Current challenges in clinical development and regulatory decision-making

Clinician's Perspective

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Disclosures

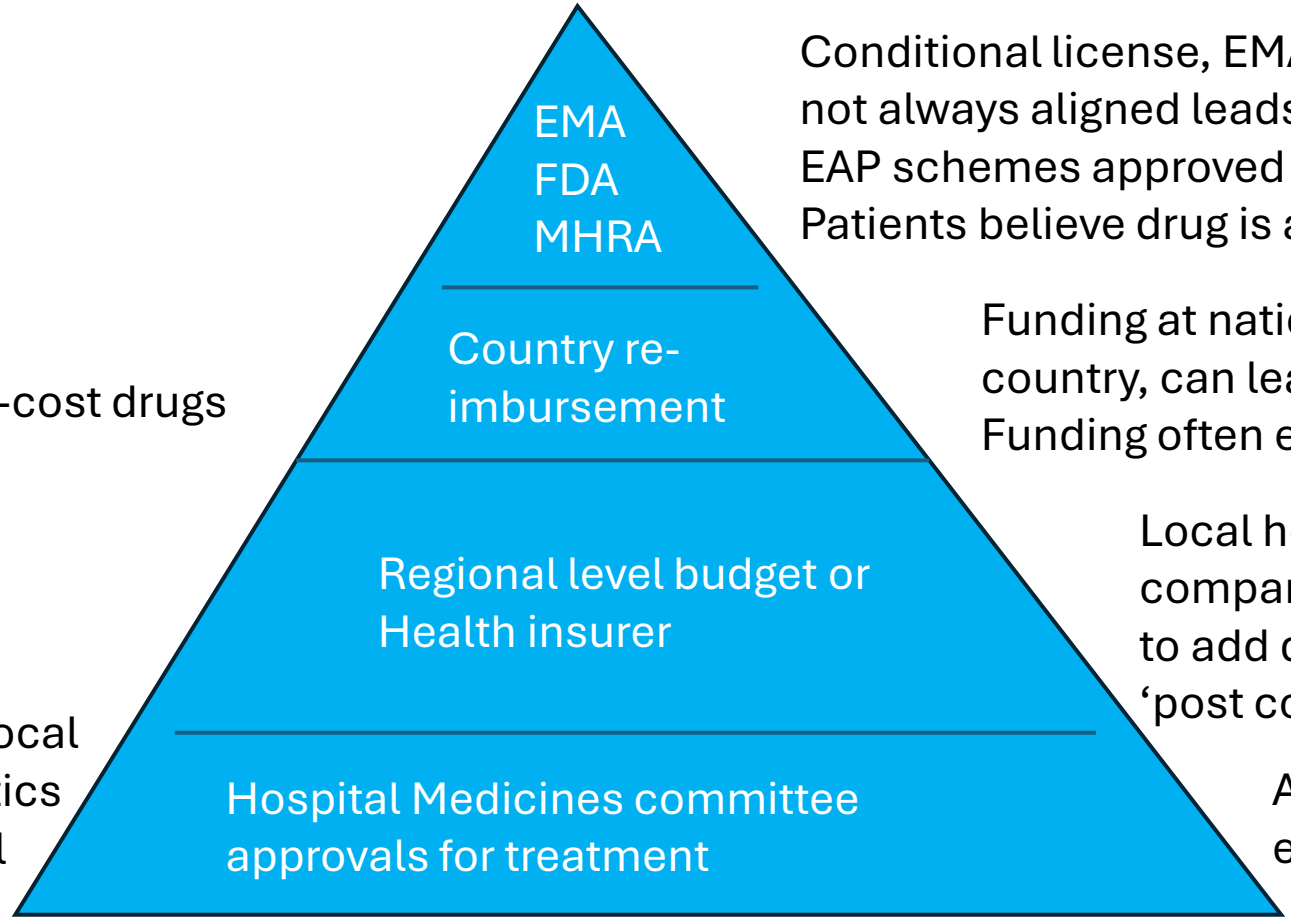
I have the following conflicts of interest to declare:

Principal investigator for trials funded by: PTCbio, Roche, Dynacure, Santhera, Reneo therapeutics, Edgewise

Honoraria for consultancy and lectures: PTCbio, Santhera, Sanofi Genzyme, Biogen, Sarepta

iDMC membership: TRiNDS, Roche

Bottlenecks to delivering treatments



Conditional license, EMA/MHRA and FDA approvals not always aligned leads to medical tourism
EAP schemes approved
Patients believe drug is available

Increased bureaucracy required to prescribe high-cost drugs

Funding at national level depends on country, can lead to medical tourism.
Funding often excludes non-ambulant DMD

Local health board or insurance company may decide not to add drug to local formulary
'post code lottery'

Huge workload to apply to local hospital drug and therapeutics committee for EAP approval

Approval for EAPs often rejected especially for non ambulant and adult DMD

Hospitals will implement high-cost drug prescribing if funded

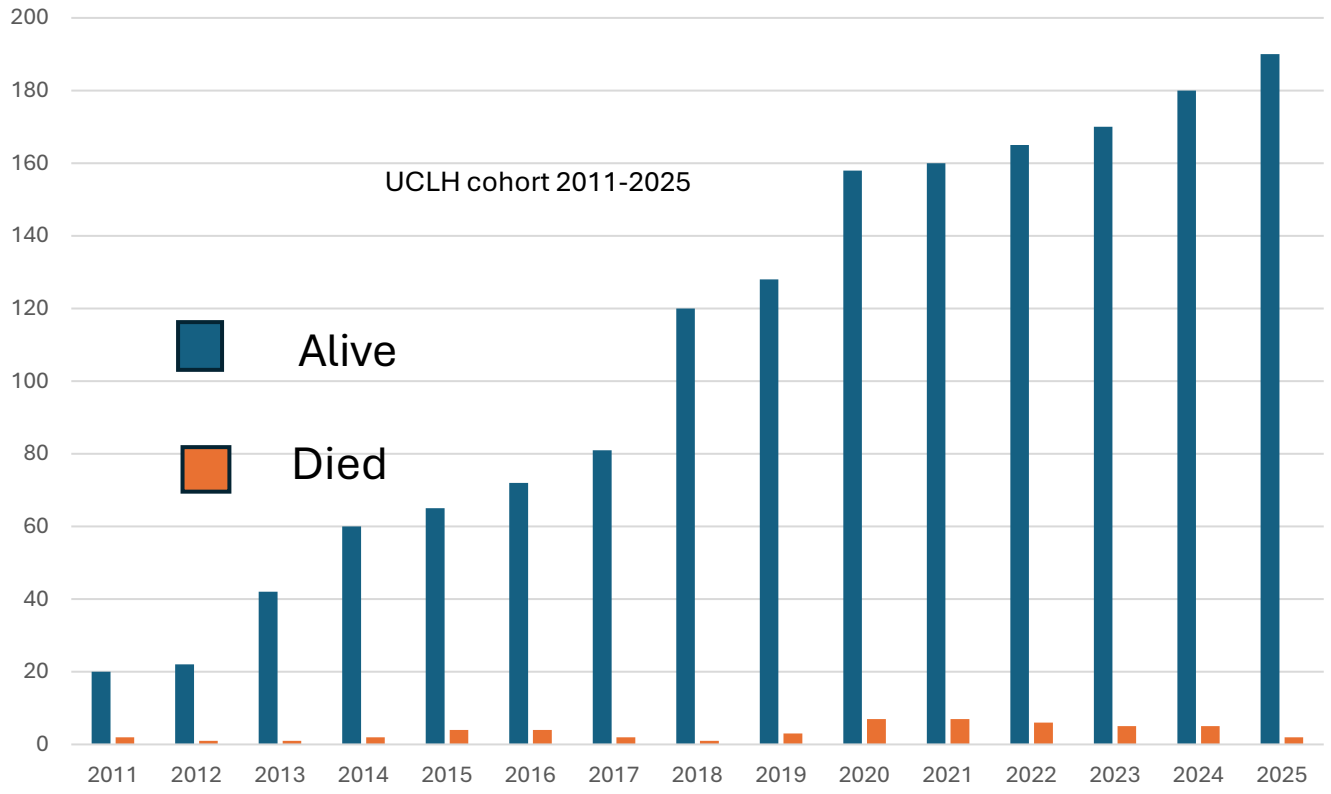
Accessing new therapies is challenging for patients with DMD (especially non-ambulant and adults) and frustrating for HCPs

- Lack of access to therapies based on
  - High cost
  - Relatively small short-term benefit i.e. based on clinical trials
  - Lack of trial data and relevant endpoints for non ambulant and adult cohorts. Clinical trials are performed on ambulant children

- Funders often assume that non-ambulant=no benefit
  - Lack of evidence is incorrectly interpreted as ‘no evidence’
  - Wheelchair use equates to ‘end-stage disease’ - an incorrect assumption
  - Disease modifying treatment may delay loss of valuable muscle function (upper limb, trunk, respiratory, cardiac and bowel)

UK Adult North Star Network and Registry

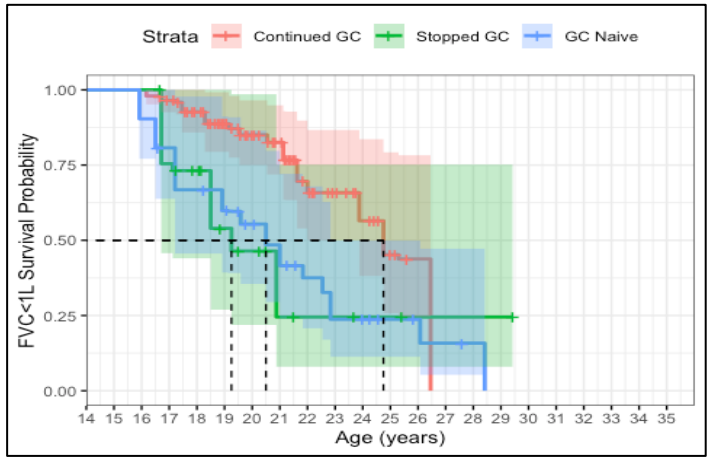
- Adult DMD cohort growing
  - UK cohort expanding by 5% per year Improved survival
    - Patients will spend longer in a wheelchair than walking
- ANSN Network established to improve care
- Data collection since 2018
  - 400/800 patients registered
  - main challenges
    - Lack of funding/ commissioning
    - Poorly organized fragmented services
    - Disease complexity increasing



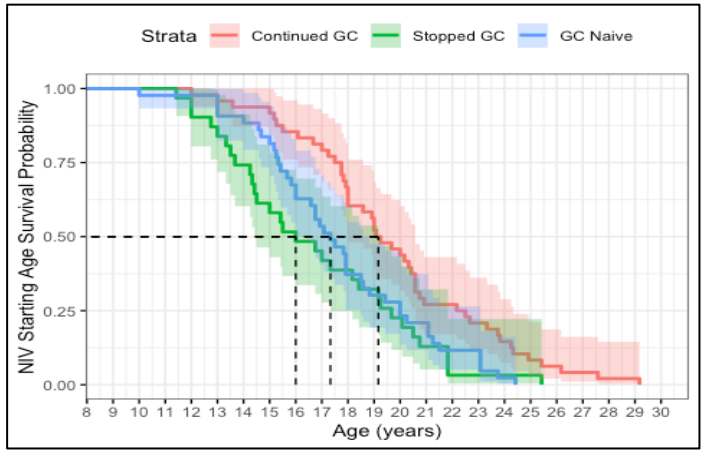
Multi-centre cohort retrospective review study of corticosteroid use in DMD (16-41 years)

- 208 DMD adults
  - corticosteroid-continued
  - corticosteroid-stopped
  - corticosteroid-naive
- Continued corticosteroid use preserved pulmonary function
  - 67% corticosteroid users not yet needing NIV
  - Delayed FVC<1l by over 5 years compared to those who stopped treatment

    24.75 years vs. 19.25 years
- Effect of stopping steroids
  - The fastest trajectory of respiratory decline occurred in steroid-stopped patients, matching or exceeding the functional decline of steroid-naive patients.



Interval from LOA of reaching FVC1litre



Interval from LOA to starting NIV

Pietrusz A et al *Muscle & Nerve*, 2026 Volume 74, Issue 2, pages 433–439

Summary

- DMD patients may live for many years, preserving function is essential for independence and quality of life
- Despite growing numbers of patients, new therapies are rarely made available to non ambulant patients due to a lack of clinical trial data
- Retrospective data shows how continuing corticosteroids can maintain essential muscle function into adult life, thus, disease modifying treatments can have a positive effect into adulthood
- Natural history registries are vital to provide real world data but need funding
- Services for adults need to improve