Unblocking the drug pipeline - treating Duchenne Muscular Dystrophy

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DMD Pathfinders – getting the life you want

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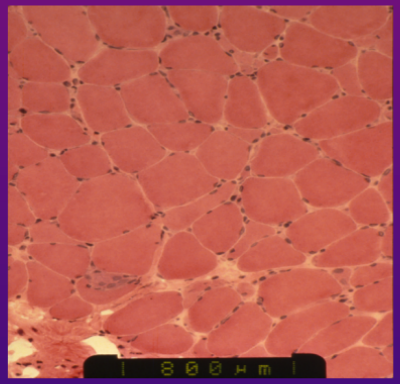
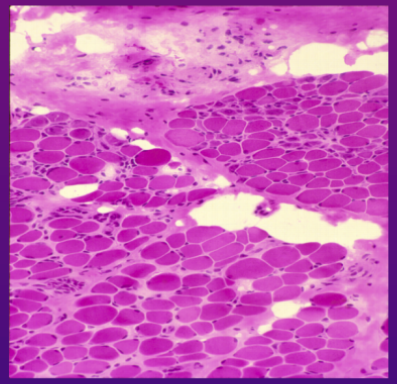
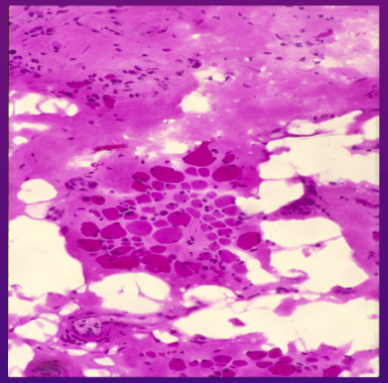
Loss of Muscle Fiber in DMD:



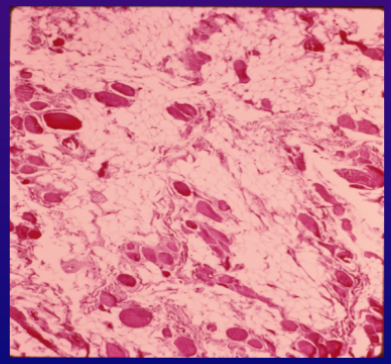
Normal

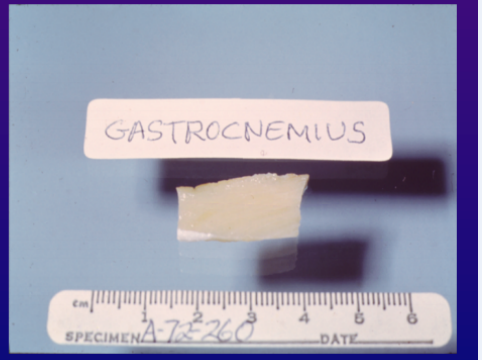


3 year old



9 year old





19 year old (Post-Mortem)

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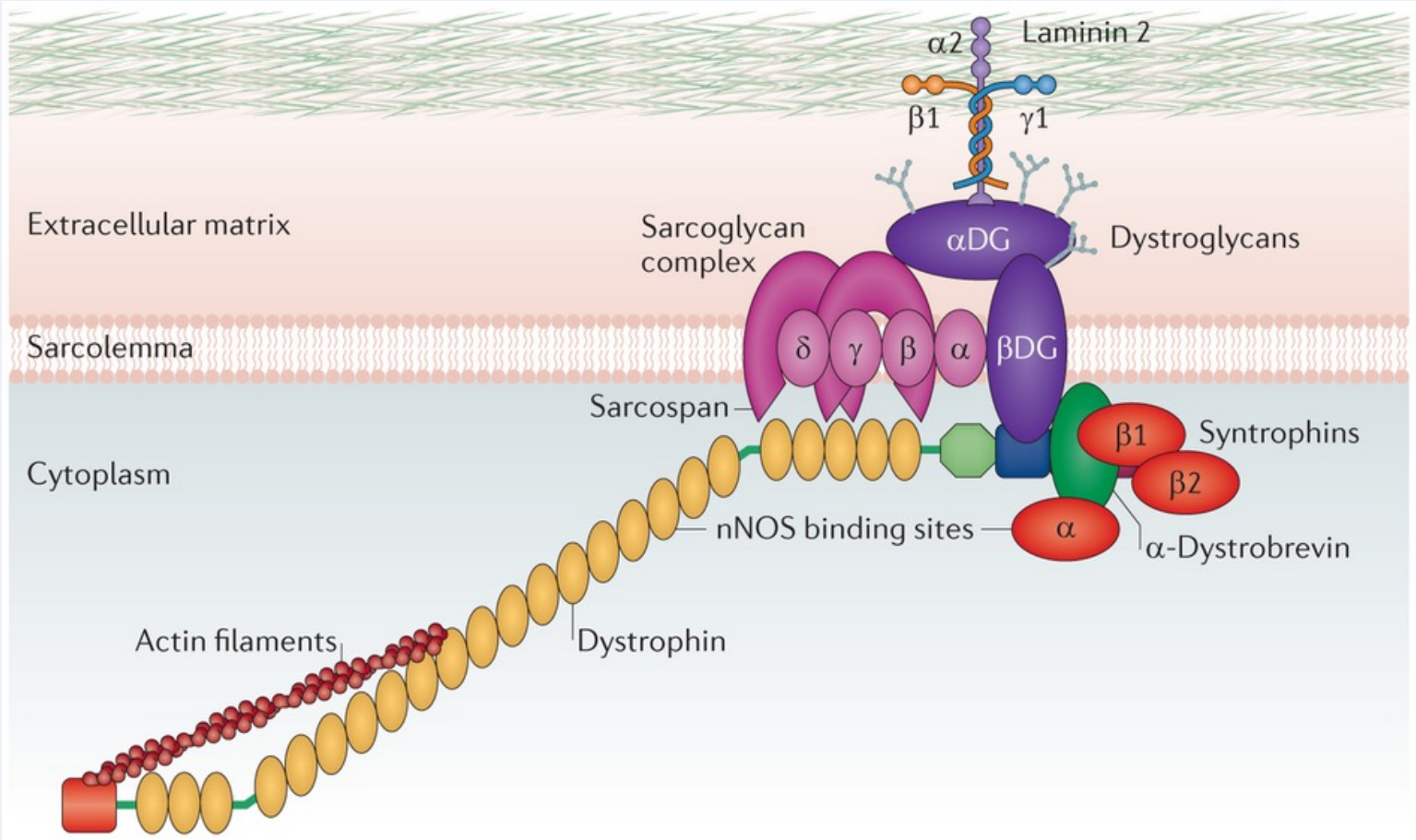
Dystrophin Protein Complex



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Duchenne Muscular Dystrophy

- Known since Duchenne described it over 150 years ago
- 1987 cloned gene named protein dystrophin
- Complex neuromuscular condition - mutations dystrophin gene
- Rare X linked condition 1:5000 (1:3500) boys about 100 every year in UK
- Changed natural progression - corticosteroids, ventilation, heart medication
- Neurodevelopmental disorder - dystrophin isoforms
- more than 80 drugs under development

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Blocked pipeline?

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Clinical Trial Design

Available online at www.sciencedirect.com

ScienceDirect

Neuromuscular Disorders ■■ (2015) ■■–■■

www.elsevier.com/locate/nmd

Personal Point of View

Challenges of clinical trial design for DMD

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Problems with clinical trial design

- Stop - Go Phased trials with small cohorts not getting data we need that shows conclusive benefit e.g. Translarna, Exon skipping trials
- Patients and families left without access to potential treatments
- Recovery in Duchenne long process - stem cells and hostile cellular environment
- Duchenne multi system requiring multi treatments - skeletal muscle, heart, brain, smooth muscle
- Boys are already on drugs and therapy regimes like physiotherapy started at different ages. Standards of Care not universal
- Spectrum of phenotype e.g. motor function varies even with steroid treatment
- Genotype variability exon 44 milder than 51 or 53

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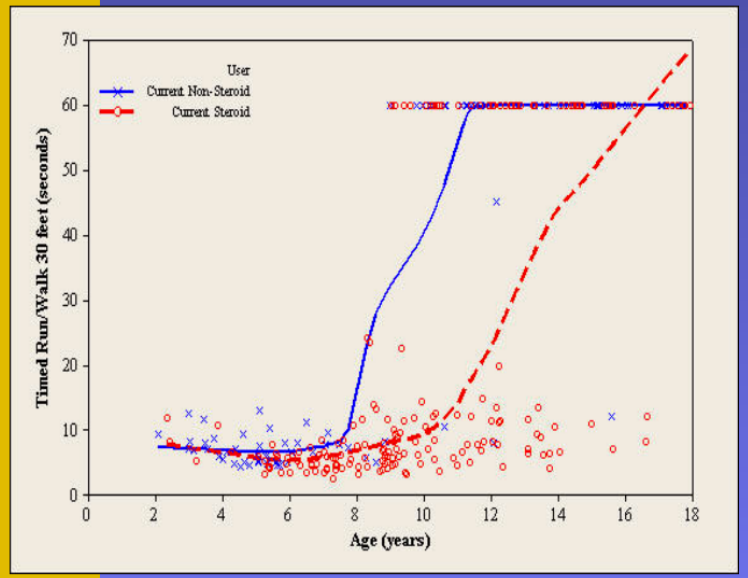
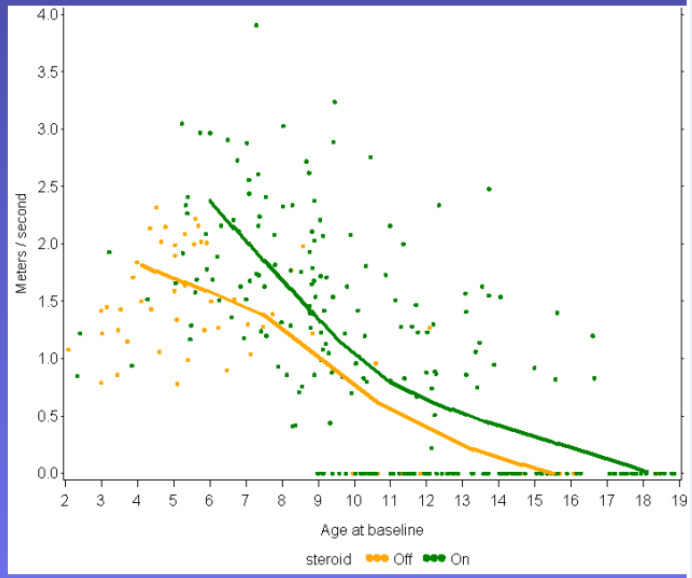
Time to Run/Walk 10 Meters





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Clinical Trial Design Solutions?

- Get rid of expensive and time consuming Phase 2 and Phase 3
- New approaches to trial design
- Use accelerated regulatory pathways e.g. FDA and EMA
- Post marketisation data collection e.g. North Star Clinical Database, DMD Registry allow long term collection data and better analysis
- Outcome measures against natural progression - account of multi system of Duchenne
- 6MWT, North Star Ambulatory Assessment, DMDSAT(patient/family)
- Biomarkers - MRI
- Expansion and funding of Expert Clinical Centres e.g. GOSH, Newcastle

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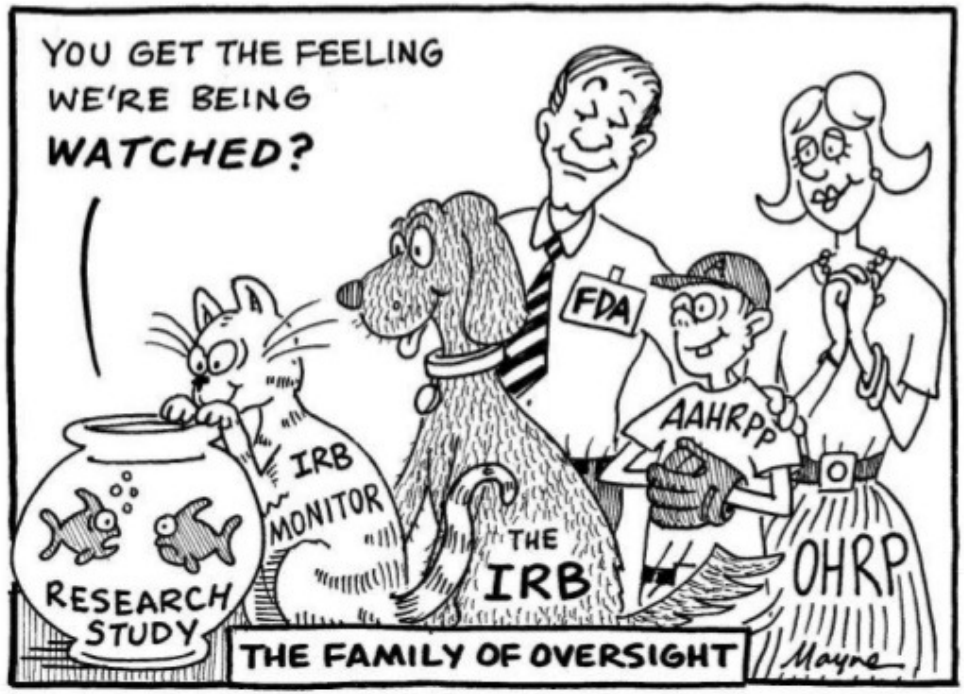
The family of oversight



Used with permission from Don Mayne. Wretched Mess Research Cartoons(2009)

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Regulatory oversight

- safety very important
- measurements of risk vs benefit important
- Use faster tracks FDA and EMA
- Translarna approved by EMA in UK - NHS England and NICE??
- NICE use of QUALY

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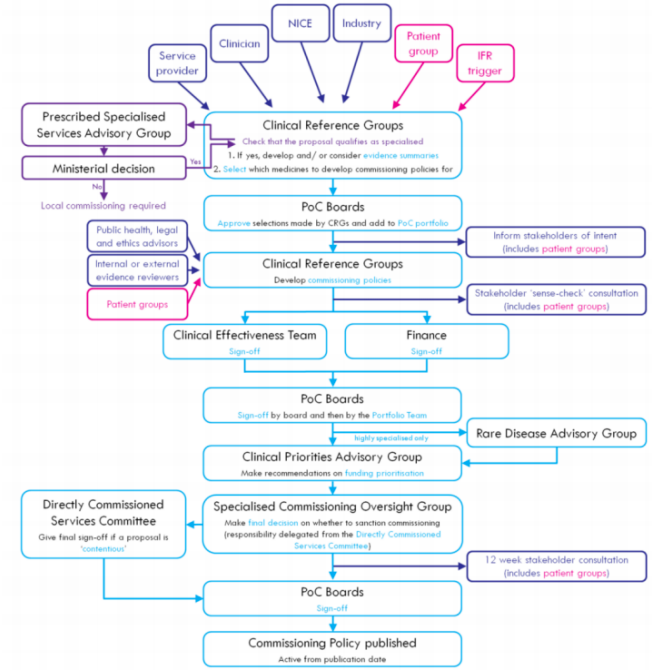
NHS England Labyrinth

The NHS England Patient Charter

Our findings – Simplify perhaps?

NHS England should streamline their unwieldy governance structure so they can make faster and fairer decisions and ensure their limited finances are spent where they are needed most.

Some progress has been made here...



The decision making process Oct 2014

Genetic Alliance UK

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First to respond to FDA decision on Biomarin drug last week?

Focus Turns to Judge in Latest Appeal of Net Neutrality Rules

Lufthansa Signs Pay Deal with 33,000 Personnel

BUSINESS

Major Shareholder Wants Inquiry Into Northwest Biotherapeutics Allegations

BUSINESS | HEALTH CARE | HEALTH

FDA Panel: BioMarin Muscular Dystrophy Drug Trials Didn't Prove Effectiveness

Committee concluded studies fell short of showing drisapersen worked in most patients

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Marketisation drug development

- Drugs are expensive to develop
- Costs per patient rare diseases is high - APPG white paper 2013
- high risk investments from venture capital - share price decisions or patient benefits?
- Promising clinical research is dropped
- Drugs and IP sit on the shelf
- commitment to follow up and collect long term data
- sharing of data
- open publication research
- Government funding vs austerity - £45bn bail out RBS
- Contributions Charities and patient groups

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time is precious

so waste it wisely!

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