Parent Project Muscular Dystrophy

JOIN THE FIGHT. END DUCHENNE.

FAST FACTS ABOUT NEWBORN SCREENING FOR DUCHENNE MUSCULAR DYSTROPHY

WHAT IS DUCHENNE?

Duchenne muscular dystrophy is the most common pediatric muscular dystrophy. It causes progressive muscle loss, cardiorespiratory failure, and ultimately premature death. Duchenne is X-linked and affects about one out of every 5,000 males at birth worldwide.

Duchenne is caused by a variant in the dystrophin gene, resulting in absent or nonfunctional dystrophin protein. Without functional dystrophin protein, muscles become damaged and are unable to repair themselves properly. This genetic disorder can be passed from parent to child, or it can result from a random spontaneous genetic mutation. In fact, most cases occur in families with no previous history of Duchenne

Duchenne progresses differently for every person, but it ultimately results in loss of muscle function. Natural history data based on treatment initiated at the typical age of diagnosis shows that the average age of loss of ambulation is 12 years. Duchenne is universally life-limiting, with an average life expectancy of mid-20s to 30s.

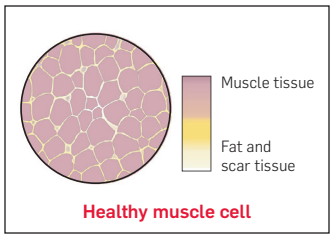
“Despite massive advances in therapy, the average age of diagnosis for Duchenne has not changed in 30 years. If we are to have any hope of getting current treatment... and curing children born with this disease in the future, we need universal newborn screening. There is simply no other way.”
- Mother of two children with Duchenne

WHY SCREEN FOR DUCHENNE AT BIRTH?

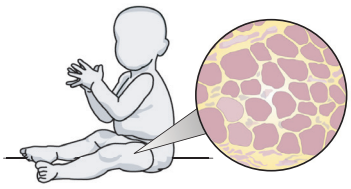
Approximately 360 babies with Duchenne are born each year in the United States. Without newborn screening (NBS), the typical family will notice symptoms of Duchenne in their child by age 2, yet most of those families will not receive a diagnosis until age 5.[1] This delay is even longer in families of color and low socioeconomic status.[2][3] Evidence of muscle damage is present in infancy. By age 5, children with Duchenne have significant and irreversible muscle damage.

There are now eight FDA-approved treatments for Duchenne, four of which are approved for use in infancy. NBS can eliminate the delay in diagnosis and provide families the opportunity for treatment years earlier, when children have more functional muscle tissue remaining.

Muscle degeneration begins well before the average age of diagnosis

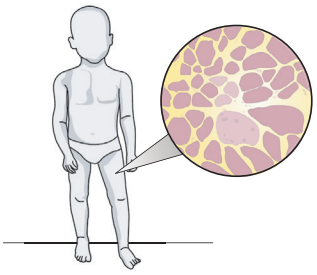


Healthy muscle cell



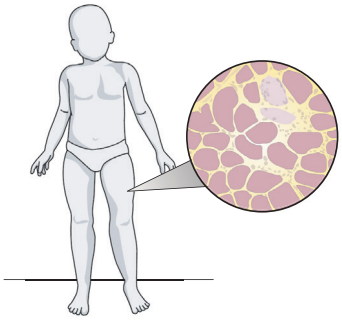
At 1 year, muscle degeneration is already evident.

Typical Duchenne muscle degeneration, as seen in muscle biopsy of 1-year-old Duchenne patient



At 3 years, the average age when parents begin noticing symptoms, muscle degeneration is more pronounced.

Typical Duchenne muscle degeneration, as seen in muscle biopsy of 3-year-old Duchenne patient



By age 5, the average age of Duchenne diagnosis, muscle degeneration is significant.

Typical Duchenne muscle degeneration, as seen in muscle biopsy of 5-year-old Duchenne patient

Illustrations based on characterization of DMD muscle phenotype. a Hematoxylin & Eosin (H&E) staining of Control (Ctr) and DMD muscles at different time points as published Cardone N, et al. Acta Neuropathologica Communications. (2023)11:167.

HOW IS NBS FOR DUCHENNE PERFORMED?

The first-tier screen for Duchenne evaluates CK-MM, the muscle isoform of creatine kinase. CK-MM is a biomarker of muscle damage and is highly elevated in newborns and children with Duchenne. In the event of elevated CK-MM, confirmatory testing—DNA sequencing of the dystrophin gene, *DMD*—is required. The presence of a pathogenic variant in *DMD* confirms the diagnosis. Both the screening and confirmatory test can be performed on the standard NBS dried blood spots, with no additional blood draw required.

IS THERE AN FDA-AUTHORIZED NBS TEST FOR DUCHENNE?

Yes. The FDA authorized the first Duchenne NBS test, manufactured by Revvity, in 2019.[4]

CAN DUCHENNE NBS BE EASILY INTEGRATED INTO EXISTING NBS?

Yes. Duchenne NBS based on CK-MM uses the same dried blood spots currently collected and the Genetic Screening Processor technology already available in most NBS laboratories.

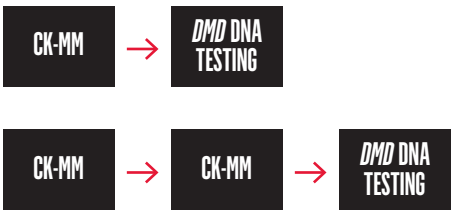
HOW ACCURATE IS DUCHENNE NBS?

Accuracy and the false positive rate will depend on the screening algorithm and cut-offs chosen. When confirmatory DNA testing is included in the algorithm, the false positive rate is essentially zero.

IS A SECOND-TIER OR CONFIRMATORY TEST REQUIRED FOR DUCHENNE NBS?

CK-MM cannot diagnose Duchenne, so second-tier or confirmatory testing is required. There are multiple potential algorithms for Duchenne NBS. A preferred algorithm in states with genetic testing capabilities or who are currently using a genetic testing laboratory for NBS for other conditions would include a confirmatory test, specifically DNA analysis of the *DMD* gene. Confirmatory testing for Duchenne could be performed on the dried blood spot.

Possible Duchenne NBS Algorithms



WHY NOT JUST SCREEN BOYS FOR DUCHENNE INSTEAD OF EVERY BABY?

NBS programs do not account for determination of sex, as it would add another step to the testing procedure and increase overall costs. Sex determination is a complex screening process and could increase false test results. In fact, of all the NBS programs across the world, not a single one includes DNA-based sex-specific screening.

Male-only testing also risks missing positive female carriers. A subset of female carriers will have Duchenne-like symptoms. By one estimate, one in every 4088 girls is a carrier of a pathogenic *DMD* variant who could be helped by early diagnosis.[5] NBS may be able to identify these girls who will benefit from intervention and may be eligible for therapies. All female carriers are at risk for cardiomyopathy, and cardiac screening is recommended for all adult female carriers.

WHAT IS THE COST TO INCLUDE DUCHENNE ON THE NBS PANEL?

The cost will depend upon the algorithm and cut-offs chosen. Each state will determine how to approach NBS for Duchenne and whether it will include genetic testing in its process. When confirmatory genetic testing is performed for the small fraction of screen-positive babies, it is estimated that it would cost approximately $8 per-infant-tested to screen for Duchenne with labor and referral costs [6].

IS DUCHENNE ON THE FEDERAL RECOMMEND UNIFORM SCREENING PANEL (RUSP)?

Duchenne is currently under consideration to be added to the RUSP. In August 2023, the federal Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) voted unanimously to move Duchenne forward to evidence review in the process of RUSP review. However, the ACHDNC is not expected to make a recommendation to the Secretary of Health and Human Services on whether to include Duchenne until mid-2024, at the earliest. With a positive recommendation, the Secretary then has six more months to decide whether to add Duchenne to the RUSP.

WHICH STATES SCREEN FOR DUCHENNE?

Since 2023, three states – Ohio, New York, and Minnesota – have approved newborn screening for Duchenne. Furthermore, several other states, such as Massachusetts, are actively reviewing the inclusion of Duchenne on their NBS panels through NBS advisory committees.

WHY DO STATES NEED TO ADD DUCHENNE TO NBS NOW?

While the federal RUSP is an important tool to help create equality among state NBS programs, it remains only a recommendation regarding what conditions states should include for NBS. What's more, with new treatments for many debilitating and fatal pediatric diseases becoming available, the RUSP has not been able to keep pace with science and innovation. While the best-case-scenario timeframe for a condition to be added to the RUSP is 18 months, on average it has taken 4 years for approved conditions to be added to the RUSP. In the 16 years since the RUSP was established, 16 conditions have been nominated for the RUSP, but only 8 have been approved.[7] It typically takes several more years before states add the new conditions and screening begins—time children and families do not have.

WHAT IS THE IMPACT OF A DELAYED DUCHENNE DIAGNOSIS?

The average delay between a family identifying symptoms and a Duchenne diagnosis is 2.5 years. This diagnostic odyssey results in significant economic and emotional impacts for the family which continue long-term, as delays in diagnosis result in higher annualized medical costs on a per patient basis.[8]

DELAYED DIAGNOSIS DRAMATICALLY INCREASES COSTS FOR FAMILIES [8]:

- $211,229 total medical cost and productivity loss per family
- 20 lost days of work for caregivers per year
- 17 out-of-state trips for medical care

WHAT ARE THE BENEFITS OF DIAGNOSIS THROUGH NBS?

An expert group of Duchenne clinicians developed and published clinical guidelines for care following a newborn screening diagnosis.[9] After NBS, families consult with pediatric neuromuscular care teams to discuss the most appropriate treatment course for each child. They have the potential to initiate therapies such as exon-skipping, gene therapy, and steroids years earlier than they would if diagnosed through traditional pathways. They may be able to enroll in clinical trials.

Establishing care in infancy also enables referrals to early intervention services such as speech, behavioral, physical, and occupational therapy. NBS diagnosis has benefits for the family, including identifying at-risk family members, like carrier mothers who are at risk for cardiomyopathy and siblings who may be carriers or affected. Many families also report using this information in future family planning.

WHAT TREATMENTS ARE AVAILABLE FOR DUCHENNE?

There are currently eight FDA-approved therapies for Duchenne muscular dystrophy, with more than 40 additional potential therapies in development. The approved therapies slow progression and enable children with Duchenne to have more years of walking, using their hands, breathing well, and spending time with their families.

DUCHENNE TREATMENT	% ELIGIBLE FOR TREATMENT	ESTABLISHED BENEFITS OF TREATMENT
EXON SKIPPING THERAPIES		
Casimersen: all ages Eteplirsen: all ages Golodirsen: all ages Viltolarsen: all ages	30%	Prolonged ambulation, slower decline in lung function, increased lifespan [10,11,12]
CORTICOSTEROIDS		
Deflazacort: age 2 and up Vamorolone: age 2 and up Prednisone: all ages	100%	Prolonged ambulation and upper limb use, slower decline in lung function, decreased scoliosis, increased lifespan [13,14]
GENE THERAPY		
ELEVIDYS: age 4 and up	94%	Gains or stabilization on functional testing [15]
SMALL MOLECULE INHIBITOR		
Duvyzat: age 6 and up	100%	Activates muscle repair mechanisms to increase muscle fiber regeneration, reduce inflammation, and reduce fibrosis

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QUESTIONS?

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