Impact of newborn screening for Duchenne muscular dystrophy: A model-based analysis

Authors

Hadley Stevens Smith (1,2*), Madison R. Hickingbotham (1), Sarah Stein (1), Ellen Kim DeLuca (1), Davene R. Wright (1,2), Marcus W. Henry (1), Caitlyn Limanto (1), Partha Ghosh (3), Niki Armstrong (4), Rachel Schrader (4), Jennifer M. Yeh (5), Ann Chen Wu (1), Kurt D. Christensen (1)

Affiliations

1. PRecisiOn Medicine Translational Research (PROMoTeR) Center, Department of Population Medicine, Harvard Pilgrim Health Care Institute, Boston, MA
2. Harvard Medical School, Boston, MA
3. Department of Neurology, Boston Children's Hospital, Boston, MA
4. Parent Project Muscular Dystrophy, Washington, DC
5. Division of General Pediatrics, Department of Pediatrics, Boston Children's Hospital, Boston, MA; Department of Pediatrics, Harvard Medical School, Boston, MA

*hadley_smith@hphci.harvard.edu

PRecisiOn Medicine Translational Research Center

Harvard Pilgrim Health Care Institute

PreEMPT Precision Medicine Policy and Treatment Model

Introduction

- Advances in treatments for Duchenne muscular dystrophy (DMD), an X-linked pediatric onset neuromuscular disorder, have increased interest in early disease detection via newborn screening.
- Patients with DMD are typically symptomatic before age 6 years, yet diagnostic delay is common.
- Untreated children usually enter non-ambulatory disease stages by age 12.
- Genomic newborn screening (gNBS) may reduce diagnostic delays and allow earlier treatment and therapy initiation, improving patient outcomes.
- The objective of this study was to understand the impact of gNBS compared with usual clinical care for DMD on treatment and clinical outcomes.

Methods

- We developed a microsimulation model to evaluate lifetime health and economic outcomes from a healthcare sector perspective of detecting DMD through:
  - Newborn screening using biochemical testing (creatine kinase, CK-MM);
  - Newborn screening using genomic sequencing (*DMD* gene);
  - Usual clinical care
- Our model incorporates clinical, patient-centered, and cost data from published literature and The Duchenne Registry, the largest and most comprehensive registry for DMD, maintained by Parent Project Muscular Dystrophy.
- We adapted a five-state partitioned survival model of disease progression (early ambulatory, late ambulatory, early non-ambulatory, late non-ambulatory, dead).
- Under CK testing and gNBS, we assumed steroid treatment would start at age 2 years, prolonging time in the early ambulatory stage by 12 months.
  - 75% of patients receive steroid treatment, reflecting real-world uptake.
- We conducted scenario analyses for two types of novel therapeutics, antisense oligonucleotides (ASOs) and gene therapy.
- We report the mean and uncertainty interval (UI) of 25 simulations.

Results

- Among a US birth cohort of 1.85 million male newborns, screening via CK testing is estimated to increase the number of patients in ambulatory disease stages at age 12 years by 8.6% (n=253) and increase the number of patients who live past age 20 years by 7.0% (n=268) compared to usual care.
  - gNBS would increase the number of patients who are ambulatory at age 12 by an additional 1.6% and who live past age 20 by an additional 1.3%.
  - Median time in early ambulatory, late ambulatory, early non-ambulatory, and late non-ambulatory disease stages under each disease detection strategy is shown in Figure 1.
- Assuming a 29-month benefit, ASO treatment after CK screening would increase the number of patients who are ambulatory at age 12 by an estimated 13.7% and who are alive at age 20 by 9.3%.
- Assuming a 12-month benefit, gene therapy after CK screening would increase the number of patients who are ambulatory at age 12 by an estimated 17.2% and who are alive at age 20 by 10.6%.
- Newborn screening via CK testing as compared to usual care would cost an estimated $436,043 per life year gained; newborn screening via gNBS as compared to CK testing would cost an estimated $760,252 per quality-adjusted life year gained (Figure 2).

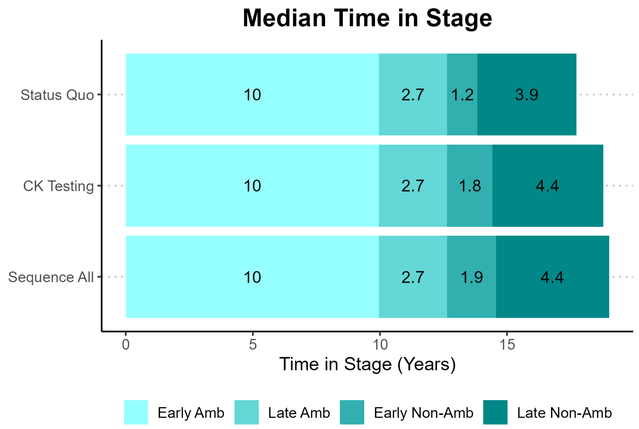

Figure 1. Median time in disease stage by disease detection strategy

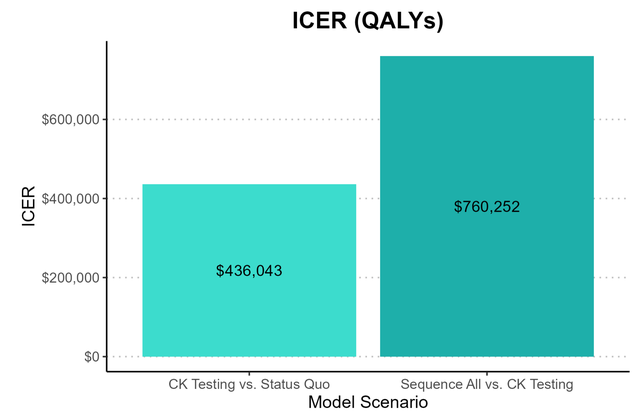

Figure 2. Incremental cost effectiveness ratios (ICERs) for newborn screening approaches

Conclusion

- Newborn screening for DMD may shorten diagnostic delay and facilitate timely treatment, thereby delaying disease progression.
- It may also allow initiation of behavioral, speech, and occupational therapies at an earlier age, which is important to families.

Acknowledgements This research is supported by a grant from the National Institute of Child Health and Human Development (R01-HD090019)