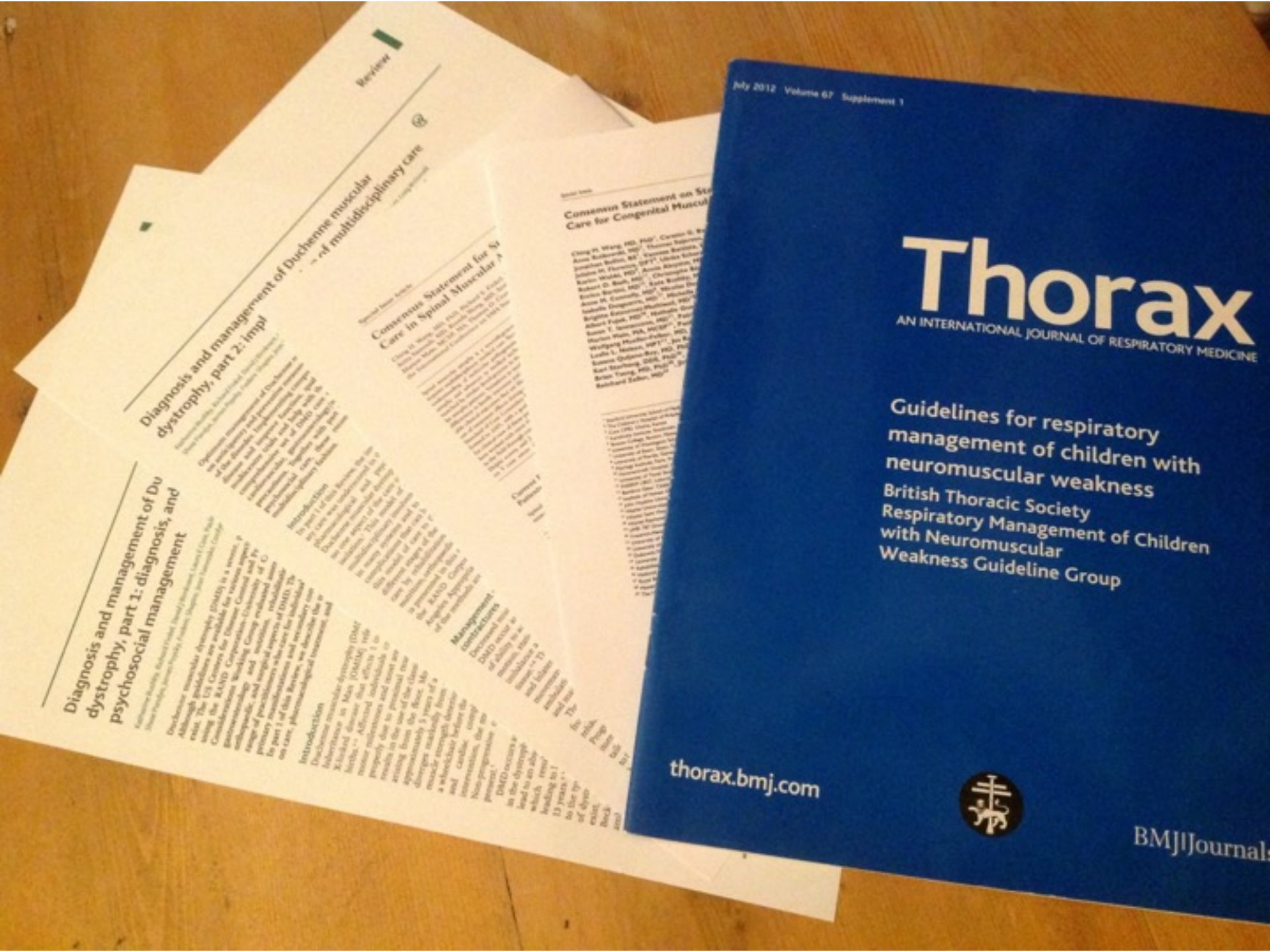
Topics

- Principles of management
- General management
- Disease specific treatment



Put simply…how small improvements in a number of different aspects of what we do can have a huge impact to the overall performance

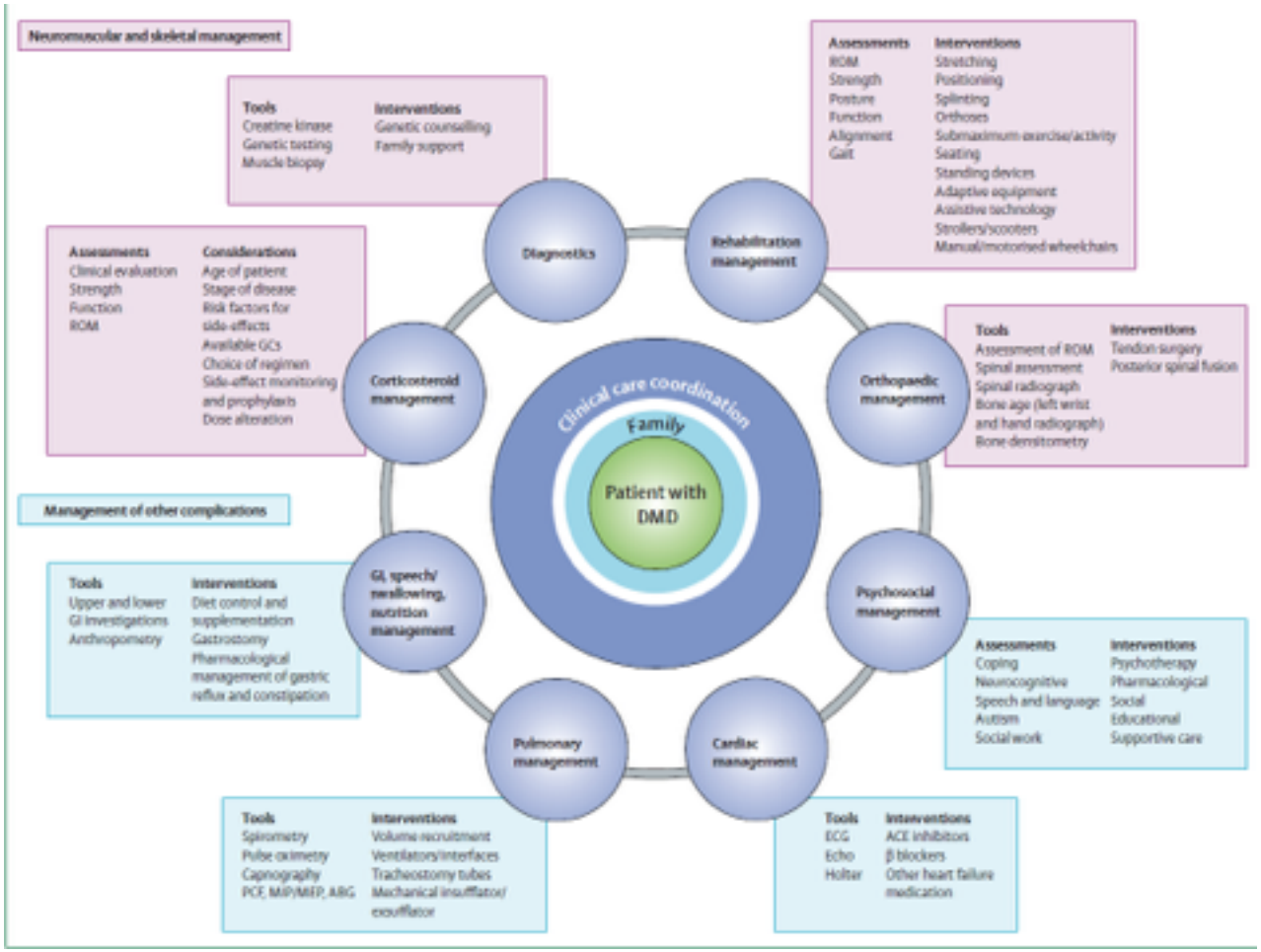
David Brailsford
Performance director
British cycling team


Review
Diagnosis and management of Duchenne muscular dystrophy, part 2: impl
of multidisciplinary care
Consensus Statement for S
Care in Spinal Muscular
Consensus Statement on St
Care for Congenital Muscul
Diagnosis and management of Du
dystrophy, part 1: diagnosis, and
psychosocial management
Introduction
Management
July 2012 Volume 67 Supplement 1
Thorax
AN INTERNATIONAL JOURNAL OF RESPIRATORY MEDICINE
Guidelines for respiratory management of children with neuromuscular weakness
British Thoracic Society Respiratory Management of Children with Neuromuscular Weakness Guideline Group
thorax.bmj.com
BMJIJournals

General

- Diagnosis & anticipation of complications
- Family support
- Swallowing/Nutrition
- Respiratory
- Cardiac
- Orthopaedic
- Rehabilitative
- End-of-life care

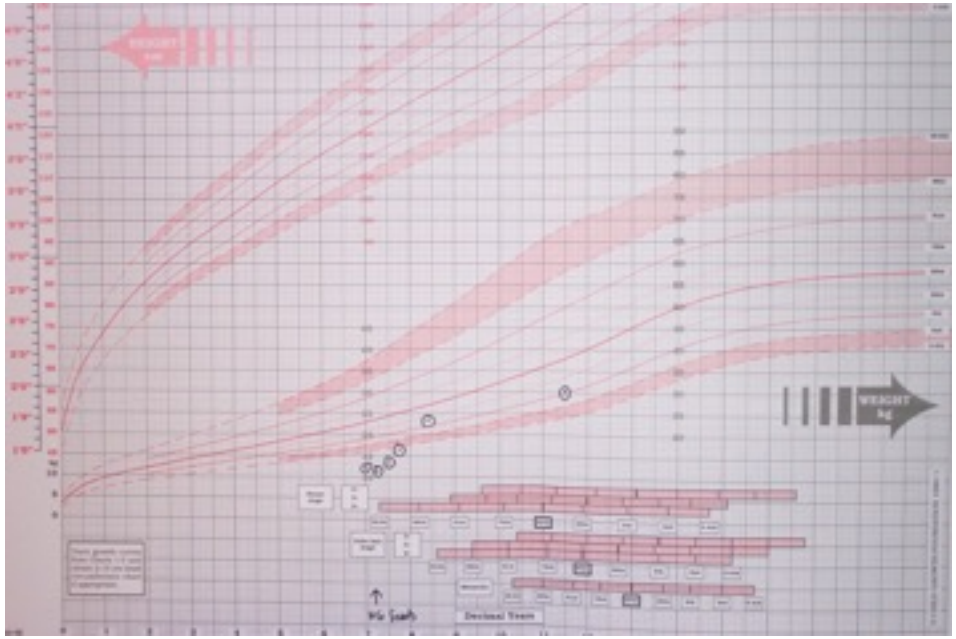
Management NMD



Diagnosis

- Accurate and timely
- Good practice diagnostic disclosure
  - Explanation of diagnosis
  - Prognosis
  - Genetics
  - Management plan
  - Support
  - Resources

Nutrition



Swallowing

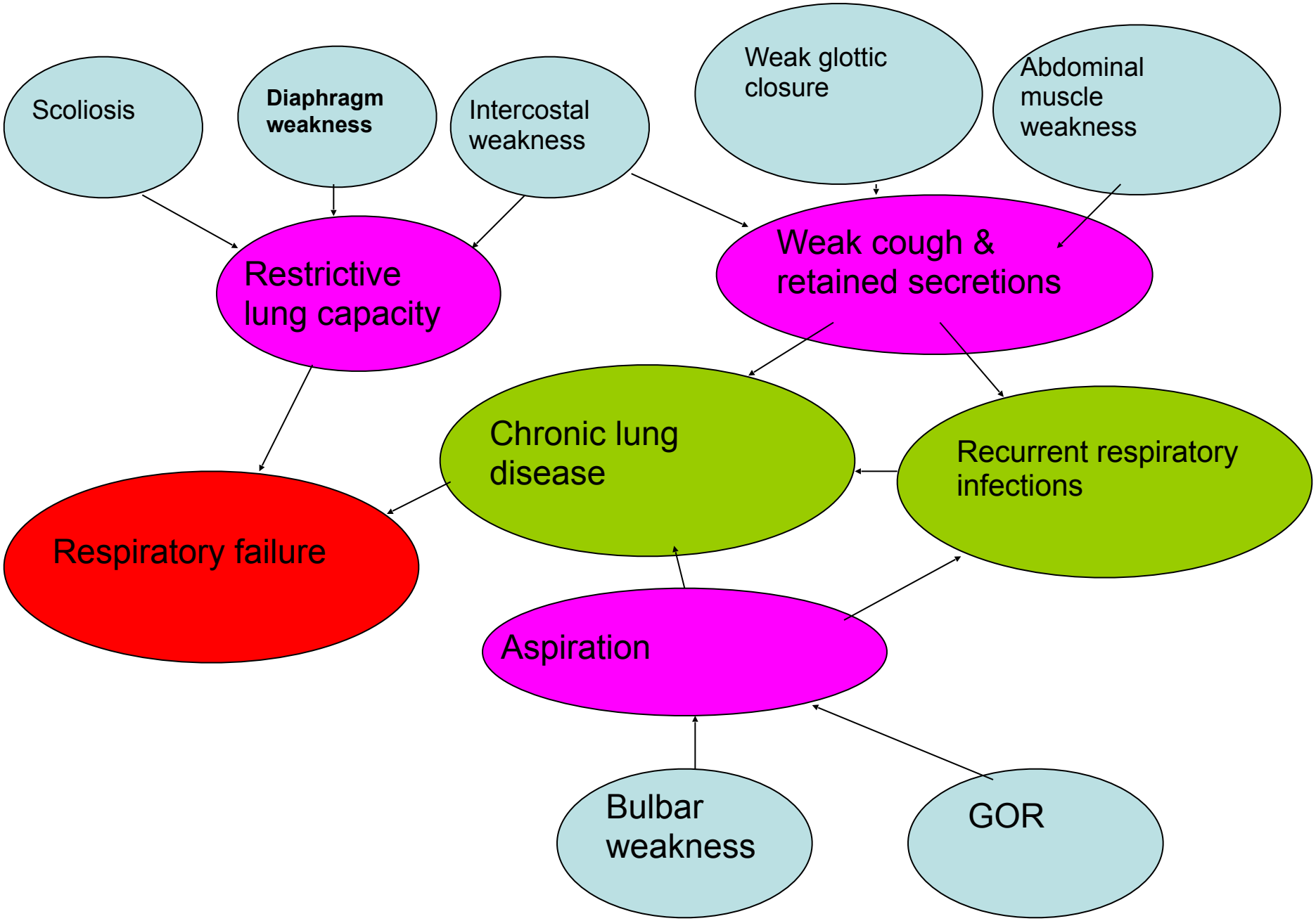
Slow at meals
Coughing on eating/drinking
SALT assessment
Videofluorscopy

Respiratory problems in NMD

- Inevitable in progressive conditions
- Different in different conditions
- Nocturnal hypoventilation first manifestation of respiratory failure

Pathophysiology of respiratory complications in NMD

- Diaphragmatic weakness
- Intercostal weakness
- Abdominal muscle weakness
- Bulbar weakness
- Weakness of glottic closure
- Gastroesophageal reflux
- Scoliosis


Scoliosis
Diaphragm weakness
Intercostal weakness
Weak glottic closure
Abdominal muscle weakness
Restrictive lung capacity
Weak cough & retained secretions
Chronic lung disease
Recurrent respiratory infections
Respiratory failure
Aspiration
Bulbar weakness
GOR

What can be done?

Management – respiratory infection

- Prevention
  - Vaccination – flu and pneumococcal
  - Feeding assessment & advice
  - GOR treatment – medical/ surgical
  - Assisted coughing – manual/mechanical
- Treatment of infection
  - Early antibiotic
  - Iv antibiotic
  - Assisted coughing

Nocturnal Hypoventilation

- Initially REM sleep
- Transient hypercapnia
- Frequent arousals
- Sleep fragmentation

Nocturnal hypoventilation

- FVC <60%
- Symptoms
  - Restless sleep
  - Morning headache
  - Lethargy
  - Loss of appetite, weight loss
- Assessment
  - Polysomnography
  - Overnight SaO_2 & pCO_2

Polysomnography

- SaO_2, pCO_2
- Sleep staging EEG, EOG, EMG
- Apnoea – cessation of airflow >10 sec
- Hypopnoea – reduction in airflow or chest wall movement with $\downarrow SaO_2$ at least 4%
- Apnoea-hypopnoea index

Benefits of NIV

- Prolongation of life

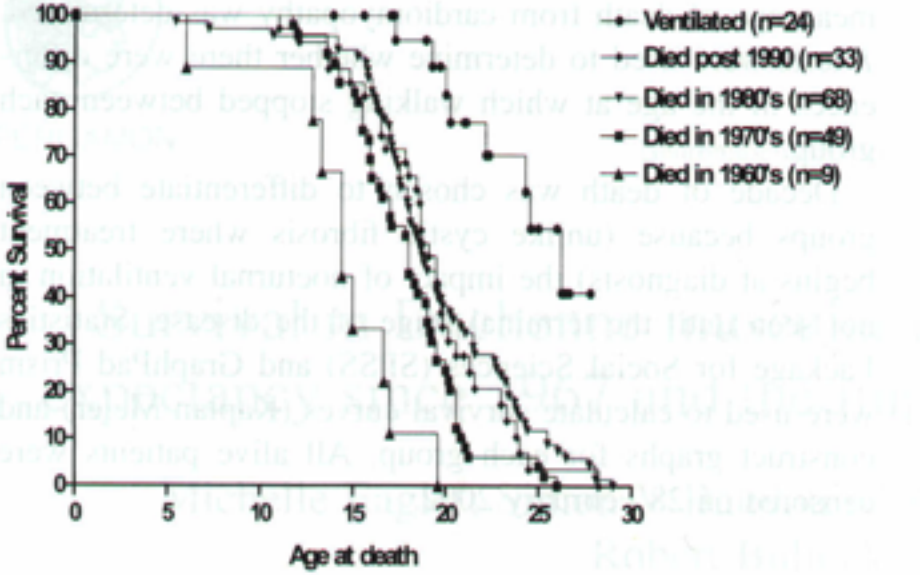


Fig. 2. Survival curves (Kaplan Meier) showing percentage survival of ventilated versus non-ventilated patients 1967–2002. (Includes live patients censored on 28th February 2002.) Legend; Log rank test for non-ventilated vs. ventilated patients post-1990 ($P = 0.0001$).

Benefit of NIV - palliation of symptoms

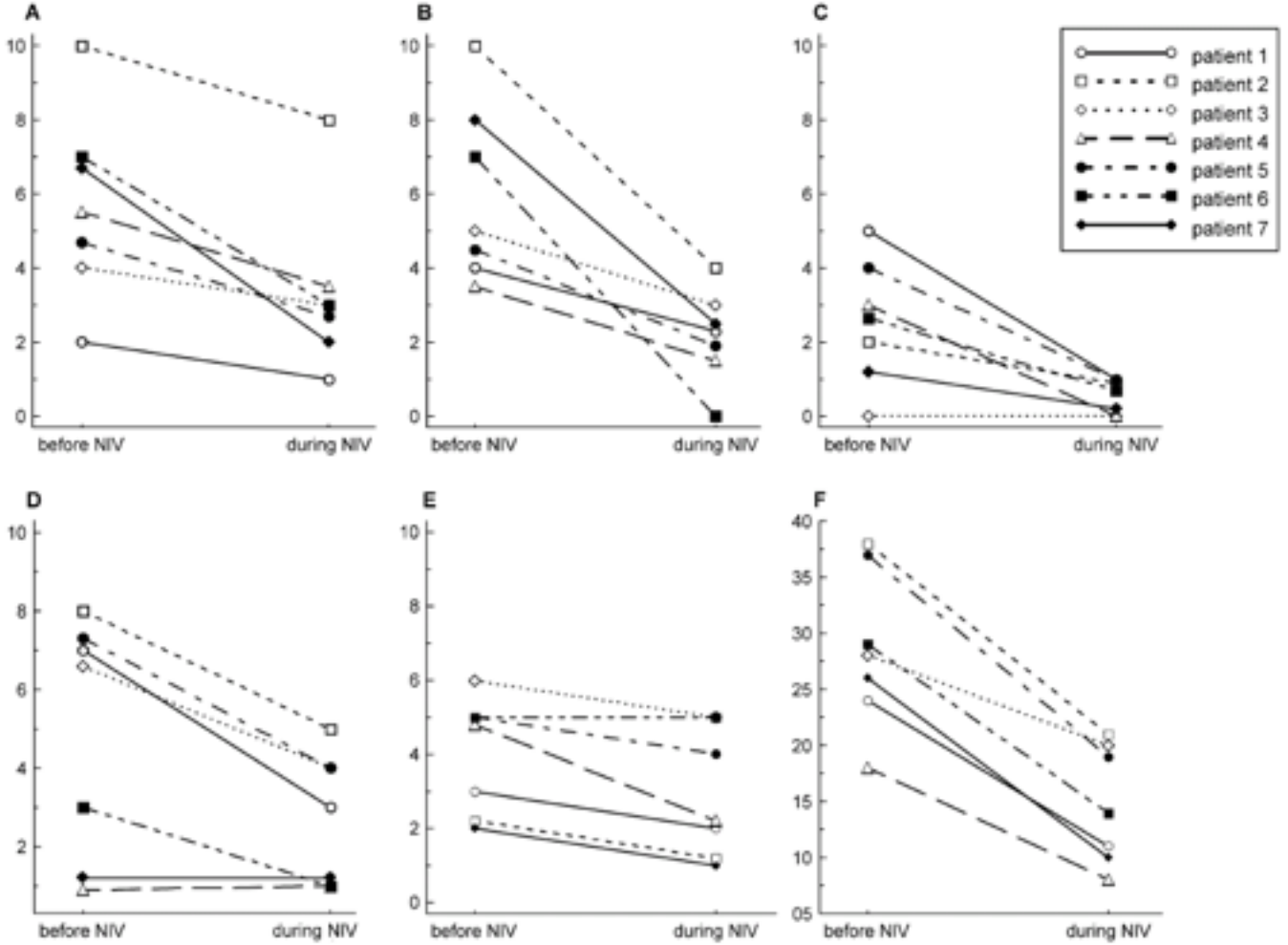


Fig. 2. Impact of NIV on symptoms (before vs. after institution of NIV). Improvements in (A) sleep disturbance (5.7±2.6 vs. 3.3±2.2 points); (B) nocturnal sweating (6.0±2.4 vs. 2.1±1.2 points); (C) morning headaches (2.6±1.7 vs. 0.6±0.5 points); (D) nausea/ lack of appetite/feeding difficulties (4.9±3.1 vs. 2.7±1.7 points); (E) impaired concentration (4.0±1.6 vs. 2.9±1.6 points) and (F) total score (28.7±7.1 vs. 14.9±5.5 points ($P < 0.005$ for all).

U. Mellies et al. / Neuromuscular Disorders 14 (2004) 797–803

Rachel's Star Chart


~~Thur~~ Wed
3 hrs


Thur
3 1/2 hrs


Fri
2 hrs


Sat
4 hrs


Sun
2 1/2 hrs


Mon
12 hrs


Tue
6 hrs


Wed
6 hrs

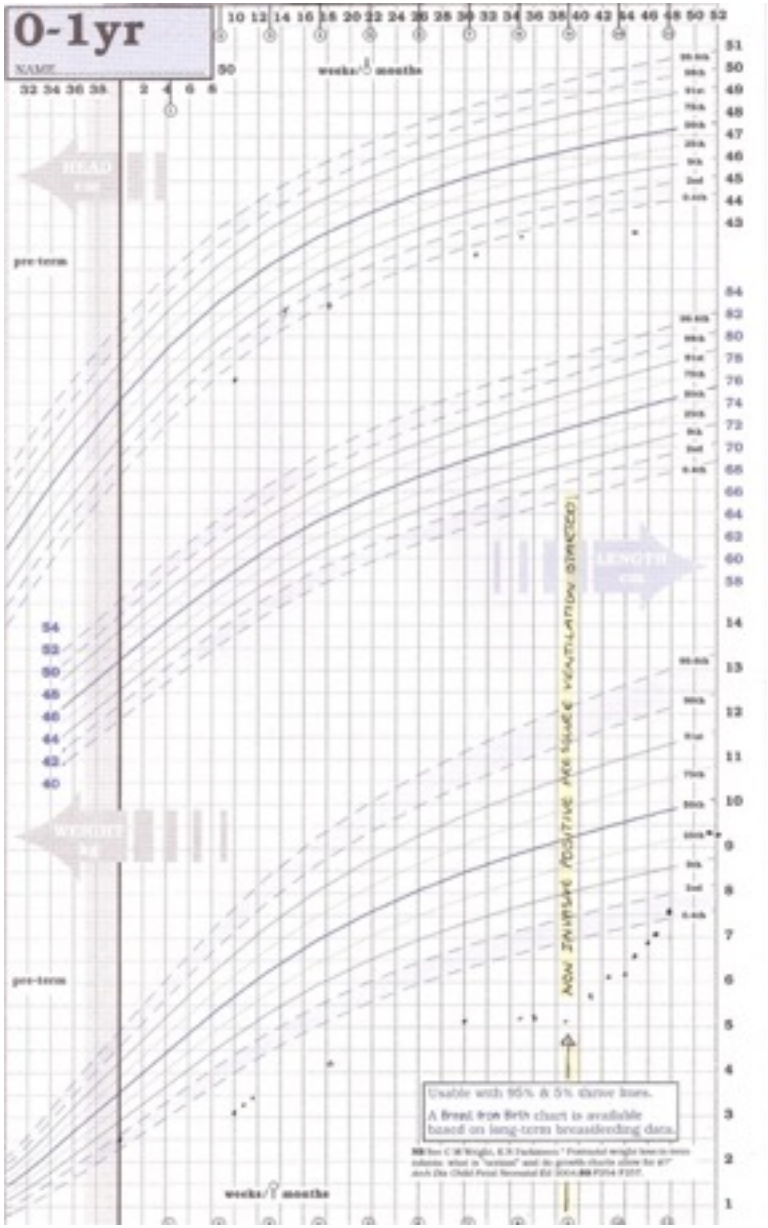

Thur
11 hrs

Benefits of NIPPV

- Prolongation of life
- Palliation of symptoms
- Improves quality of life
- Is well tolerated
- Reduces hospital & PICU admission

NIV Complications

- Skin breakdown
- Dry mouth (65%)
- Nasal congestion & dryness (25%)
- Eye irritation (24%)
- Runny nose (35%)
- Sinusitis (8%)
- Nose bleeds (4-19%)
- Gastric distension (sporadic)
- Pneumothorax (rare)


0-1yr
NAME
weeks/ months
pre-term
pre-term
HEAD
WEIGHT
LENGTH
NOW ENTERING POSITIVE PRESSURE VENTILATION (DIRECTED)
Usable with 95% & 5% curve lines.
A Breast Iron Birth chart is available based on long-term breastfeeding data.
weeks/ months

Patterns of respiratory involvement

DMD

- Fairly predictable
- Loss of ambulation
- Scoliosis
- Sleep disordered breathing
- Respiratory infections
- Cardiomyopathy
- Natural history modified by steroids

SMA

- Intercostal weakness
- Diaphragmatic sparing
- Bulbar weakness
- Retained secretions, recurrent infections

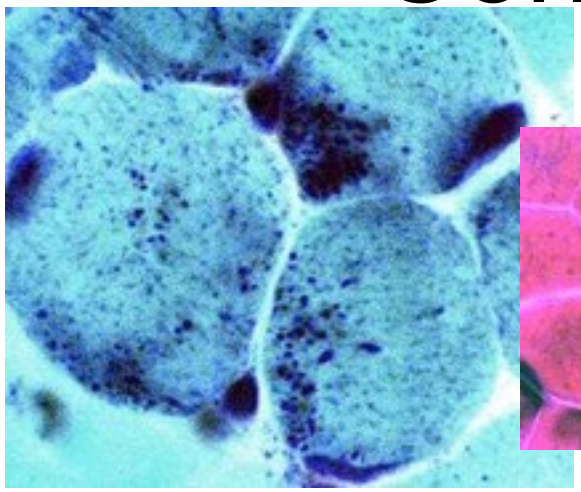
Rigid spine syndromes

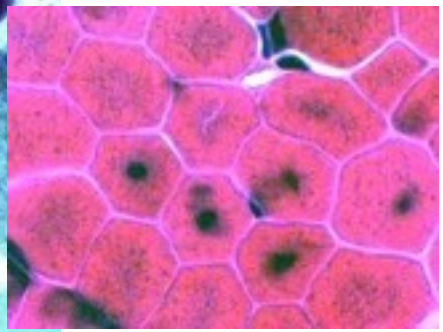
- RSMD, Minicore disease, EDMD
- Early respiratory failure

Selective diaphragmatic involvement

SMARD
EMARD
BVVL

Congenital myopathy

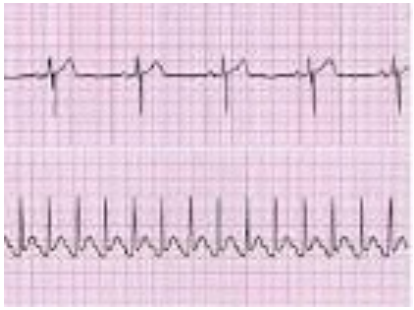


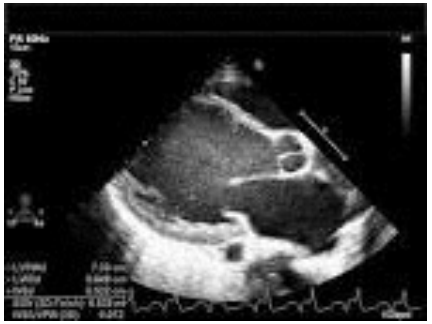


- Neonatal respiratory failure – nemaline & myotubular myopathy
- Core myopathy may develop respiratory failure while ambulant

Cardiac

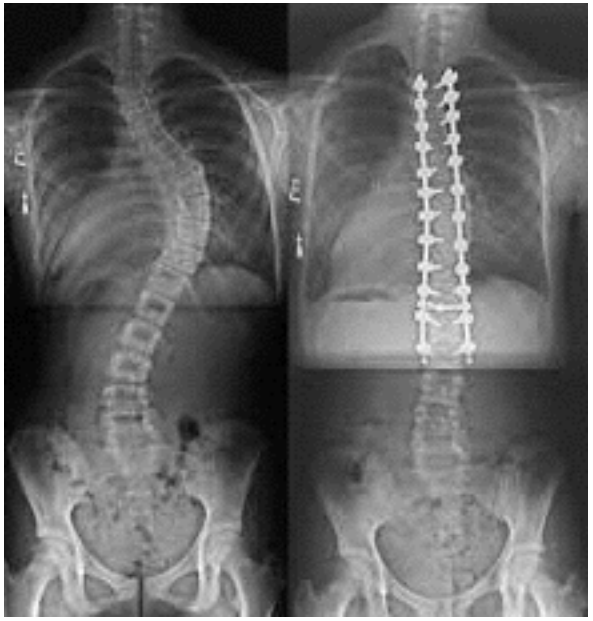
- DMD <10 every 2 years, >10 annual
- Myotonic dystrophy annual ECG
- EDMD, LGMD1B, MYH7, predisposition to arrythmia





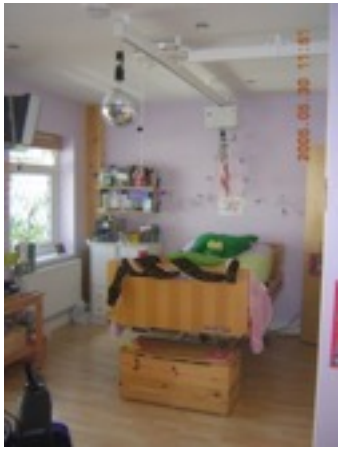
Orthopaedic

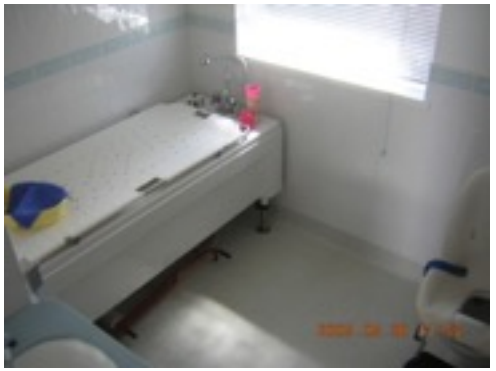
- Contractures
  - Splinting
  - Serial casting
  - Surgery
- Scoliosis
- Postural management



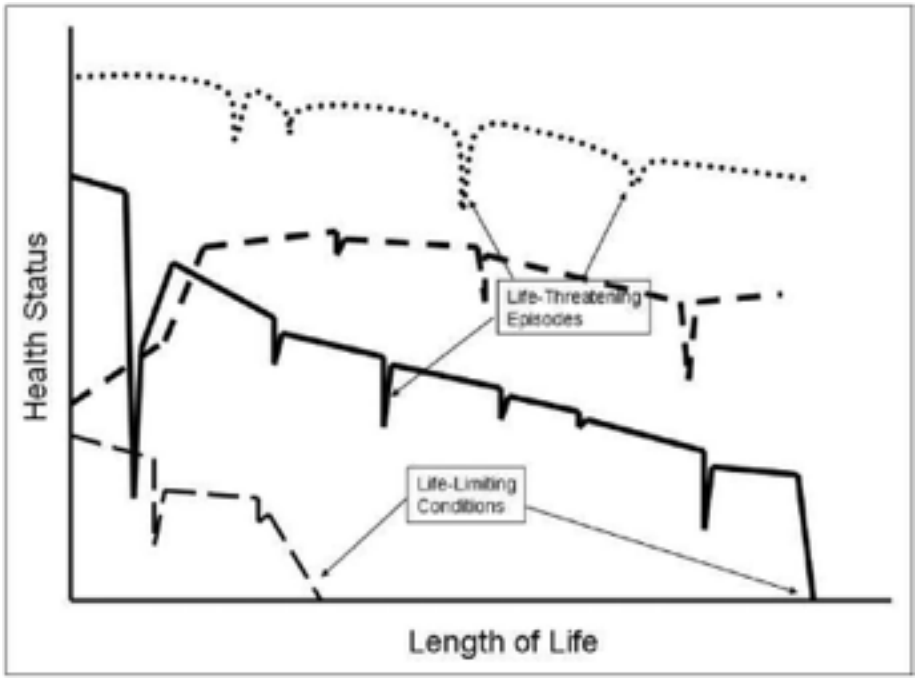
Rehabilitative

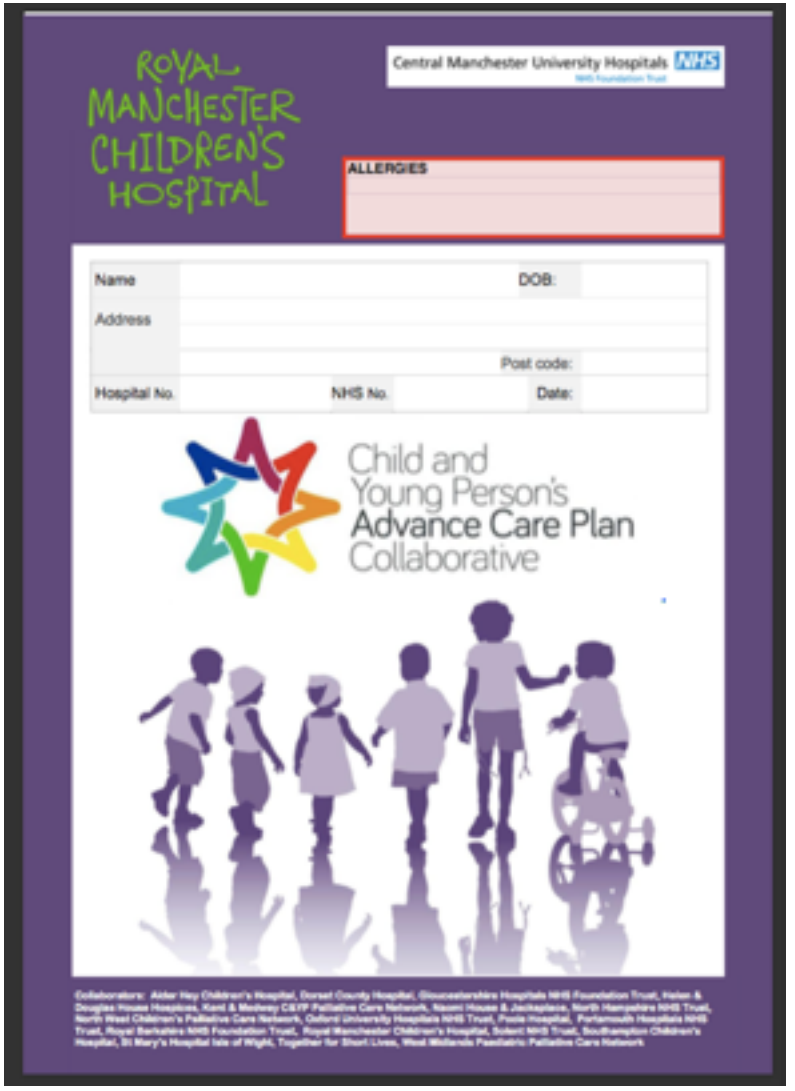
- Mobility
- Education
- Housing



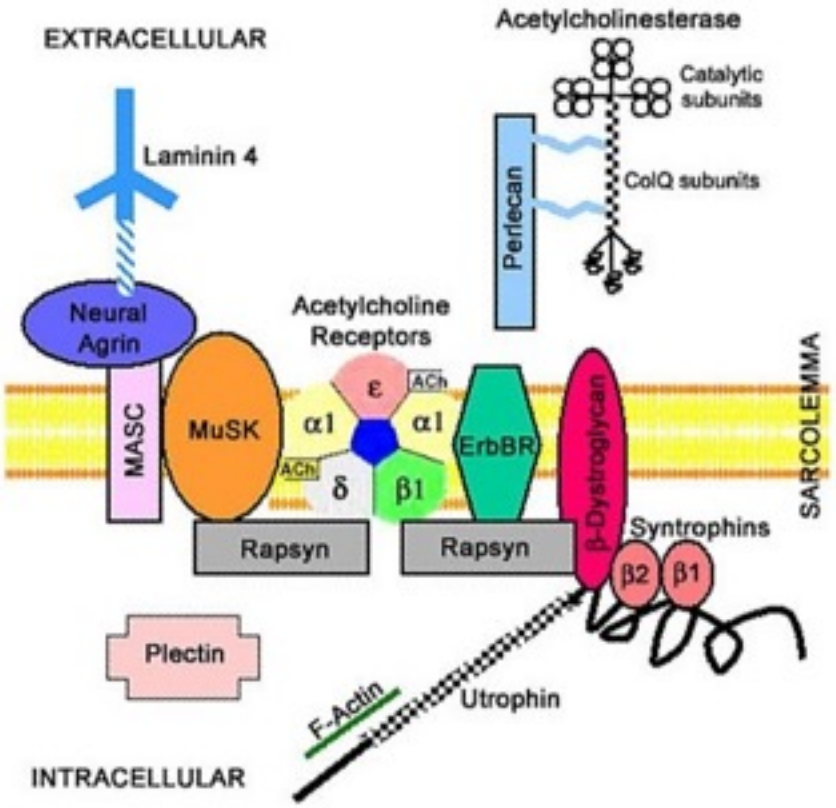


Palliative & End-of-life care





Congenital Myasthenic syndromes



- Weakness fluctuates, worse in intercurrent illnesses
- May be episodic apnoea
- May be treatable

Disease specific treatment

- DMD
  - steroid
  - ataluren
  - idebenone
  - eteplirsen
- Congenital myasthenic syndromes
  - pyridostigmine, salbutamol, 3,4-DAP, ephedrine
- Pompe disease ERT
- SMA Nusinersen
- Inflammatory myopathy, CIDP immune modulation
- Myasthenia gravis pyridostigmine, immune modulation

Glucocorticoid corticosteroids for Duchenne muscular dystrophy (Review)

Manzur AY, Kuntzer T, Pike M, Swan A

Authors' conclusions

There is evidence from randomised controlled studies that glucocorticoid corticosteroid therapy in Duchenne muscular dystrophy improves muscle strength and function in the short-term (six months to two years). The most effective prednisolone regime appears to be 0.75 mg/kg/day, given daily. In the short term, adverse effects were significantly more common but not clinically severe. Long-term benefits and hazards of glucocorticoid treatment cannot be evaluated from the currently published randomised studies. Non-randomised studies support the conclusions of functional benefits but also identify clinically significant adverse effects of long-term treatment. These benefits and adverse effects have implications for future research studies and clinical practice.

DMD natural history

- Mean age of diagnosis 4.6 years
- Median age wheelchair dependence 10 years
- Median age death 15 years

Steroid benefits

- Prolonged ambulation
- Preserved pulmonary function
- Reduced scoliosis
- ? Preserved cardiac function

Steroid side effects

- Weight gain
- Short stature
- Behaviour
- Reduced bone mass and vertebral fractures
- Delayed puberty
- Adrenal suppression
- Cataract
- Hypertension
- Gastrointestinal symptoms
- Cushingoid appearance
- Hirsutism
- Death

Variations in practice
Griggs et al Muscle & Nerve 2013;48:27-31

- 105 Treat-NMD clinicians
- Steroids not used in 10 clinics
- 29 different regimens
  - 0.75mg/kg/day prednisolone
  - Intermittent (10 days)
  - 0.9mg/kg/day deflazacort
  - 5mg/kg/day weekends

Benefits & adverse events intermittent v daily steroids Ricotti et al

- Median loss of ambulation
  - 12 yrs intermittent
  - 14.5 yrs daily
- Divergence after 7 years
- Cushingoid features, behaviour & hypertension more common in daily
- BMI mean z score higher in daily
- Height restriction more severe in daily

Steroids – unanswered questions

- Long term benefits v side effects
- Which steroid?
- What dosage regimen?
- When to start?

FOR-DMD

- Randomised controlled multicenter
- 3 arms
  - Prednisolone 0.75mg/kg/day
  - Deflazacort 0.9mg/kg/day
  - Prednisolone 0.75mg/kg intermittent (10 days)

Summary

- Management is:
  - Interdisciplinary
  - Multifaceted
  - Requires attention to detail