THE DIAGNOSIS AND MANAGEMENT OF
DUCHENNE MUSCULAR DYSTROPHY

A GUIDE FOR FAMILIES

UW Health

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DISCLAIMER

The information and advice published or made available in this booklet is not intended to replace the services of a medical provider (physician, nurse, nurse practitioner, etc.), nor does it constitute a doctor-patient relationship. This advice should be taken in conjunction with medical advice, which you should consult in all matters relating to your health, in particular with respect to symptoms that may require diagnosis or medical attention. Any action on your part in response to the information provided in this booklet is at your own discretion. Although every effort has been taken to ensure the accuracy and completeness of the information contained in this booklet, accuracy cannot be guaranteed, and care in each situation must be individualized.

INTRODUCTION

Duchenne muscular dystrophy (DMD or Duchenne) is a difficult, complex diagnosis to understand and manage. This is not a world that anyone enters willingly. The Muscular Dystrophy Association (MDA), Parent Project Muscular Dystrophy (PPMD), TREAT-NMD and the World Duchenne Organization (UPPMD) all understand the heartache and angst that parents feel with this diagnosis, and the support that is needed thereafter. As you journey through this diagnosis, it is important to all of us that you or your child receive the very best in care, support, and resources. For this reason, we have worked together to develop this 2018 Duchenne Family Guide.

Duchenne is one of a spectrum of muscle diseases known as "dystrophinopathies." Dystrophinopathies result from the absence of the muscle protein "dystrophin" and range from the more severe phenotype (symptoms that you see) Duchenne muscular dystrophy to the milder yet variable phenotype of Becker muscular dystrophy. For simplicity, we primarily refer to Duchenne throughout this Family Guide.

"This is a guide to the 'medical' aspects of Duchenne, but always bear in mind that the medical side isn't everything. The idea is that by minimizing medical problems, your child can get on with his life and you can get on with being a family. It's good to remember that most Duchenne children are happy kids and most families do very well after the initial shock of the diagnosis."

Elizabeth Vroom, World Duchenne Organization (UPPMD)

We have written this Family Guide to be directed toward the parent in the Diagnosis and Early Ambulatory Phase, and to the person living with Duchenne. For the purposes of this document, "you" refers to the person living with Duchenne.

BACKGROUND OF THE DUCHENNE "CARE CONSIDERATIONS"

The US Centers for Disease Control and Prevention (CDC) guidelines for Duchenne care are affectionately known in the community as the "care considerations." Both the original and updated care considerations are based on an extensive study by international experts in Duchenne diagnosis and care, chosen to represent a broad range of specialties. They independently "rated" methods of care used in the management of Duchenne to say how **"necessary," "appropriate,"** or **"inappropriate"** each one was at different stages of the course of Duchenne. In total they considered more than 70,000 different scenarios. This allowed them to establish guidelines that the majority agreed represented the **"best practice"** for Duchenne care. The updated guidelines were developed using the same process.

The 2018 Duchenne Family Guide summarizes the results of the updates for the medical care of Duchenne muscular dystrophy. Both the original effort, as well as the updated guidelines, were supported by the CDC in collaboration with patient-advocacy groups and the TREAT-NMD network. The documents are published in Lancet Neurology and are

INTRODUCTION *(continued)*

available on the websites of PPMD, MDA, UPPMD, TREAT-NMD and the CDC. Additionally, thanks to TREAT-NMD and the UPPMD, multiple translations are available through TREAT-NMD.

In addition, each subspecialty area developed a separate article, for a deeper dive into a specific area of care. These articles will be published in a Pediatric Supplement volume of the journal *Pediatrics*, the official journal of the American Academy of Pediatrics, in 2018 and will be available through the websites listed below.

REFERENCES FOR THE MAIN DOCUMENT:
ADVOCACY WEBSITES

www.mda.org

www.parentprojectmd.org

www.treat-nmd.eu

https://worldduchenne.org/

PUBLISHED CARE GUIDELINES

- Diagnosis and management of Duchenne muscular dystrophy, an update, part 1: Diagnosis, neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management
- Diagnosis and management of Duchenne muscular dystrophy, an update, part 2: Respiratory, cardiac, bone health, and orthopedic management
- Diagnosis and management of Duchenne muscular dystrophy, an update, part 3: Primary care, emergency management, psychosocial care, and transitions of care across the lifespan

LANDING PAGES

- **CDC:** www.cdc.gov/ncbddd/musculardystrophy/care-considerations.html
- **Parent Project Muscular Dystrophy:** www.parentprojectmd.org/careguidelines
- **MDA:** www.mda.org
- **World Duchenne Organization:** www.worldduchenne.org
- **TREAT NMD:** http://www.treat-nmd.eu/resources/care-overview/dmd-care/diagnosis-management-dmd/

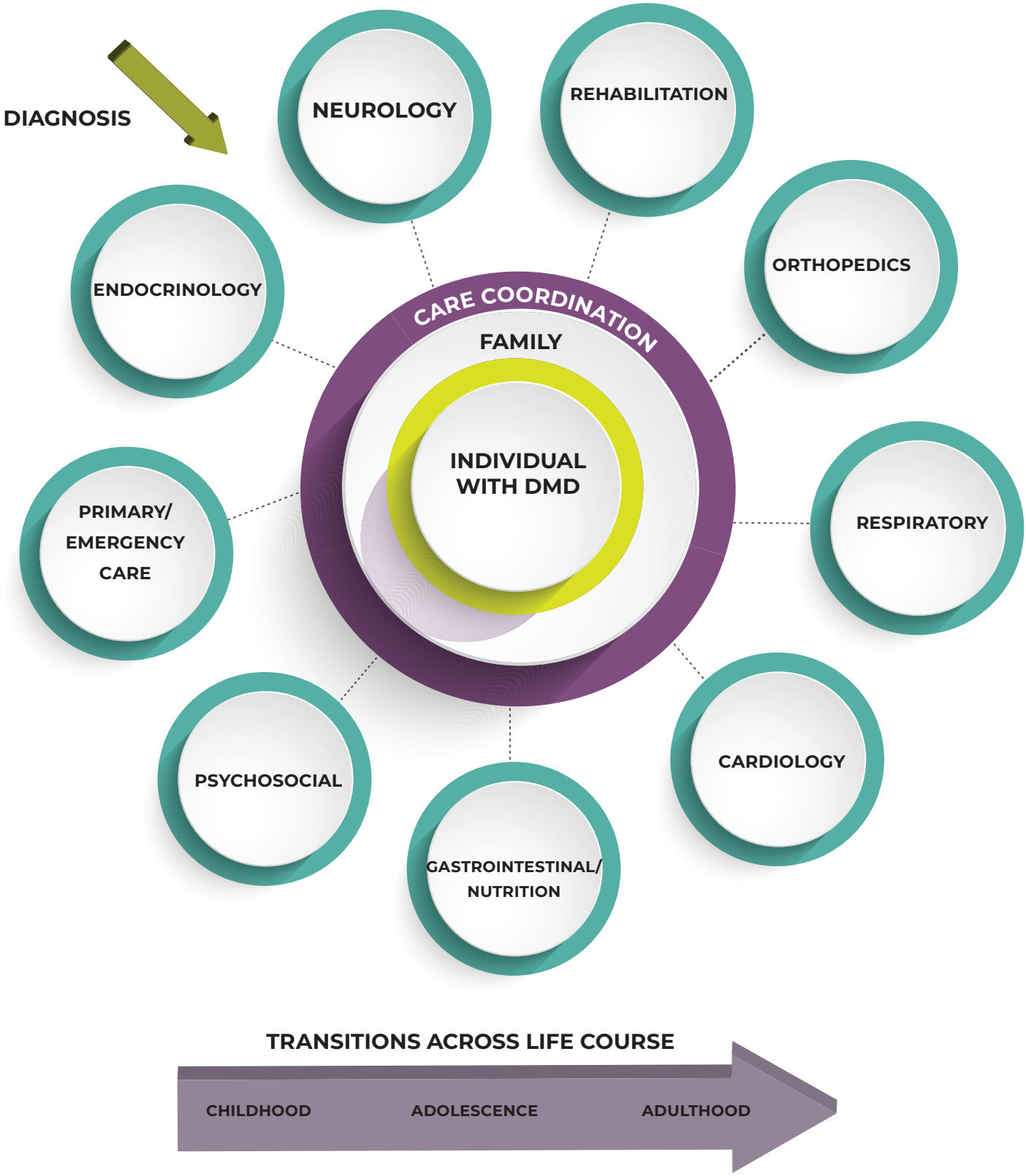

DIAGNOSIS
NEUROLOGY
REHABILITATION
ENDOCRINOLOGY
ORTHOPEDICS
CARE COORDINATION
FAMILY
INDIVIDUAL WITH DMD
PRIMARY/ EMERGENCY CARE
RESPIRATORY
PSYCHOSOCIAL
CARDIOLOGY
GASTROINTESTINAL/ NUTRITION
TRANSITIONS ACROSS LIFE COURSE
CHILDHOOD
ADOLESCENCE
ADULTHOOD

Figure 1

2. HOW TO USE THIS DOCUMENT

YOU CAN USE THIS GUIDE IN TWO DIFFERENT WAYS:

1. To concentrate on a specific stage of Duchenne
2. To concentrate on a specific area of Duchenne care

This next section, including Table 1, demonstrates the progression of Duchenne as a step-by-step process that varies from person to person. This guide is meant to be an overview of what care needs you might anticipate.

Additionally, if you want to read specific care-management sections that may be relevant to you now, you can find them easily within the table of contents.

PUTTING TOGETHER YOUR CARE TEAM

The best management of Duchenne requires a multidisciplinary approach, with the input of specialists in many different areas who will provide your comprehensive care. A neuromuscular specialist (NMS) will act as the lead clinician of your neuromuscular team, taking responsibility for your overall care across your lifetime. As you move from pediatric to adult care, this specialist may change from a pediatric NMS to an adult NMS but will remain the lead clinician for your team. A care coordinator is an important member of the team who will help to make sure that communication and care are coordinated between team members, between you and the team, and between the team and your local/primary care providers (pediatrician, family practice provider, etc.). If your neuromuscular team does not include a care coordinator, be sure to ask who you should call for questions/concerns/emergencies between appointments.

This Family Guide will provide you with basic information to allow you to participate effectively in the process of obtaining comprehensive care. Your NMS must be aware of all potential issues in Duchenne and must have access to the interventions that are the foundations for appropriate care and input from essential subspecialties. As you age, the emphasis of some interventions, as well as the inclusion of some subspecialists, will change. The Family Guide takes you through the different areas of Duchenne care (Figure 1). Not all of these subspecialists will be needed at all ages or stages, but it is important that they are accessible if necessary and that the person coordinating care has support in all these areas.

YOU are at the center of your care team – it is important that you and your family are **actively engaged with a medical professional** who will coordinate and individualize your clinical care (Figure 1).

TAKING DUCHENNE STEP-BY-STEP (TABLE 1)

Duchenne is a condition that changes very slowly over time. We have separated key stages of Duchenne to help you anticipate recommendations for care. Although these stages can be somewhat blurred in distinction, you may find it useful to use the stages to identify the kind of care and interventions that are recommended at any particular time and what you should expect of your care team at that time.

1. DIAGNOSIS (infancy/childhood)

Currently, most children with Duchenne remain undiagnosed during the presymptomatic stage (when children show few, if any, symptoms) unless there is a family history of the condition, or unless blood tests are done for other reasons. Symptoms such as delayed walking and crawling or speech are present, but are typically subtle and are often unrecognized at this stage.

Parents are often the first to notice differences in their child's development, the first to ask questions, and the ones requesting further testing to explain perceived developmental delays. The American Academy of Pediatrics has develped a tool to help parents evaluate their child's development, look for possible delays, and address these concerns with their primary care providers. This tool can be found at: **motordelay.aap.org.**

Psychosocial and emotional support is extremely important when a new diagnosis of Duchenne is confirmed. Receiving a diagnosis of Duchenne is tremendously difficult. There are so many unanswered questions, and families often feel alone and overwhelmed, with few places to turn. Primary care providers and neuromuscular specialists can be especially helpful during this time, facilitating connections to appropriate care and advocacy organizations that can help to provide the resources, information, and support parents need to help themselves and their families. In the US, PPMD has developed a special page with resources parents can use to help during the first 3 months of a new diagnosis (ParentProjectMD.org/for-newly-diagnosed). In addition, both PPMD and MDA have resources available for communicating with children, siblings, and extended family about a Duchenne diagnosis. Connecting with local advocacy groups will help you to know what resources are available.

2. EARLY AMBULATORY (childhood)

In the early **ambulatory** or **walking stage**, children will be showing what are typically regarded as the "classical" signs of Duchenne. These signs may be very subtle, and may include:

- Difficulty lifting the head or neck
- Not walking by 15 months
- Difficulty walking, running, or climbing stairs
- Tripping and falling frequently
- Difficulties with jumping and hopping
- Not speaking as well as other children the same age
- Needing help getting up from the floor or walking the hands up the legs in order to stand (see **Gowers' Maneuver,** Figure 2 below)

Figure 2. Gowers' Maneuver

- Calves that look bigger than normal (pseudohypertrophy)
- Walking with legs apart
- Walking on toes and waddling
- Walking with chest pointed out (or having a sway back, saddle back, or arched back)
- Elevated creatine kinase (called a “CK” or “CPK”; this is an enzyme released by the muscle when it is damaged. The level of CK is measured in the blood; if a CK is higher than 200, further testing for Duchenne is needed)
- Elevated liver enzymes (AST or ALT; an elevated AST or ALT can also be signs that further testing is needed for Duchenne. Further liver evaluations should never be done until testing for Duchenne is complete)

DIAGNOSING DUCHENNE:

When there is suspicion of Duchenne, the first test is often a bloodtest to see if serum CK is elevated. People with Duchenne often have a CK level 10 to 100 times the normal value. If this is found, specific tests will be recommended in order to identify the change in the DNA (called the “genetic mutation”) that causes Duchenne. Input from specialists, specifically genetic counselors, may be needed in order to interpret these genetic tests and to discuss how the results may impact your child and possibly other family members. Diagnosis is often made during the early ambulatory phase.

PSYCHOSOCIAL, LEARNING, AND BEHAVIOR:

People living with Duchenne have a higher chance of learning and behavioral challenges. Some challenges are due to the lack of dystrophin in the brain; others may be due to adjusting to physical limitations. Some medications such as steroids, which are often started in the early or late ambulatory stage (see below), can also play a role. Some children taking steroids may have difficulty with impulse control, anger, mood changes, attention, and memory, and others may not. If delays in development and/or learning are found, an evaluation by a psychologist or neuropsychologist may help to define the specific issues, as well as give recommendations to help reach full potential. Emotional and behavioral issues are not uncommon and are managed best if they are addressed early. Developmental pediatricians and psychologists may be very helpful in these areas. Speech and language should also be evaluated, and therapies started as soon as possible, if needed. If your family is having difficulty accessing resources, social workers can be very helpful in connecting you. Family support is essential, and input from specialists may be needed to address specific psychosocial, learning, and behavior issues (Section 14).

PHYSICAL THERAPY/PHYSIOTHERAPY:

An introduction to the physical therapy team (Section 10) at this early stage will allow for exercise/stretching regimes to be introduced gradually to keep muscles flexible and prevent or minimize tightness at the joints. The rehabilitation team can also advise on appropriate exercise during playtime/recess, as well as adaptive physical education, to keep your child safe while supporting school participation. A physical therapy exercise program should focus on stretching and maintaining range of motion rather than strengthening. Night splints (often called “ankle foot orthoses,” or “AFOs”) may be recommended at this stage to provide a prolonged stretch and prevent loss of ankle range of motion. A home stretching program recommended by your physical therapist should become part of your daily routine.

STEROIDS:

Corticosteroids, or “steroids,” should be discussed preferably at diagnosis and may be started at this stage (Section 6). In planning for the use of steroids, it is important to discuss the benefits of steroids, ensure all immunizations are complete, and discuss any risk factors for the side effects of steroids, as well as how they can be anticipated and minimized. This includes receiving nutrition education (preferably from a registered dietitian) to help avoid side effects such as weight gain and altered bone health.

BONE HEALTH AND HORMONES:

Taking steroids can lead to weak bones and may affect the levels of several hormones, such as growth hormone and testosterone (the male sex hormone) (Section 7). Nutrition is important for keeping bones strong, and diets containing Vitamin D and calcium should be encouraged (Section 8 & 13). It may be appropriate to discuss your nutritional needs with a registered dietitian at your neuromuscular visits. Heights and weights should be checked at every neuromuscular visit and should be plotted on a graph to monitor growth and weight over time (Section 7). Measuring the length of the bone in your forearm (“ulnar length”), or your lower leg (“tibial length”), or adding the lengths of your upper and lower arms together (“segmental arm length”) are alternate ways to record accurate “heights” and should be tracked as well for baseline measurements. A baseline bone-density level should be obtained, using dual energy X-ray absorption (or “DEXA”), when steroids are started (see Section 8).

HEART AND BREATHING MUSCLES:

Typically, issues with the heart and breathing muscles are not likely to be present at this stage, but surveillance should start at diagnosis to establish the baseline (what is “normal” for you) and then continue at regular follow-up visits. Starting pulmonary function testing at a young age will help you get used to the equipment and “practice” for subsequent visits. Cardiac monitoring (ECG and cardiac MRI or echocardiogram) is recommended at diagnosis and annually up to age 10, and then more frequently as necessary (Section 12). It is also important that you have pneumococcal (pneumonia) and yearly influenza vaccinations (flu shots) to avoid illness (Section 11).

3. LATE AMBULATORY (late childhood/adolescent/young adult)

In the late ambulatory stage, walking will become increasingly difficult, with greater struggle during motor activities, such as climbing stairs and getting up from the floor.

PSYCHOSOCIAL, LEARNING, AND BEHAVIOR:

Continued evaluation of learning delays or specific learning disabilities is important at this stage. Psychologists and neuropsychologists can help identify the interventions best suited to meet your educational needs. Continued support from professionals will be necessary to help with any learning and behavior issues, and specific interventions may be necessary to address coping strategies for dealing with the loss of physical strength and functions (Section 14). At this stage, you should start to set goals for the future so that you and your family can work with your school to organize the education and training needed to meet those goals. For some, a neuropsychology evaluation may be indicated to help identify possible cognitive impairments and provide strategies for home and classroom settings to help you function at your best.

Caregiving requires emotional and physical energy. Carving out time for oneself, as well as relationships with others, is extremely important. Developing support networks that include extended family and trusted community members can be very helpful in giving caregivers time to rest and recharge.

PHYSICAL THERAPY/PHYSIOTHERAPY:

Rehabilitation input will continue to focus on maintaining range of movement, strength, and function in order to maintain independence (Section 10). If joint tightness cannot be managed by physical therapy, assessment and input from orthopedic specialists may be necessary. A physical therapist has many roles in the care team, including overseeing stretching regimens, recommending equipment such as wheelchairs and standers, and promoting continued weight bearing and standing (this will help with both bone health and digestion). It is important to make sure that mobility aids, such as wheelchairs, are equipped with supportive seating to promote body alignment, proper positioning, and comfort. A daily home stretching program is of continued importance.

STEROIDS:

Ongoing management of steroid treatment is important at this stage, with attention to the specific regimen and dose used (Section 6), as well as attention to side-effect prevention, surveillance, and management. Twice-yearly assessments to monitor skeletal muscle strength and function are important. Continued attention to weight control needs to take into account any tendency to be under- or overweight with appropriate intervention if there is a concern (Section 13).

BONE HEALTH AND HORMONES:

Ongoing surveillance of bone health and risk for fractures is important while on steroids, especially as mobility decreases. It is important for your NMS to monitor the risk for fractures through blood tests that check vitamin D levels (“25 OH vitamin D”), as well as imaging tests such as a DEXA scan or spinal X-rays that can assess bone density/health (Section 8). Diet should be assessed at each visit to ensure that you are eating adequate amounts of vitamin D and calcium. Height, lengths, and weight should continue to be monitored for signs of growth delays (Section 7).

HEART AND BREATHING MUSCLES:

Ongoing assessments of the heart and breathing muscles are necessary. ECG, cardiac MRI or echocardiogram, and other types of tests should be done at least annually from diagnosis and more frequently as needed after age 10. The cardiologist will recommend interventions if there are any changes observed on the ECG, cardiac MRI, or echocardiogram (Section 12).

4. EARLY NON-AMBULATORY (childhood/adolescent/young adult)

In the **early non-ambulatory** phase, you may begin getting tired after walking long distances. When this happens, a scooter, larger stroller (if appropriate), or wheelchair may be helpful for assistance with mobility (Section 10).

PSYCHOSOCIAL, LEARNING, AND BEHAVIOR:

Conversations about "transitioning" from an adolescent to an adult should begin at least by age 13 or 14. While your pediatric and adult medical teams, social worker, school professionals, and others will help you plan for a smooth transition, one or two individuals on your neuromuscular team should help guide the development of your personal transition plan. Conversations about your future goals should include education goals, as well as where you would like to live, study, work, and receive medical care. As you become an adult, it is important to maintain independence so you can continue to enjoy activities at home, at school, and with your friends. It is important for you to stay connected to friends – forming and maintaining relationships at this stage is very important. While some people living with Duchenne have no psychosocial issues, some do. Screening for anxiety and depression should happen at each neuromuscular visit. If anxiety or depression is identified, it should be treated early and appropriately.

PHYSICAL THERAPY:

In addition to the current home stretching program, attention to tightness in your upper limbs (shoulders, elbows, wrist, and fingers) becomes very important, as does the need for (supported, if needed) standing. Spinal curvature (scoliosis) is seen much less often with the use of steroids, but monitoring for this is still very important following the loss of ambulation. In some cases, scoliosis may progress quite rapidly, often over a period of months (Section 9). Orthopedic input may also be needed to deal with issues of foot positioning, which can cause pain or discomfort and limit the choice of footwear. Surgical options to assist with ankle and foot joint tightness, if appropriate, may be discussed.

STEROIDS:

Maintenance of steroid treatment continues to be an important part of management in this phase (Section 6) whether started previously, continued into this phase, or started at this stage.

BONE HEALTH AND HORMONES:

Close surveillance of bone health should continue, with special attention on signs for spinal compression fractures (Section 8). Ongoing observation of height, lengths, and weight is important to monitor growth. Alternate height measurements from the forearm ("ulnar length"), lower leg ("tibial length"), and the lengths of your upper and lower arms together ("segmental arm length") will be tracked when standing becomes difficult. Starting around age 9, it is important to monitor puberty. If puberty has not started by age 14, you should be referred to an endocrinologist. If your testosterone level is low, testosterone therapy may be needed (Section 7).

HEART AND BREATHING MUSCLES:

Monitoring of cardiac function at least anually is still essential and any changes in function, or evidence of fibrosis (scarring) in the cardiac muscle (seen only by cardiac MRI), should be treated promptly (Section 12). Respiratory function should be monitored every 6 months through pulmonary function testing. If respiratory function begins to decline, interventions to help with breathing and to aid with coughing should be discussed and introduced when appropriate (Section 11).

PALLIATIVE CARE:

The palliative care team includes medical providers who are focused on helping you achieve your highest quality of life, providing relief from pain and discomfort, and helping ensure that your life goals match your treatment choices. While palliative care is sometimes confused with “end-of-life” care, the palliative care team will help you to meet challenges at every stage of your diagnosis and be a supportive resource for you and your family with many types of transitions across your lifespan.

All people, with or without Duchenne, need to make decisions around emergency care – what they would like done to their body in an emergency, what they might not want done, who will be their medical power of attorney to make medical decisions if they cannot. The palliative care team is especially helpful in making your emergency care plan and deciding what it should include and where it should be kept.

5. LATE NON-AMBULATORY (Young adult/adult)

In the late **non-ambulatory** phase, core strength and upper limb strength may weaken, making function and maintenance of good posture increasingly difficult.

PHYSICAL THERAPY:

It is important to discuss with your physical therapist what types of stretching, exercises, and equipment can best support your desired level of independence and function. An occupational therapist on your rehabilitation team can help with activities such as eating, drinking, using the bathroom, and transferring to and turning in bed, if needed. Assistive technology evaluations can also be conducted to assess opportunities for extending independence and safety.

STEROIDS:

You should continue to discuss steroid regimens, nutrition, puberty, and weight management with your neuromuscular care team. Current recommendations encourage the lifelong continuation of steroids (Section 6) to preserve respiratory and upper limb strength and function.

BONE HEALTH AND HORMONES:

Close surveillance of bone health should continue throughout your lifespan. Bone problems may lead to issues with pain and should be addressed with your neuromuscular care team (Section 8).

HEART AND BREATHING MUSCLES:

Monitoring of heart and lung function at least every 6 months is recommended, and often more intensive investigations and interventions may need to be implemented (section 11 & 12).

PALLIATIVE CARE:

The palliative care team continues to be important at this stage. As mentioned above, this team includes medical providers who are focused on helping you achieve your highest quality of life, providing relief from pain and discomfort, and helping ensure that

your life goals match your treatment choices. While palliative care is sometimes confused with “end-of-life” care, the palliative care team will help you meet challenges at every stage of your diagnosis, and be able to help you and your family with many types of transitions across your lifespan. All people, with or without Duchenne, need to make decisions around emergency care – what they would like done to their body in an emergency, what they might not want done, who will be their medical power of attorney to make medical decisions if they cannot.

LIVING AS AN ADULT WITH DUCHENNE:

A full and productive life as an independent adult living with Duchenne requires planning. Developing a plan to transition from adolescence to adulthood should begin at least by age 13 or 14. Your personal transition plan should be based on the expectations and goals that you have visualized for your future. Your transition plan should include considerations for education, employment, housing, transportation, and mobility within the community, and transferring medical care from pediatric to adult providers (this may not be needed if your medical providers are able to continue to care for adults living with Duchenne). Regardless of whether your medical care/providers change, your resources and benefits will be impacted as you move from childhood to adulthood. Planning for these changes should include you, your family, your school, and your health care teams. This process, and all that it entails, is discussed in Section 17. Living as an adult with Duchenne is more expensive than living as an adult without Duchenne. You will require resources to support the assistance needed to reach your personal goals. Your neuromuscular team will help you to explore available resources and your eligibility to receive them, and the team will help you to navigate state and federal systems of support. It is also important to continue to find creative ways to stay connected with friends at this stage, especially as your life starts to change. While many people do not experience psychosocial problems, some adults with Duchenne may experience anxiety or depression that benefit from treatment. Screening for anxiety and depression should happen at each neuromuscular visit. If you have issues with anxiety or depression, they should be treated early and appropriately.

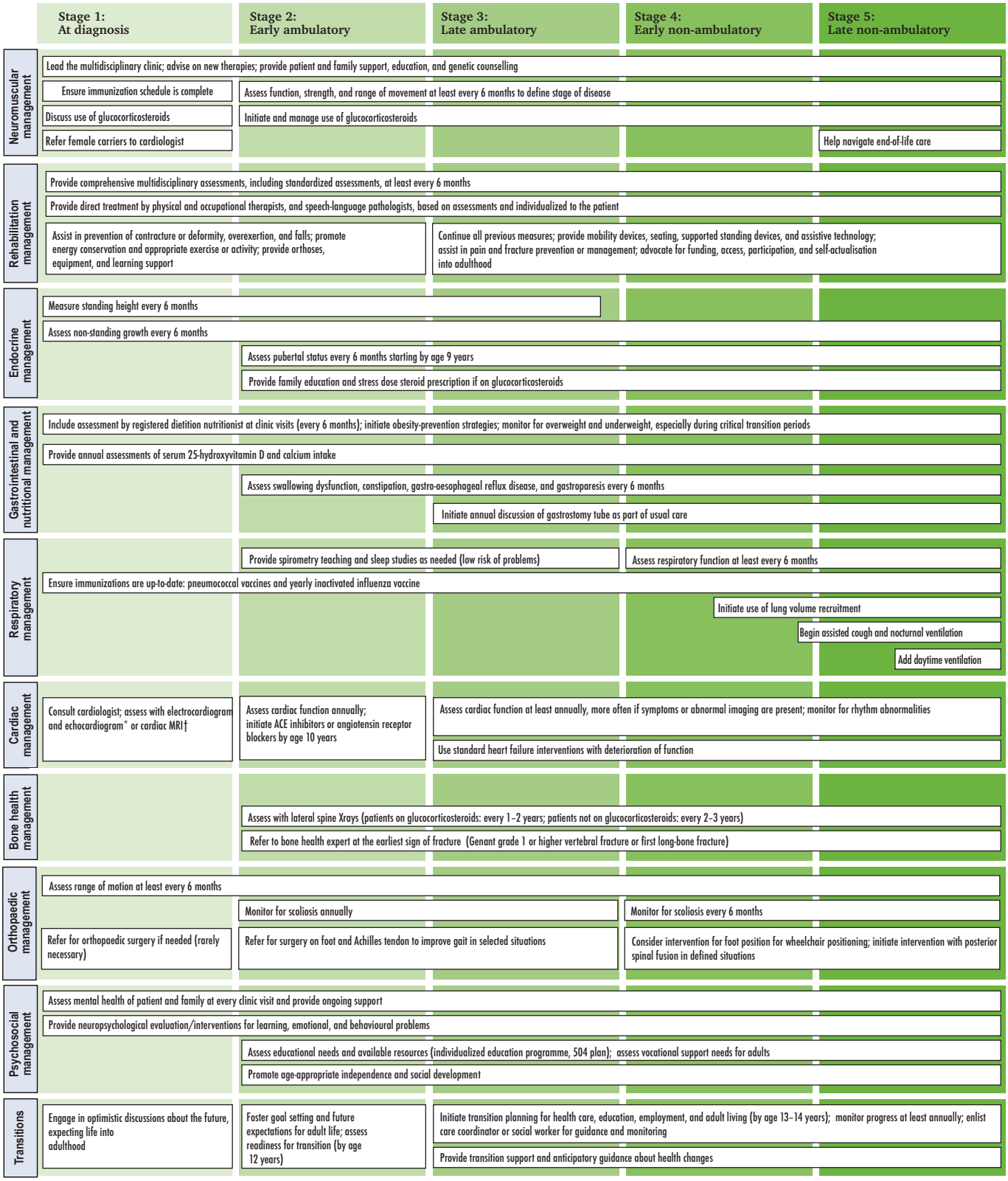


Table 1[1]: Subspecialty management encouraged across each stage of Duchenne

3. CARE AT DIAGNOSIS

The specific cause of a medical disorder is called the "diagnosis." It is very important to establish the exact diagnosis when Duchenne is suspected. Depending on one's health system, a primary care provider (PCP) may be the first medical professional to hear concerns regarding a child's weakness or delays. PCPs are typically those physicians, nurse practitioners, or physician assistants who specialize in pediatrics, general practice, family medicine, or internal medicine and provide a "medical home."

The aim of care at this time should be to provide an accurate diagnosis as quickly as possible. A prompt diagnosis will help everyone in the family become informed about Duchenne, provided with information regarding genetic counseling, and told of treatment plans. Appropriate care, ongoing support, and education are essential at this stage. Ideally, a neuromuscular specialist (NMS) will assess a child and can help to start and/or interpret lab and genetic tests correctly, giving an accurate diagnosis (Section 4).

ChildMuscleWeakness.org is a tool to help professionals evaluate patients for developmental delays and possible neuromuscular diagnoses.

The American Academy of Pediatrics (AAP) realizes that parents are most often the first to recognize delays in their child's development. The AAP developed the "motor delay tool." This tool helps parents watch the development of their child, assess what is normal development versus delayed development, and know when to be concerned. This tool can be found at: www.HealthyChildren.org/MotorDelay.

At the time of diagnosis, it is very important that children see a NMS familiar with Duchenne. Centers offering Duchenne care may be found at the websites listed below:

MDA Care Centers in the US:
www.mda.org/services/your-mda-care-center

PPMD Certified Duchenne Care Centers in the US:
www.ParentProjectMD.org/CareCenters

TREAT-NMD:
http://www.treat-nmd.eu/

World Duchenne Organization (UPPMD):
http://worldduchenne.org/

This is also a time when contact with a patient advocacy organization can be of particular help. Patient organizations are listed at www.treatnmd.eu/dmdpatientorganisations.

WHEN TO SUSPECT DMD (FIGURE 3)

There may be suspicions of Duchenne raised by one of the following signs (even when there is no family history of Duchenne):

- Development and/or speech delay
- Problems with muscle function, with the Gowers' sign (Figure 2) being the classical sign of Duchenne
- Enlarged calf muscles (called "pseudohypertrophy")
- Elevated CK and/or increase in transaminases, or liver enzymes AST and ALT, in blood tests

Although suspicion can be raised in a variety of ways, the figure below can help to describe the steps taken in diagnosing Duchenne.

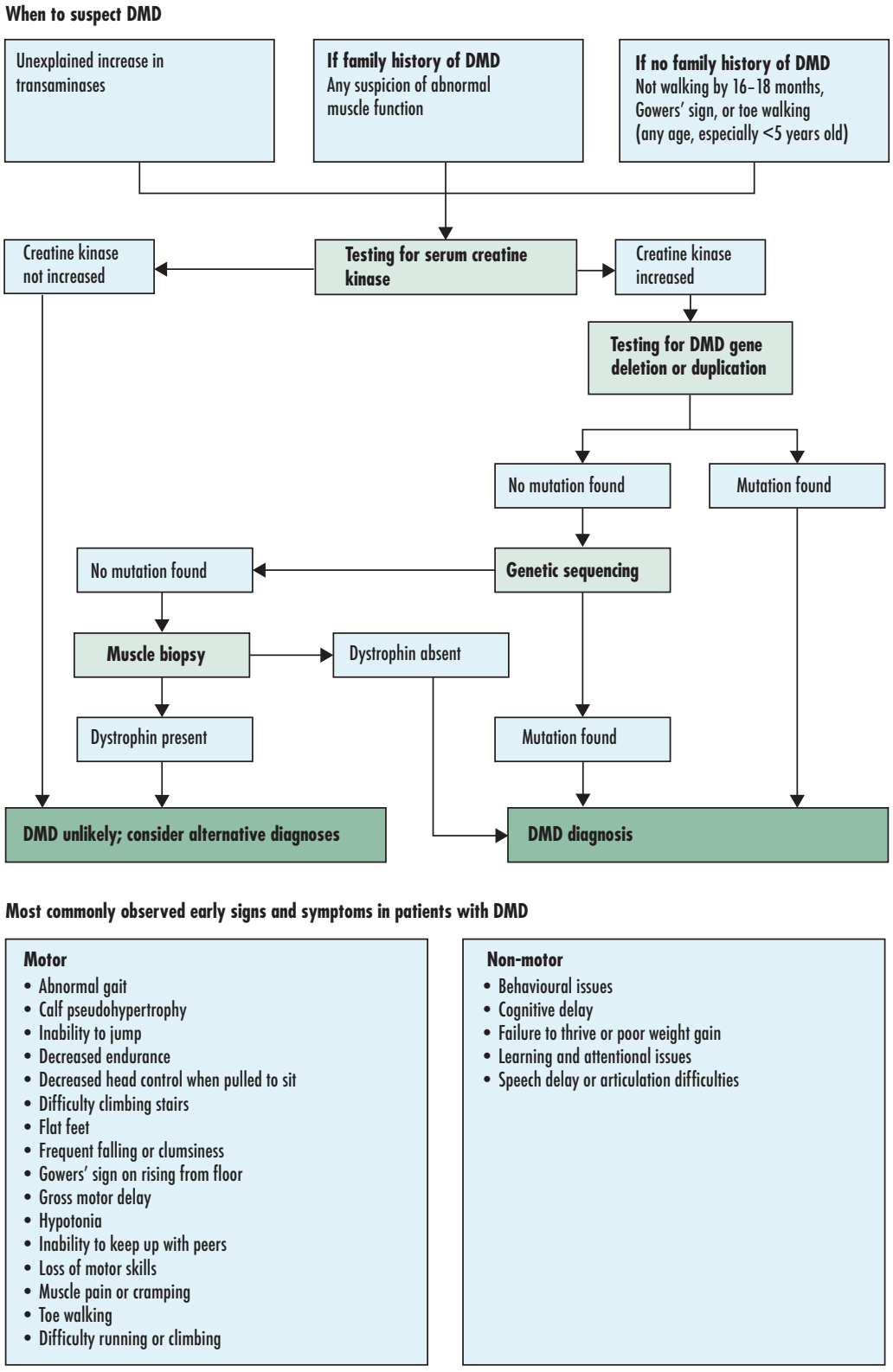


Figure 3[1]

ROLE OF THE PRIMARY CARE PROVIDER (PCP) IN THE CARE TEAM

After the diagnosis is confirmed by a NMS, information and resources should be sent to your PCP about Duchenne. PCPs are typically those physicians, nurse practitioners, or physician assistants who specialize in pediatrics, general practice, family medicine, or internal medicine and provide your "medical home." An ongoing medical relationship with your PCP will provide a continued, much-needed source of stability and support.

Your PCP's responsibilities should include:

- First-line care for acute and chronic medical issues
- Age/developmentally appropriate care at all stages of development
- Coordination of care with appropriate specialists
- Annual screening for hearing and vision
- Annual screening for mood disorders, substance abuse, and other mental health problems
- Ensuring all vaccinations are up-to-date, including annual influenza vaccinations (the flu shot should be given, rather than the live virus nasal vaccine)
- Annual screening for cardiovascular risk factors, such as high blood pressure (hypertension) and high cholesterol levels (hypercholesterolemia)

4. DIAGNOSING DUCHENNE

WHAT CAUSES DUCHENNE?

Duchenne is a genetic disease caused by a mutation, or change, in the gene that encodes for dystrophin. Dystrophin is a protein that is present in every muscle fiber in the body. Dystrophin acts as a "shock absorber" that allows muscles to contract and relax without being damaged. Without dystrophin, muscles are not able to function or repair themselves properly. Additionally, the muscle membrane is easily damaged by normal day-to-day activity, creating tiny microtears in the cell membrane. Without dystrophin, the muscles are not able to repair themselves. These tiny tears let calcium come into the cell, which is a toxic substance to muscle. The calcium damages and eventually kills the muscle cells, allowing them to be replaced with scar tissue and fat. The loss of muscle cells results in a loss of strength and function over time.

CONFIRMING THE DIAGNOSIS

The diagnosis of Duchenne must be confirmed by genetic testing. This testing is typically from a blood sample, but other tests may be performed as well.

1) GENETIC TESTING (FIGURE 2)

Genetic testing is always necessary and should be offered to every patient. Different types of genetic tests are able to provide specific and more detailed information about the change in the DNA known as the genetic mutation. Having genetic confirmation of the diagnosis is very important, and it may help to determine eligibility for a number of mutation-specific clinical trials.

Once the exact genetic mutation is known, mothers should be offered the opportunity for genetic testing to check whether they are carriers. This information will be important for other female family members on the mother's side (sisters, daughters, aunts, cousins) to understand if they may be carriers as well. Having this information will help the family to gain knowledge about the risk of having more children with Duchenne and make decisions regarding prenatal diagnosis and reproductive choices. Families should be offered genetic counseling following diagnosis (Box 2).

TYPES OF GENETIC TESTING

- **Multiplex ligation-dependent probe amplification** (MLPA): MLPA tests for deletions and duplications, and is able to identify 70 percent of Duchenne genetic mutations
- **Gene sequencing:** If MLPA testing is negative, gene sequencing can pick up mutations other than deletions or duplications (i.e., point mutations [non-sense or missense] and small duplications/insertions); this test is able to identify the other 25 to 30 percent of Duchenne genetic mutations that the MLPA test does not identify

2) MUSCLE BIOPSY

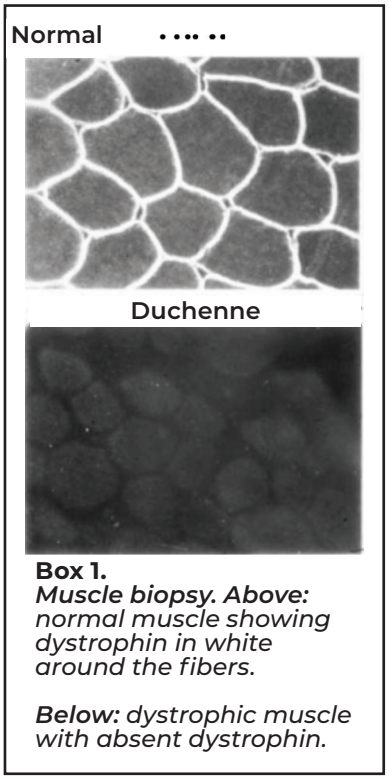
If you have a high CK level and signs of Duchenne but no genetic mutations were found using genetic testing, you may need to have a muscle biopsy. A muscle biopsy is done by surgically taking a small sample of muscle for analysis. The genetic mutation in Duchenne means the body cannot produce the protein dystrophin, or doesn't produce enough of it. Tests on the muscle biopsy can provide information on the amount of dystrophin present in the muscle cells (see Box 1).

Most people with Duchenne do NOT need a muscle biopsy.

There are two types of tests normally performed on a muscle biopsy: immunochemistry and western blot test. These tests are done to determine the presence or absence of dystrophin in the muscle. Immunohistochemistry involves putting a tiny piece of muscle on a slide, putting a stain on the muscle, then looking at the muscle cells under a microscope for evidence of dystrophin. Western blot test is a chemical process that tests for the chemical presence of dystrophin.

3) OTHER TESTS

In the past, the tests known as electromyography (EMG) and nerve conduction studies (needle tests) have been a traditional part of the assessment for a suspected neuromuscular disorder. **The experts agree that EMG and nerve conduction tests are NOT appropriate or necessary for the evaluation of Duchenne.**



Box 1.
Muscle biopsy. Above: *normal muscle showing dystrophin in white around the fibers.*

Below: *dystrophic muscle with absent dystrophin.*

WHY GENETIC CONFIRMATION IS IMPORTANT

GENETIC COUNSELLING AND CARRIER TESTING:

- Sometimes the genetic mutation causing Duchenne arises by chance. This is considered to be a "spontaneous mutation." In these cases, there is no family history of Duchenne. Thirty percent of people who are born with Duchenne have a spontaneous mutation in the gene that encodes for dystrophin rather than an inherited disease from a family member
- If the mother has a mutation in her DNA that she passes to her child, she is called a "carrier." A carrier has a 50 percent chance with each pregnancy to pass the genetic mutation on to her children. Boys who receive the mutated gene will have Duchenne, while the girls who receive the mutated gene will be carriers themselves. If the mother is tested and is found to have the mutation, she can make informed decisions about future pregnancies, and her female relatives (sisters, aunts, and daughters) can also be tested to see if they are also carriers
- A female who is a carrier and shows some signs of Duchenne (muscle weakness, fatigue, pain, etc.) is known as a "manifesting carrier." There is no test to show if a female carrier will be a manifesting carrier
- Even when a woman is not a carrier, there is a small risk that future pregnancies may be affected by Duchenne. The genetic mutation causing Duchenne may occur only in her ova or egg cells rather than in all of her cells. This is called "germline mosaicism." There is no blood test for germline mosaicism
- A female who is a carrier also has an increased risk of developing cardiac and skeletal muscle weakness and dysfunction. Female carriers should have cardiac monitoring (ECG and cMRI or echo) by a cardiologist every 3 to 5 years if tests are normal (or more frequently as prescribed by the cardiologist). Knowing carrier status helps to identify this risk in order to get appropriate advice and treatment
- A genetic counselor can explain all this in detail

ELIGIBILITY FOR CLINICAL TRIALS:

- There are a number of clinical trials underway in Duchenne that are targeted to specific genetic mutations causing Duchenne. Genetic testing is important to know whether you might be eligible to participate in these trials. To help clinical trial sites find you when you might be eligible for trials, be sure to register in your national Duchenne patient registry – a list can be found here: http://www.treat-nmd.eu/resources/patient-registries/list/DMD-BMD/
- If previously performed genetic testing did not meet currently accepted standards, allowing the exact mutation to be defined, further/repeated testing might be needed. You should discuss this with your neuromuscular specialist and/or genetic counselor. The precise genetic mutation is also needed to register in the Duchenne registries. You can find details about the kind of tests that might be done and how effective they are at detecting the detail of the mutation in the main document
- Adults who have not had genetic testing, or who have had it in the past and require testing using more current methods (ask your genetic counselor if your testing should be repeated), should consider obtaining genetic testing in order to be considered for clinical trial participation

5. NEUROMUSCULAR MANAGEMENT

In Duchenne, skeletal muscles will gradually get weaker because they do not have dystrophin. You should have regular checkups with a neuromuscular specialist (NMS) familiar with Duchenne. The NMS understands the progression of muscle weakness and can help you and your family prepare for the next step in care. It is important for the NMS to know how your muscles are working so that they can start the right therapies as early as possible.

NEUROMUSCULAR ASSESSMENTS

It is recommended that you see your NMS every 6 months and see a physical and/or occupational therapist for evaluation about every 4 months. This is important in order to make decisions about new treatments or modification of existing treatments at the most appropriate time, as well as to anticipate and prevent problems to the maximum extent possible.

Tests used to evaluate disease progression may vary from clinic to clinic. It is extremely important that you have regular evaluations using these same tests every time so any changes can be detected. Regular evaluations should include tests that monitor the progression of the disease and assess if interventions are appropriate. Those evaluations should include:

STRENGTH:

Skeletal muscle strength may be measured in a number of different ways to see if the force generated by specific muscles is changing.

RANGE OF JOINT MOTION:

This is done to monitor whether contractures or joint tightening are developing and to help to determine what stretches and/or interventions will be most helpful for you.

TIMED TESTS:

Many clinics routinely time activities such as getting up off the floor, walking a certain distance, and climbing several steps. This gives important information on how your muscles are changing and responding to different interventions.

MOTOR FUNCTION SCALES:

There are a large number of different scales, but your clinic should routinely use the same one each time they evaluate you. Different scales may be needed at different times.

ACTIVITIES OF DAILY LIVING:

This allows the team to determine whether some additional help might be needed to assist your independence.

DRUG TREATMENTS FOR SKELETAL MUSCLE

A lot of research is happening at the moment in the area of novel therapies for Duchenne. The updated care considerations include recommendations only for therapies for which there is sufficient evidence regarding treatment. These recommendations will change in the future when new evidence for new therapies becomes available. These guidelines will be reviewed and updated as new results become available.

Although it is expected that in the future a wider range of treatment options will be available, at the present time this is limited. Currently, steroids are the only drug recommended for the treatment of musculoskeletal symptoms of Duchenne because

experts in the field agree there is sufficient evidence to recommend it. Steroids are discussed in detail in Section 6. Drug treatments for other specific symptoms of the disease, such as heart problems, are discussed later.

6. STEROID MANAGEMENT

Corticosteroids, or steroids, are used in many other medical conditions worldwide. There is no doubt that steroids can benefit many people with Duchenne, but this benefit needs to be balanced with proactive management of possible side effects. Use of steroids is very important in Duchenne and should be discussed before a decline in physical function is seen.

THE BASICS

Steroids are known to slow the loss of muscle strength and motor function in Duchenne. Corticosteroids are different from the anabolic steroids that are sometimes misused by athletes who want to become stronger. The goal of steroid therapy in Duchenne is to maintain muscle strength and function, helping you to walk longer, preserve your upper limb and respiratory function, and avoid surgery to treat scoliosis (curvature of the spine).

- Steroids should be discussed at the time of diagnosis. The optimal time to start steroid use is during the ambulatory stage before there is significant physical decline (see Figure 4)
- The recommended national vaccination schedule should be complete before steroid treatment is started and varicella (chicken pox) immunity should be established. Vaccination recommendations from the CDC for the US can be found here: www.parentprojectmd.org/vaccinations. Consult your regional authorities for vaccination recommendations in your country
- Prevention and management of steroid side effects needs to be proactive and anticipatory (see Table 1)

THE DIFFERENT STEROID DOSING REGIMENS

Neuromuscular specialists may prescribe different regimens of steroids. These guidelines have tried to establish a clear method to using steroids effectively and safely based on regular assessments of function and side effects (see Figure 4).

- Prednisone and deflazacort (sold as Emflaza in the US) are the two types of steroids that are mainly used in Duchenne. They are believed to work similarly. Ongoing trials of these drugs are important and should help us understand the relative benefits of each better
- The choice of which steroid to use depends upon your/your family's preference, your specialist's preference, availability of the steroid in your country, the cost of the steroid, and the perceived side effects. Prednisone has the advantage of being inexpensive. Deflazacort may be preferred to prednisone by some because there may be a slightly lower risk of weight gain and behavioral problems, but it also comes with a slightly increased incidence of growth delay and cataract development

STEROID DOSING, MANAGEMENT, AND SIDE EFFECTS (FIGURE 4, TABLE 2)

- Attentive management of steroid-related side effects is crucial. While steroid therapy is currently the mainstay of medication therapy for Duchenne, it should not be undertaken casually and should be overseen only by a NMS with appropriate expertise
- Factors to take into account in maintaining or increasing steroid dosing include response to therapy, weight, growth, puberty, bone health, behavior, cataracts, and whether side effects are present and manageable

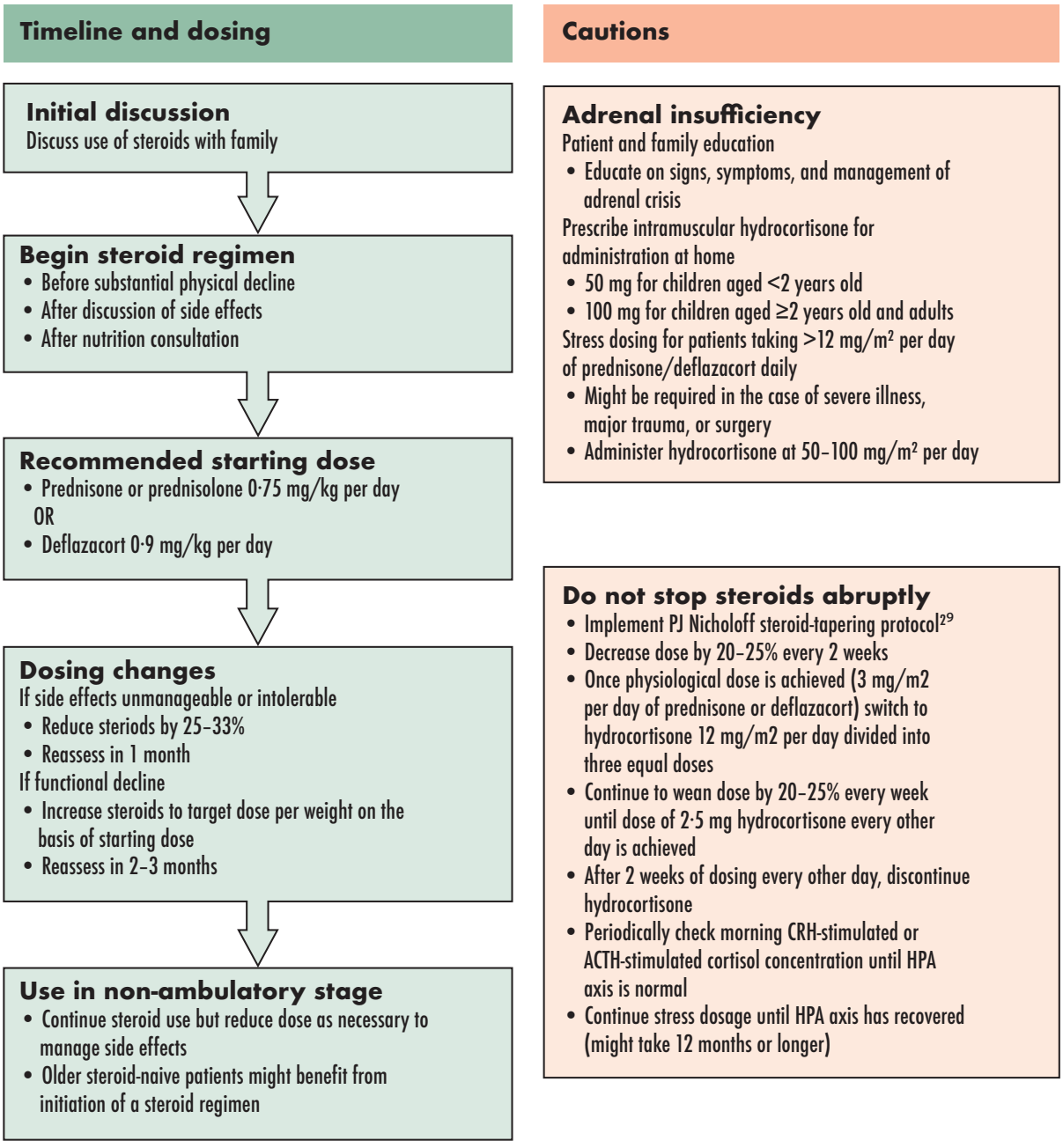


Figure 4, Table 2[1] Steroid Dosing and Management

ADRENAL INSUFFICINECY AND CRISIS

The adrenal glands sit on top of the kidneys and produce a hormone (cortisol) that helps the body deal with stress (i.e., severe illness or injury). While you are taking daily steroids, the adrenal glands stop producing cortisol (called "adrenal insufficiency") and become inactive. If steroids are discontinued, it can take weeks or months for your body to begin making cortisol again. Without cortisol, your body is unable to deal with stress, resulting in "adrenal crisis" which may be life threatening. For this reason, you should never stop your daily steroids suddenly (or without a doctor's help) or miss doses for more than 24 hours.

In addition, when your body is under additional stress (e.g. high fever, surgery, fractures) additional doses of steroids, or stress doses, may be needed. Information for dosing and recognizing/treating/preventing acute adrenal insufficiency can be found in the PJ Nicholoff Steroid Protocol, available here: www.parentprojectmd.org/pj.

OTHER DRUGS AND DIETARY SUPPLEMENTS

Along with steroids, other drugs approved for use in Duchenne include EXONDYS 51 (eteplirsen), which is approved in the US by the Food and Drug Administration (FDA), and ataluren (Translarna), which is approved for use in several European countries by the European Medicines Agency (EMA) but not in the US. Both EXONDYS 51 and ataluren are for use in people with distinct types of Duchenne mutations.

EXONDYS 51 is indiciated for people living with Duchenne who have genetic mutations amenable to exon 51 skipping (about 13 percent of cases). This drug aims to "skip" over the flawed portion (exon) to produce partially functional dystrophin.

Ataluren is indicated for people living with Duchenne who have a non-sense mutation (about 13 percent of cases). Although ataluren's mechanism of is action unknown, it is thought to interact with the part of the cell that "reads" proteins, allowing the cell to "read through" non-sense mutations to produce a functional protein.

There are a number of clinical trials underway in Duchenne that are targeted to specific genetic mutations causing the disease. Genetic testing is important to know whether you might be eligible to participate in these trials. To help clinical trial sites find patients who might be eligible for trials, be sure to register in your national Duchenne patient registry – a list can be found here: http://www.treat-nmd.eu/resources/patient-registries/list/DMD-BMD.

In addition to the medications discussed above, there are many other drugs and supplements that may be used in Duchenne but are not approved by the FDA or EMA. Though some of the drugs mentioned in Box 3 are widely used, there is just not enough evidence to say whether these supplements may be helpful or harmful to you. It is important to discuss all medication with your NMS before you think about adding or stopping medication.

BOX 3. OTHER DRUGS AND DIETARY SUPPLEMENTS NOT APPROVED FOR USE IN DUCHENNE

The experts considered a range of other drugs and supplements that have been used in some cases for Duchenne treatment. They reviewed published data on these substances to see if there was enough evidence for their safety and efficacy to be able to make recommendations.

The experts concluded the following:

- The use of oxandrolone, an anabolic steroid, is not recommended
- The use of Botox is not recommended
- There was no support for the systematic use of creatine. A randomized controlled trial of creatine in Duchenne did not show a clear benefit. If a person is taking creatine and has evidence of kidney problems, this supplement should be discontinued
- No recommendations can be made at this time about other supplements or other drugs that are sometimes used in Duchenne treatment, including co-enzyme Q10, carnitine, amino acids (glutamine, arginine), anti-inflammatories/antioxidants (fish oil, vitamin E, green tea extract, pentoxifylline), and others including herbal or botanical extracts. The experts concluded that there was not enough evidence in the published literature to support their use
- The experts agreed that this is an area where additional research is needed. Active involvement of families in activities that develop further knowledge, such as patient registries and clinical trials, was encouraged

TABLE 2. STEROID SIDE EFFECTS: RECOMMENDED MONITORING AND INTERVENTION

Some of the more common side effects of long-term steroid administration are listed here. It is important to note that different people will have very different responses to steroids. The key to successful steroid management is to be aware of the potential side effects and work to prevent, or reduce, them where possible. Reduction in steroid dose may be necessary if side effects are unmanageable or intolerable (Figure 4). If this is unsuccessful, changing to another type of steroid or dosing regimen is necessary before abandoning treatment altogether. This should be done with your NMS.

TABLE 2. STEROID SIDE EFFECTS

Steroid side effect	Additional Information	Discuss with your NMS
Weight gain and obesity	You should be warned that steroids may increase appetite; dietary advice should be provided before starting steroids	It is important that the whole family eat sensibly in order to prevent excess weight gain. Healthy eating plans can be found at https://www.choosemyplate.gov
Cushingoid features ("moon face")	Fullness in the face and cheeks may become more noticeable over time	Careful monitoring of diet, minimizing sugar and salt, will help with weight gain and may help to minimize Cushingoid features
Excessive growth of hair on the body (hirsuitism)	Steroids often cause excessive hair growth on the body	This is not usually severe enough to warrant a change in medication
Acne, fungal infections of the skin (tinea), warts	This may be more noticeable in teenagers	Use specific treatments (topical prescription) and do not rush to change the steroid regimen unless there is emotional distress
Short stature	Height should be checked at least every 6 months as part of general care	If growth has slowed or stopped, or if height increase is < 1.5 inches (4 cm)/year, or if height is < 3rd percentile, referral to endocrine specialist may be necessary
Delayed puberty	Puberty should be checked at each visit beginning at 9 years old Tell your NMS about any family history of delayed sexual maturation Testosterone replacement therapy is generally recommended for boys who have not started puberty by age 14	If you are concerned about delayed pubertal development, or if puberty has not started by age 14, referal to an endocrine specialist for evaluation may be necessary

TABLE 2. STEROID SIDE EFFECTS

Steroid side effect	Additional Information	Discuss with your NMS
Delayed puberty	Puberty should be checked at each visit beginning at 9 years old Tell your NMS about any family history of delayed sexual maturation Testosterone replacement therapy is generally recommended for boys who have not started puberty by age 14	If you are concerned about delayed pubertal development, or if puberty has not started by age 14, referral to an endocrine specialist for evaluation may be necessary
Adverse behavioral changes *(for additional information about behavior, see Section 10)*	Tell your NMS about any baseline mood, temperament, and ADHD issues Be aware that these often temporarily worsen in the initial six weeks on steroid therapy	Baseline behavior issues should be treated prior to starting steroid therapy, e.g. ADHD counseling or prescription It may help to change the timing of steroid medication to later in the day - discuss this with your NMS, who may also consider a behavioral health referral
Immune suppression	Taking steroids may reduce immunity (the ability to fight infections) Be aware of risk of serious infection and the need to promptly address minor infections	Obtain chicken pox immunization prior to starting steroid therapy; if not done, seek medical advice if in contact with chicken pox If there is a regional problem with tuberculousis, there may need to be specific surveillance

TABLE 2. STEROID SIDE EFFECTS

Steroid side effect	Additional Information	Discuss with your NMS
Adrenal suppression	Inform all medical personnel that you are taking steroids, and carry a steroid alert card It is very important that steroid doses are not missed for more than 24 hours, as this may cause adrenal crisis Know when stress dose steroids should be given (severe illness, major trauma, or surgery) to prevent adrenal crisis Know the signs and symptoms of adrenal crisis (stomach pain, vomiting, lethargy) Have a prescription for hydrocortisone intramuscular injection at home (you may need to know how to administer in case of adrenal crisis) Never stop taking steroids abruptly	Ask your NMS for a stress dose steroid plan that explains: • What to do in the case of a missed steroid dose >24 hours (because of fasting, illness, or prescription unavailability) • When to give stress dose steroids, at what dose, and in what form (by mouth, by intramuscular injection, or by IV); consult the PJ Nicholoff Steroid Protocol for an example plan: www.parentprojectmd.org/pj • If you are going to stop taking steroid medications, ask your NMS for a tapering plan. They can refer to the PPMD PJ Nicholoff Steroid Protocol for an example plan: www.parentprojectMD.org/PJ
High blood pressure (hypertension)	Your blood pressure (BP) should be checked at each clinic visit	If BP is elevated, reducing salt intake and weight reduction may be useful first steps If ineffective, your primary care provider may consider additional medication

TABLE 2. STEROID SIDE EFFECTS

Steroid side effect	Additional Information	Discuss with your NMS
Glucose intolerance	Your urine should be tested for glucose (sugar) with dipstick test at clinic visits Tell your NMS about increased urine or increased thirst Blood test should be done once a year to monitor for development of type 2 diabetes and other complications of steroid-induced weight gain	Further blood tests for type 2 diabetes may be needed if urine tests or symptoms are positive for glucose
Gastritis/ gastroesophageal reflux (GERD)	Steroids can cause reflux symptoms (heartburn). Tell your NMS if you have these symptoms	Avoid non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen, naproxen Antacid can be used for symptoms
Peptic ulcer disease	Report symptoms of stomach pain as this can be a sign of damage to the lining of the stomach Your stool can be checked for blood if you are anemic or if there is suspicion of bleeding in the gut	Avoid NSAIDs (aspirin, ibuprofen, naproxen) Prescription medications and antacids can be used if you are having symptoms You may need to see a gastrointestinal (GI) physician for evaluation and treatment
Cataracts	Steroids can cause benign cataracts; evaluation with an annual eye exam is needed	Consider switching from deflazacort to prednisone if cataracts evolve that affect vision (deflazacort has been shown to have a higher risk of cataract development) If cataracts are present, an ophthalmology consultation may be needed Cataracts will need to be treated only if they interfere with vision

TABLE 2. STEROID SIDE EFFECTS

Steroid side effect	Additional Information	Discuss with your NMS
Osteoporosis	Tell your NMS about fractures and back pain at each visit Spine X-rays should be done every 1-2 years to monitor for vertebral compression fractures DEXA every 2-3 years to monitor bone density Yearly vitamin D blood levels should be checked using a 25 OH vitamin D test (ideally late winter in seasonal climates); vitamin D supplements with vitamin D3 may be needed if levels are low Your diet should be evaluated each year to make sure you are eating/ drinking adequate amounts of calcium	Vitamin D supplements may be needed depending on level in blood Check 25 OH vitamin D levels annually; supplement as needed. Make sure that your dietary calcium intake meets recommendations for your age Calcium supplements may be needed if your diet does not include adequate amounts of calcium Weight-bearing activities (standing) can be helpful for bone health Discuss with your NMS/PT before starting an exercise/ weight-bearing program
Myoglobinuria *(Urine looks reddish-brown colored because it contains breakdown products of muscle proteins. This needs to be tested for in a hospital lab.)*	Report any reddish-brown urine to your NMS Urine can be tested for myoglobin Urine should also be checked for infection	Avoid vigorous exercise and eccentric exercises, such as running downhill or trampolining Good fluid intake is important Kidney investigations are needed if it this continues

7. ENDOCRINE MANAGEMENT

A number of hormones can be negatively affected by the steroids used to treat Duchenne. Most commonly these include growth hormone (affecting growth, leading to short stature) and testosterone (the male sex hormone, leading to delayed puberty). Your NMS may recommend that you see a pediatric endocrinologist (hormone doctor) if there are any concerns about growth, puberty, or adrenal suppression.

GROWTH AND PUBERTY

Short stature and delayed puberty may be distressing and you should feel comfortable discussing these topics with your NMS. Short stature can be a sign of other medical problems and testosterone deficiency may worsen bone health, so it is important that your neuromuscular team follow your growth and pubertal development closely (Figure 5).

GROWTH HORMONE THERAPY

- You may be prescribed growth hormone for short stature if you are found to be growth-hormone deficient
- There is no evidence or literature assessing the safety or efficacy of growth-hormone in people living with Duchenne who are not growth-hormone deficient
- There may be potential risks associated with growth-hormone use, including headaches, idiopathic intracranial hypertension (high pressure in the brain and eyes), slipped capital femoral epiphyses (a hip disorder that can cause pain and may need surgery to fix), worsening of scoliosis, and increased risk of developing diabetes
- Before deciding whether to use growth hormone, your endocrinologist should discuss the potential risks and benefits of treatment

TESTOSTERONE THERAPY

- Testosterone is important for bone health, as well as for psychosocial/emotional development
- Testosterone therapy should be started at low doses and increased slowly to mimic normal puberty
- Testosterone comes in multiple forms, including intramuscular injections, gels, and patches
- Your endocrinologist should discuss the expected response to treatment before testosterone is started, which will likely include: the development of body odor, facial hair, acne, a growth spurt, closing of the growth plates, and increased libido (interest in sex)
- Potential side effects include: infection at injection site, allergic reaction, mood swings, and increases in red blood cell count
- You will need to have your blood drawn regularly while taking testosterone in order to monitor your body's response to treatment

ADRENAL CRISIS

The adrenal glands, sitting on the kidneys, produce a hormone (cortisol) that helps your body deal with stress (i.e., severe illness or injury). When you are taking steroids, the adrenal glands stop producing cortisol ("adrenal suppression"). Once the steroids are discontinued, it can take weeks or months for your body to begin making cortisol again. Without cortisol, your body is unable to deal with stress, resulting in adrenal crisis that may be life threatening.

Adrenal suppression and crisis are potentially life-threatening complications of long-term steroid use (See Figure 5). It is important to know that you may be at risk of an adrenal crisis if your steroids are stopped suddenly or if doses are missed because of illness or other reasons for more than 24 hours. All patients taking chronic daily steroids should have a plan in place that outlines what to do in case of missed doses or during times of major illness or severe trauma, when extra doses, or "stress doses," of steroids may be needed. Information about preventing, recognizing, and managing adrenal insufficiency, as well as when and how to use stress doses of steroids, are in included in the PJ Nicholoff Steroid Protocol, which can be found here: www.parentprojectmd.org/pj.

SYMPTOMS OF AN ADRENAL CRISIS

You should should receive information about the signs and symptoms of an adrenal crisis:

- Severe fatigue
- Headache
- Nausea/vomiting
- Low blood sugar
- Low blood pressure
- Passing out

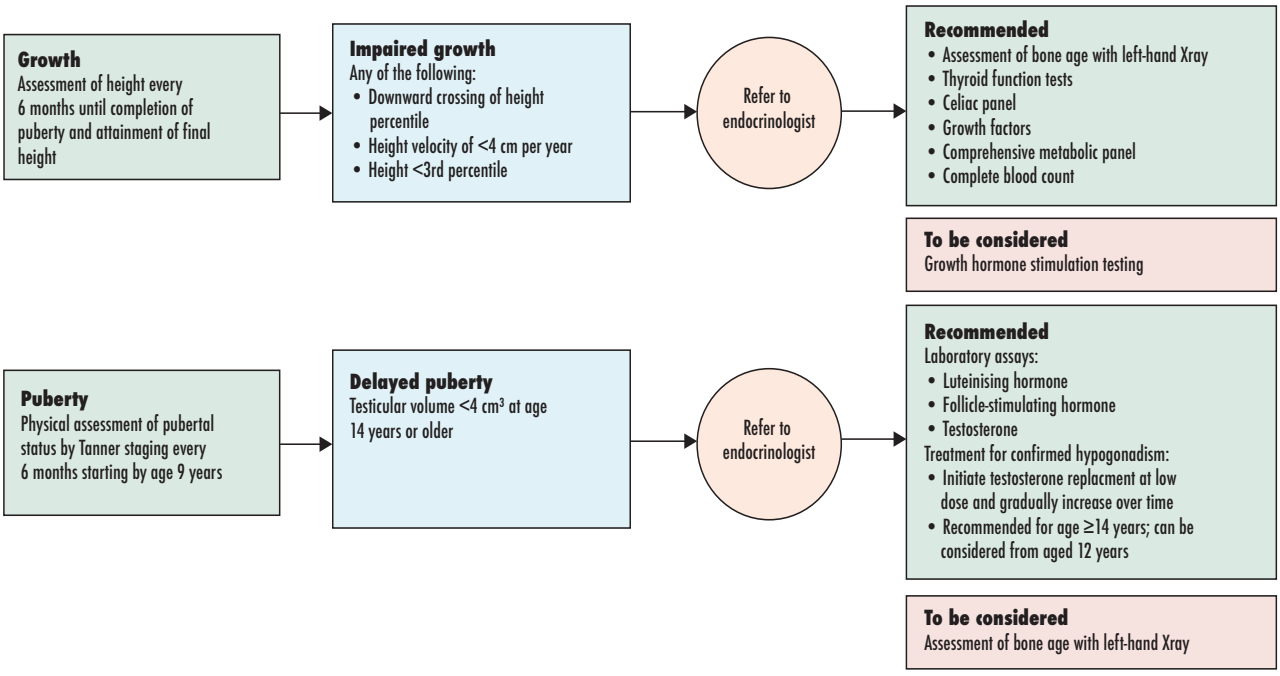


Figure 5 Assessment and management of growth and puberty while taking corticosteriods

8. BONE HEALTH (OSTEOPOROSIS) MANAGEMENT *(Figure 6)*

Bone health is important in both the ambulatory and non-ambulatory phases of Duchenne. People living with Duchenne at all ages have weak bones, especially if they are taking steroids. Steroids cause bones to have a lower bone mineral density, increasing the risk of fractures (broken bones) compared to the general population. Muscle weakness and decreased mobility are also risk factors for weak bones.

Dual energy X-ray absorption (DEXA) is a non-invasive test that measures bone mineral density of the long bones (usually the leg or arm). Thinner bone is less healthy and is more susceptible to fractures. Measuring your bone mineral density is important in monitoring overall bone health. It is recommended you have DEXA scans at least every 2 to 3 years.

People living with Duchenne, especially those taking steroids, are at risk for vertebral compression fractures. Vertebral compression fractures occur when vertebrae (the bones of the spine) sustain small fractures, causing them to become misshapen and to collapse on one another. These fractures, and resultant vertebral collapse, can cause pain. Vertebral compression fractures can be seen on a lateral side-view spinal X-ray, even without having back pain. Vertebral fractures may be treated with bisphosphonates, especially if pain is present. It is recommended you have lateral spine X-rays every 1 to 2 years or more frequently if you experience back pain.

Bone is constantly being broken down, reabsorbed into the blood stream, and rebuilt. Steroids slow down the rebuilding phase of bone growth. Bisphosphonates are medications that bind to the surface of bone, slowing down the breaking down and reabsorbtion process, helping bone to be built more effectively. This process keeps bones thicker and, hopefully, healthier and less susceptible to fracture. The use of bisphosphonates may be discussed if there are signs of decreased bone density, long bone fractures that occur without significant trauma, and/or vertebral compression fractures (see Figure 6).

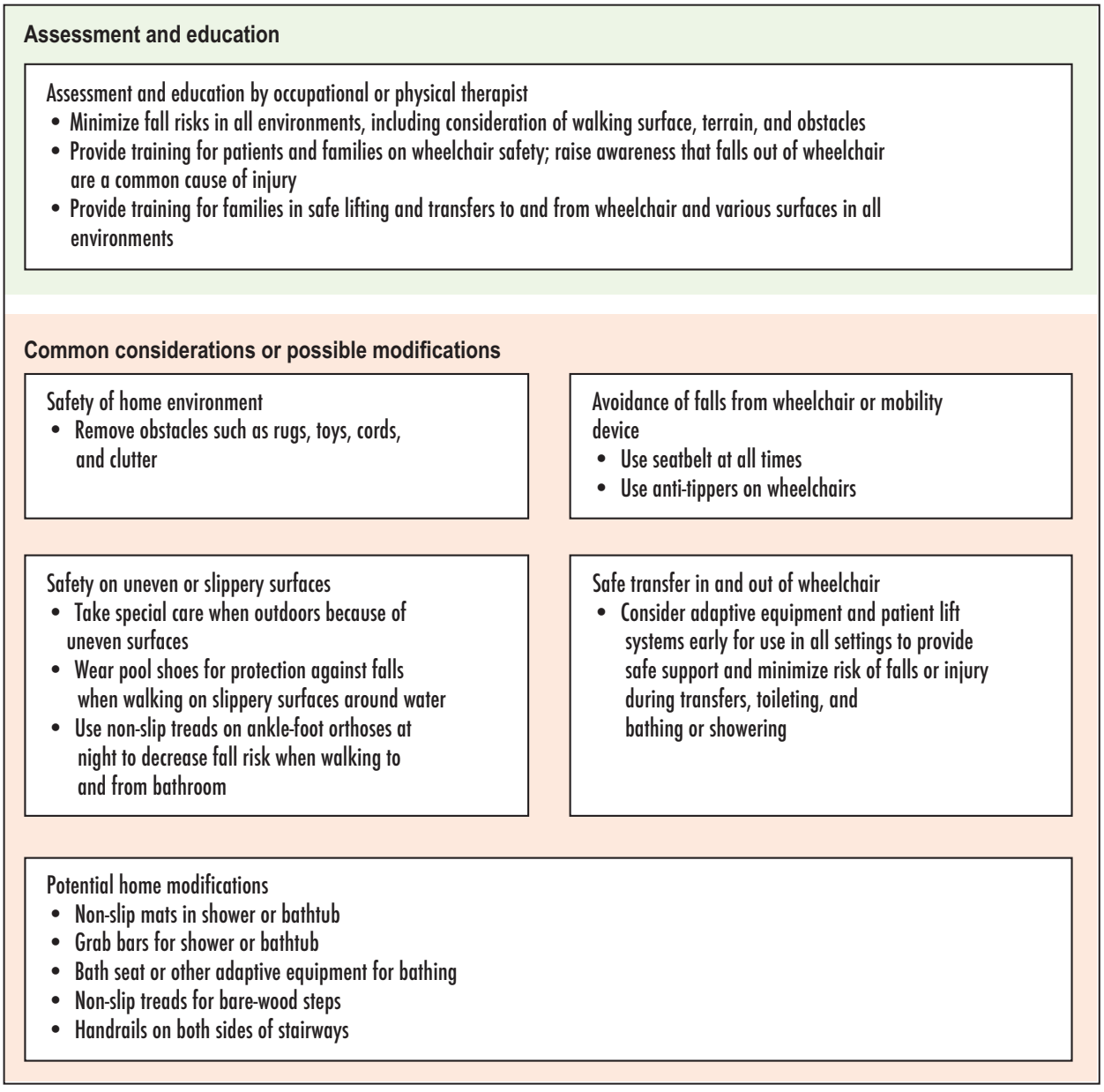


Figure 6[2] Considerations for Safety and Fall Prevention

9. ORTHOPEDIC MANAGEMENT *(Figure 7)*

The main goals of orthopedic care are to maintain walking and/or motor function as long as possible, and to minimize joint contractures. The ability to walk or stand will help you to maintain a straight spine and will help to promote bone health.

CONTRACTURES

As muscles become weaker and you find moving your joints more difficult, joints are at risk for becoming locked in one position, known as a contracture. Having correct posture may help the prevention of contractures in the back, feet, and ankles while you are walking. While sitting, it is important to make sure your posture is in good alignment, with weight bearing even on both sides of the body. Your feet and legs should be in proper alignment, with good positioning and proper support. A proper seating system in your wheelchair, giving support of spinal and pelvic symmetry and spinal extension, is crucial. There may be surgical options to help maintain the alignment of feet and legs if that is appropriate for you.

SCOLIOSIS

People living with Duchenne who are not treated with corticosteroids have a 90 percent chance of developing progressive scoliosis (a sideways curvature of the spine that may get worse over time). Daily steroid treatment has been shown to reduce the risk of scoliosis, or to significantly delay its onset. Paying attention to your posture and positioning is critical for preventing scoliosis. Continued assessment of your spine throughout your lifespan is essential.

LONG BONE FRACTURES

A broken leg can be a significant threat to the continued ability to walk. If you break, or fracture, your leg, ask if treatment with surgery should be considered. Surgical correction can often allow people living with Duchenne to get back up on their feet as soon as possible. If you do experience a fracture, make sure that your neuromuscular team is notified before any treatment decisions are made. Your neuromuscular team will help to both guide the care for your fracture, as well as your post-fracture therapy.

Fat embolism syndrome (FES) is a risk in Duchenne and presents a medical emergency. A fat embolism is caused by a tiny piece of fat being released into the blood stream after a bone is broken or significantly bumped. This piece of fat (called an “embolism”) can travel through the blood to the lungs, preventing the body from getting enough oxygen. Symptoms of a fat embolism may include confusion, disorientation, “not acting like yourself,” rapid breathing and heart rate, and/or shortness of breath. ***If you have had a bump, fall, and/or fracture and are showing any of the signs of FES, get to the emergency room as quickly as possible. Let the staff know that you suspect you have a fat embolism. This is a medical emergency.***

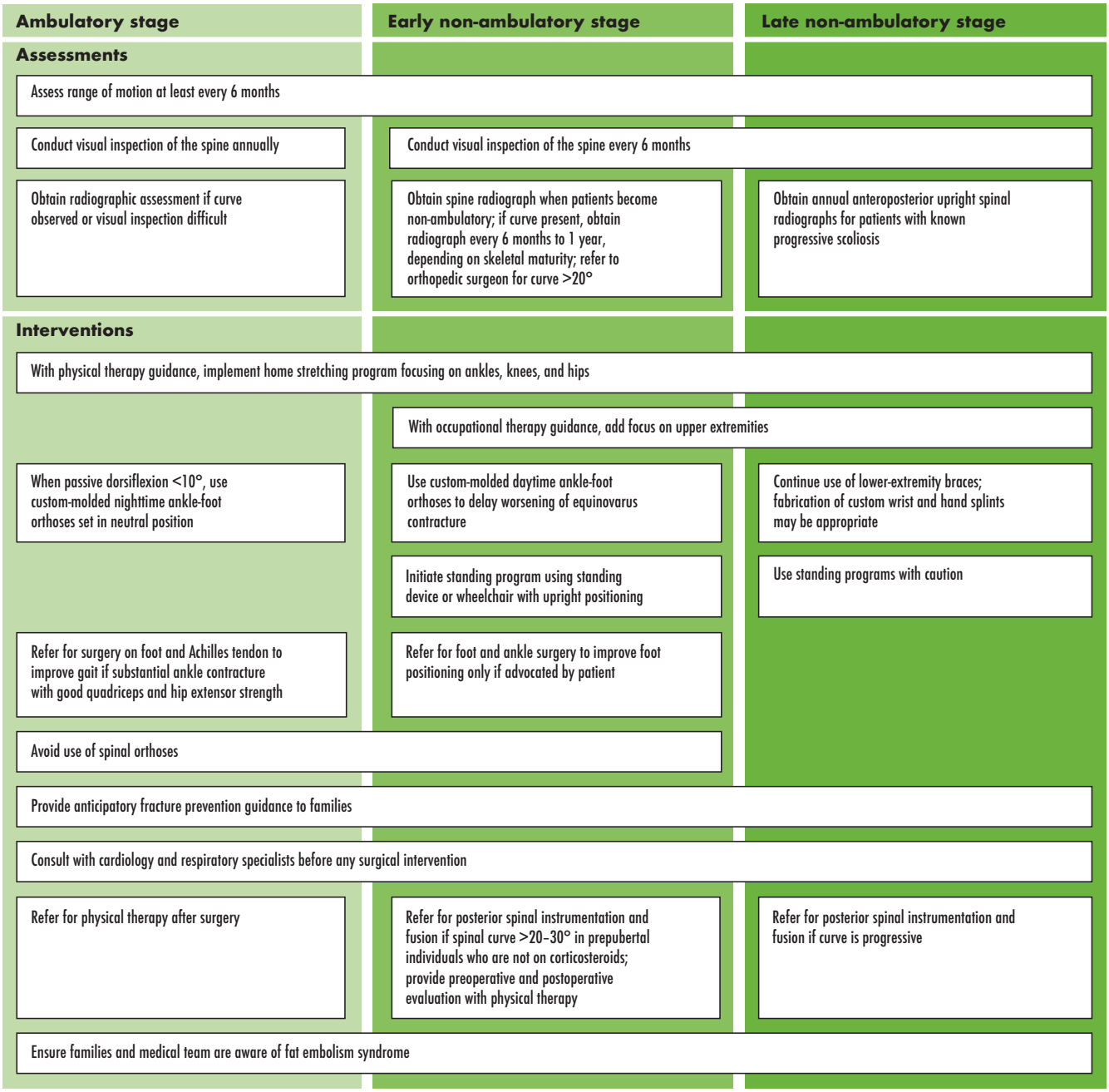


Figure 7[2] Assessment and Management of the Spine and Joints

10. REHABILITATION MANAGEMENT

Physical, occupational, and speech therapy

People living with Duchenne need access to different types of rehabilitation management throughout their lives. The rehabilitation team can include physicians, physical therapists (PTs), occupational therapists (OTs), speech-language pathologists (SLPs), orthopedists, orthotists, and durable medical equipment providers.

The rehabilitation team should consider your goals and lifestyle in order to provide you with consistent preventative care, minimize the impact of Duchenne on your life and activities, and optimize quality of life. Rehabilitation can be provided in outpatient clinic and school settings, and should continue throughout your life. You should be assessed by a rehabilitation specialist at least every 4 to 6 months.

RANGE OF MOTION, EXERCISE, AND STRETCHING (FIGURE 8)

- There are many factors in Duchenne that contribute to the tendency for joints to get tight, or "contracted," including: muscles becoming less elastic because of limited use and muscles around a joint getting out of balance (one stronger than another)
- Maintaining good range of movement and symmetry at different joints helps to maintain the best possible function, prevents the development of contractures, and prevents pressure problems with the skin
- Aerobic exercise or activity is recommended; swimming is a great example of safe exercise. Some exercise (such as bouncing on a trampoline or bouncey house) may be harmful to muscles. Therefore, all exercise should be monitored and guided by your physical therapist or physiotherapist
- Stretching will be monitored by the physical therapist but needs to become part of your daily routine
- The goal of stretching and bracing, from diagnosis onwards, is to preserve function and flexibility and maintain comfort

Panel 2: Rehabilitation assessments and interventions across all disease stages for patients with Duchenne muscular dystrophy

Assessment

Multidisciplinary rehabilitation assessment every 6 months or more frequently if concerns, change in status, or specific needs are present (appendix)

Intervention

Direct treatment

Direct treatment implemented by physical therapists, occupational therapists, and speech-language pathologists, tailored to individual needs, stage of disease, response to therapy, and tolerance, provided across the patient's lifespan

Prevention of contracture and deformity

- Daily preventive home stretching 4–6 times per week; regular stretching at ankles, knees, and hips; stretching of wrists, hands, and neck later if indicated by assessment
- Stretching for structures known to be at risk of contracture and deformity* and those identified by assessment
- Orthotic intervention, splinting, casting, positioning, and equipment:
  - AFOs for stretching at night—might be best tolerated if started preventatively at a young age
  - AFOs for stretching or positioning during the day in non-ambulatory phases
  - Wrist or hand splints for stretching of long and wrist finger flexors/extensors —typically in non-ambulatory phases
  - Serial casting—in ambulatory or non-ambulatory phases
  - Passive/motorised supported standing devices—when standing in good alignment becomes difficult, if contractures are not too severe to prevent positioning or tolerance
  - KAFOs with locked knee joints—an option for late ambulatory and non-ambulatory stages
  - Custom seating in manual and motorised wheelchairs (solid seat, solid back, hip guides, lateral trunk supports, adductors, and head rest)
  - Power positioning components on motorised wheelchairs (tilt, recline, elevating leg rests, standing support, and adjustable seat height)

Exercise and activity

Regular submaximal, aerobic activity or exercise (eg, swimming and cycling) with assistance as needed, avoidance of eccentric and high-resistance exercise, monitoring to avoid overexertion, respect for the need for rests and energy conservation, and caution regarding potentially reduced cardiorespiratory exercise capacity as well as risk of muscle damage even when functioning well clinically

Falls and fracture prevention and management

- Minimisation of fall risks in all environments
- Physical therapist support of orthopaedics in rapid team management of long-bone fractures and provision of associated rehabilitation to maintain ambulation and/or supported standing capabilities

Management of learning, attentional, and sensory processing differences

Management in collaboration with team, based on concern and assessment

Assistive technology and adaptive equipment

Planning and education with assessment, prescription, training, and advocacy for funding

Participation

Participation in all areas of life supported at all stages

Pain prevention and management

Pain prevention and comprehensive management, as needed, throughout life

AFOs=ankle-foot orthoses. KAFOs=knee-ankle-foot orthoses. *Areas typically at risk of contracture and deformity include hip flexors, iliotibial bands, hamstrings, plantar flexors, plantar fascia, elbow flexors, forearm pronators, long wrist and finger flexors and extensors, lumbricals, and cervical extensors; isolated joint contracture into hip and knee flexion and plantar flexion, varus at hindfoot and forefoot, elbow flexion, wrist flexion or extension, and finger joints; and deformity of the vertebral column and chest wall including scoliosis, excessive kyphosis or lordosis, and decreased chest wall mobility.

Figure 8[1]

WHEELCHAIRS, SEATING, AND OTHER ADAPTIVE EQUIPMENT (FIGURE 9)

- While you are walking, a scooter, stroller, or wheelchair may be used for long distances to conserve your strength
- When you start needing to use a wheelchair for longer periods, it is important that you are using a chair that keeps your posture in proper alignment and provides good support for all parts of your body
- As difficulty with walking increases, it is recommended that a power wheelchair is provided sooner rather than later. Additionally, a power standing feature is recommended if available
- Physical and occupational therapists will be helpful in recommending assistive devices to help maintain your independence and promote safety
- It is best to think ahead about the kind of equipment that will continue to support your independence and participation in activities you enjoy and to plan accordingly

BOX 4. PAIN MANAGEMENT

It is important to let your NMS know if pain is a problem so that it can be addressed and treated properly. This should be reviewed at every neuromuscular visit. Unfortunately, very little is currently known about pain in Duchenne. More research is needed. If you are in pain, you need to talk to your NMS and explain that this is a problem.

- For effective pain management, it is important to determine why there is pain so your neuromuscular team can provide appropriate interventions
- Pain may result from problems with posture and difficulty getting comfortable. Interventions may include appropriate and individualized orthoses (braces), seating, bedding, and mobility as well as standard drug treatment approaches (e.g. muscle relaxants, anti-inflammatory medications). Interactions with other medications (e.g. steroids and non-steroidal anti-inflammatory drugs [NSAIDs]) and associated side effects, especially those that might affect cardiac or respiratory function, should be considered
- Rarely, orthopedic surgical intervention might be indicated for pain that cannot be managed in any other way. Back pain, especially in people using steroids, may be a sign of vertebral compression fractures, which respond well to bisphosphonate treatment.
- Narcotic pain medication should be used with extreme caution, especially if there is pulmonary dysfunction. Narcotics can cause more shallow breathing or may cause breathing to stop

- You may need additional adaptations to help with getting upstairs and transferring, eating and drinking, turning in bed, toileting, and bathing
- Simple devices such as elevated lap trays and adaptive straws can optimize function
- Advanced technologies such as robotics, Bluetooth, and infrared environmental controls may be helpful. Advanced Assistive Computer Technologies such as Tecla Home Automation devices and Dragon Naturally Speaking, and voice-recognition devices such as Google Home and Amazon Echo, can help to control your environment and assist with daily tasks

It is very important that you do everything, inside and outside your home, to stay safe. Below are some suggestions to help you to avoid accidents and potential broken bones.

Assessment and education

Assessment and education by occupational or physical therapist
- Minimise fall risks in all environments, including consideration of walking surface, terrain, and obstacles
- Provide training for patients and families on wheelchair safety; raise awareness that falls out of wheelchair are a common cause of injury
- Provide training for families in safe lifting and transfers to and from wheelchair and various surfaces in all environments

Common considerations or possible modifications

Safety of home environment
- Remove obstacles such as rugs, toys, cords, and clutter

Avoidance of falls from wheelchair or mobility device
- Use seatbelt at all times
- Use anti-tippers on wheelchairs

Safety on uneven or slippery surfaces
- Take special care when outdoors because of uneven surfaces
- Wear pool shoes for protection against falls when walking on slippery surfaces around water
- Use non-slip treads on ankle-foot orthoses at night to decrease fall risk when walking to and from bathroom

Safe transfer in and out of wheelchair
- Consider adaptive equipment and patient lift systems early for use in all settings to provide safe support and minimise risk of falls or injury during transfers, toileting, and bathing or showering

Potential home modifications
- Non-slip mats in shower or bathtub
- Grab bars for shower or bathtub
- Bath seat or other adaptive equipment for bathing
- Non-slip treads for bare-wood steps
- Handrails on both sides of stairways

Figure 9[2] Surveillance and Management of the Rehabilitation Team

11. PULMONARY MANAGEMENT

People with Duchenne typically do not have trouble breathing or coughing while they are still walking. As you get older and coughing muscles weaken, you may be at risk for chest infections due to an ineffective cough. Later on, the muscles that support breathing may weaken as well, and you may develop problems with breathing during sleep. It is important to let your neuromuscular team know if you have headaches or morning fatigue, as these may be signs of breathing too shallowly during sleep and indicate the need for a sleep study.

If your cough is weakening, it is extremely important to use devices to make your cough more effective, especially if you are sick. A sleep study evaluates how well you are breathing while asleep. If your oxygen levels are found to be too low while you are sleeping, you will need to use bi-level positive airway pressure (BI-PAP) to help improve your breathing during sleep. You may find, as you get older, that you may need help with breathing during the day as well.

A planned and proactive approach to respiratory care is necessary and should be based on close monitoring, prevention of problems, and early intervention when indicated. Your pulmonary team should include a doctor (pulmonologist) and respiratory therapist with experience in evaluating breathing in people with Duchenne. Their treatment goals typically include implementing techniques that expand the lungs and keep the chest wall muscles supple (lung volume recruitment), manually and mechanically assist cough for effective airway clearance, and deliver non-invasive or invasive nighttime and daytime ventilatory support.

SURVEILLANCE & PREVENTION (FIGURE 10)

- You should begin to see a pulmonologist yearly starting at diagnosis and begin pulmonary function testing as soon after diagnosis as possible. Testing should include measurement of forced vital capacity (or “FVC;” the largest breath that a person can fully and forcefully breathe out). Starting these tests early will allow children to become familiar with the equipment and the team and to assess baseline respiratory function
- When you are unable to walk without support, a scheduled pulmonary assessment should occur at least every six months. The assessment should include pulmonary function testing with measurements of FVC, maximum inspiratory (MIP – how strongly you can breathe in) and expiratory pressure levels (MEP – how strongly you can breathe out), and peak cough flow (PCF – the strength of your cough). These values will be trended over time by your pulmonary team
- In addition, the assessment should include pulse oximetry (SpO2 – measures the oxygen in your blood while you are awake) and when available, end-tidal or transcutaneous measurement of blood carbon dioxide levels (PetCO2/PtcCO2 – measures the levels of carbon dioxide in your blood while you are awake)
- A sleep study may be needed if there are signs of restless sleep, morning headaches, or extreme tiredness during the day. This study assesses breathing and measures oxygen levels and blood carbon dioxide levels while you are asleep
- Pneumococcal vaccination (to prevent pneumonia) and yearly influenza vaccinations (flu shots; avoid live virus influenza nasal spray) will help prevent episodes of severe flu and pneumonia

CONTACT YOUR NEUROMUSCULAR SPECIALIST OR PULMONOLOGIST IF YOU ARE:

- Experiencing a prolonged illness with only minor upper respiratory infections
- More tired than usual or sleepy for no reason during the day
- Short of breath, seeming as if you cannot catch breath or have difficulty finishing sentences
- Having headaches most mornings or all the time
- Having trouble sleeping, waking up a lot, having trouble waking up, or having nightmares
- Waking up trying to catch your breath or feeling your heart pounding
- Having trouble paying attention during the day at home or at school

Figure 10[2] Surveillance, Assessment and Management of the Pulmonary Team

INTERVENTIONS (FIGURE 10)

There are ways to help your lungs to function as well as they can, for a long time.

- It may be helpful to use ways to increase the amount of air that can enter the lungs by stretching breathing muscles through deep breathing ("lung volume recruitment," lung inflation, or breath stacking techniques)
- If coughing becomes weak, manual or mechanically assisted cough techniques ("cough assist") are helpful to clear the airway and keep mucus and germs out of the lungs. This reduces the risk of pneumonia
- With time, support will be needed initially for breathing overnight (non-invasive nocturnal assisted ventilation via bi-level airway pressure, or Bi-PAP) and then later during the daytime (non-invasive daytime assisted ventilation) as symptoms listed under the surveillance section develop
- The transition to assisted ventilation can be difficult to get used to. There are many different types of "interfaces" (masks and mouthpieces) that you can use. It is important to find an interface that is right for you. Your pulmonary team can offer various different types of interfaces until they find the most comfortable type for you
- Ventilation may also be assisted via a surgically placed tube in the trachea at the base of the throat ("tracheostomy tube") depending on local practice. This is known as invasive ventilatory support. There are no guidelines as to when a tracheostomy might be needed. It is often a personal decision between you and your pulmonologist
- The above interventions can help to keep you breathing more easily and avoid acute respiratory illnesses
- It is essential to keep up with your vaccination schedule, including the pneumococcal and annual influenza vaccine. People living with Duchenne should always opt for the influenza injection, rather than the live virus nasal spray
- Particular attention to breathing is required around the time of planned surgery (see Section 15)
- If you get a respiratory infection, ask for antibiotics in addition to the use of manually or mechanically assisted cough
- Always use caution if supplemental oxygen is necessary; be sure medical personnel know to use non-invasive bi-level positive airway pressure ventilation at the same time and monitor your carbon dioxide (CO_2) levels closely

12. CARDIAC MANAGEMENT *(Figure 11)*

The heart is a muscle, and it is also affected in Duchenne. Heart muscle disease is called "cardiomyopathy." In Duchenne, cardiomyopathy is a result of a lack of dystrophin in the heart muscle. Cardiomyopathy causes decreased function of the heart, or heart failure over time. There are many levels of heart failure, and people can live with managed heart failure for many years with the use of medication and regular visits to a cardiologist (heart doctor). The aim of cardiac management in Duchenne is early detection and treatment of heart muscle changes. Unfortunately, heart problems can often be silent and you may not notice symptoms. For this reason, it is extremely important to involve a cardiologist as a member of your care team from the time of diagnosis.

SURVEILLANCE

- You should see your cardiologist at least once a year from diagnosis, or more frequently if recommended
- Evaluation of your heart function should include an electrocardiogram (ECG – evaluates the electrical impulses of the heart and measures the heart rate) and echocardiogram ("echo," shows pictures of the heart structure and function) or cardiac MRI (gives exact images of the heart structure and function, and shows if there is fibrosis, or scarring, in the heart muscle)
- Female carriers of Duchenne need to have their hearts checked every 3 to 5 years if their hearts are normal (more often if recommended) as they can also have the same type of heart problems as people living with Duchenne

TREATMENT

- Cardiac medicines should be started with the first sign of cardiac fibrosis (scar tissue forming in the heart muscle, seen on MRI), decreased heart function (seen by decreased ejection or shortening fraction on MRI or echocardiogram), or by age 10, even if all your tests are normal as this will help to protect your heart
- Angiotensin converting enzyme inhibitors (ACEi – lisinopril, captopril, enalapril, etc.) or angiotensin receptor blockers (ARB – losartan) should be considered as first-line therapy. These medicines open up the blood vessels leading out of your heart, so your heart doesn't need to squeeze as hard to pump blood to the body
- Other medicines, such as beta-blockers, slow the heart rate down so that the heart can fill and pump blood effectively. Diuretics ("water pills" that cause the body to get rid of fluid, reducing the volume of the blood, allowing the heart to not pump as fast and hard) may also be prescribed with progession of heart failure
- Abnormal heart rhythms shown on an ECG should be promptly investigated and treated. It is a good idea to keep a copy of your baseline ECG on hand
- A Holter monitor will evaluate your heart rate and rhythm for 24 or 48 hours; this is done if changes in your heart rate or rhythm are suspected and need further evaluation
- A fast heart rate and/or palpitations (occasional abnormal heart beats) are common in people living with Duchenne and are typically not harmful. However, these can also be associated with more serious heart problems and need to be investigated by a cardiologist

- If you are experiencing severe, persistent chest pain, this may be a sign of cardiac damage, and you should be evaluated immediately in an emergency department
- People taking steroids should be monitored for potential cardiac side effects, such as hypertension (high blood pressure) and hypercholesterolemia (high cholesterol); steroid dose may require adjustment or further treatment may need to be added (see Table 2)

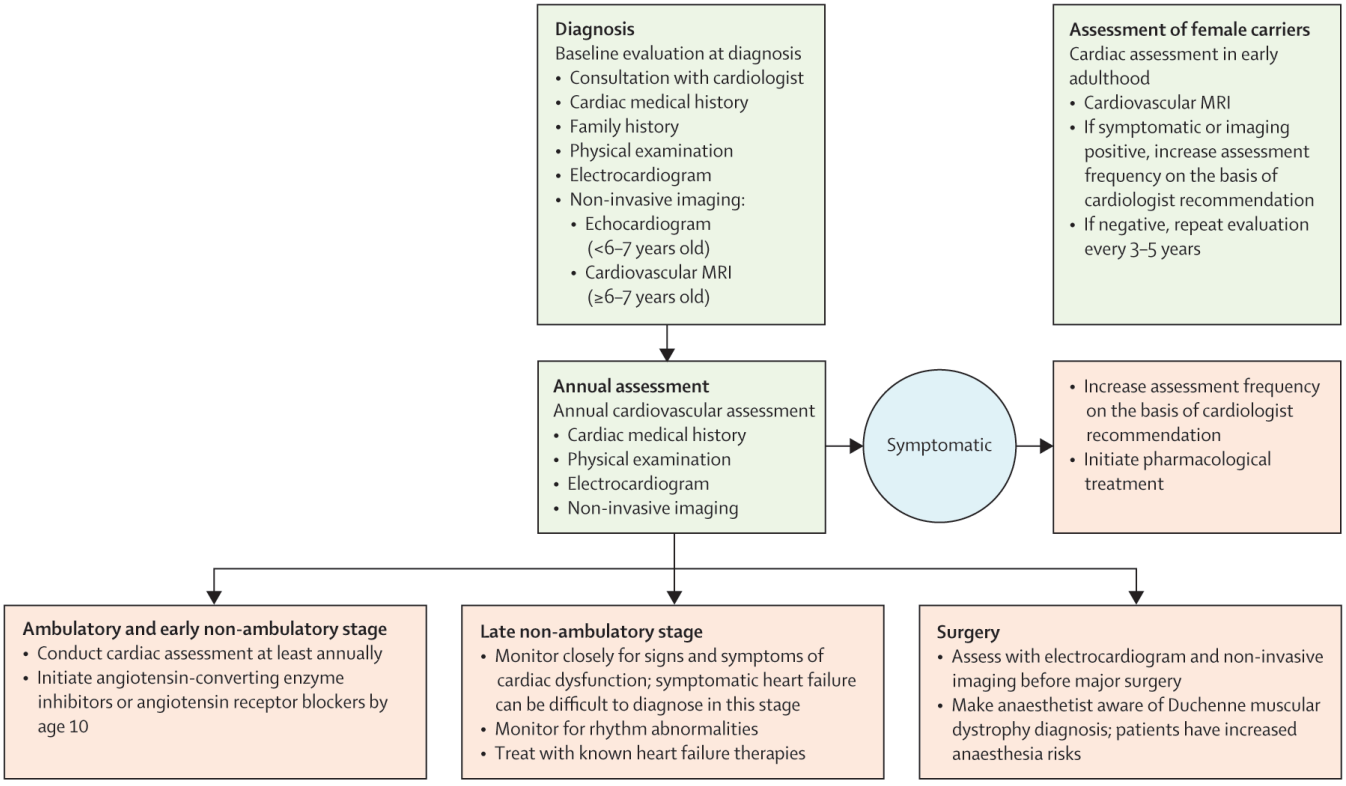


Figure 1[2] Surveillance, Assessment, and Management of the Cardiac Team

13. GASTROINTESTINAL MANAGEMENT

Nutrition, swallowing, and other gastrointestinal issues

You may need to see the following experts at different ages: a registered dietician nutritionist (RDN), physical therapist (PT), speech language pathologist (SLP), and a gastroenterologist. Gastrointestinal concerns for people living with Duchenne include: becoming overweight or underweight, chronic constipation, and difficulty swallowing (dysphagia).

NUTRITIONAL MANAGEMENT (FIGURE 12)

A registered dietician (RD) can help you to evaluate how many calories you need per day by calculating your resting energy expenditure (REE), using your height, age, and activity level.

- Maintaining good nutritional status will help to prevent both undernutrition and becoming overweight. This is essential from diagnosis throughout life
- It is important that your weight or body mass index (BMI) for age is kept between the 10th and 85th percentile on national percentile charts (see resource section)
- Eating a healthy, well-balanced diet with a full range of food types is necessary for maintaining a healthy body; information for the whole family on eating a well-balanced diet can be found from most national sources, including Dietary Guidelines for Americans (www.choosemyplate.gov/Dietary-Guidelines) and other reputable resources in your country
- You should pay extra attention to diet at diagnosis, when starting steroids, when loss of ambulation occurs, and when swallowing problems arise
- Your diet should also be assessed for calories, protein, fluid, calcium, vitamin D, and other nutrients each year
- Proper fluid intake is necessary for the prevention of dehydration, constipation, and renal (kidney) issues
- If there is too much weight gained, a decrease in calories and increase in safe physical activity is recommended
- Gastroparesis, or delayed stomach emptying, can occur as you get older, causing abdominal pain after eating, nausea, vomiting, loss of appetite, and feeling full quickly
- If you have an unexpected weight loss, it is important to consider that this may be a complication of issues in other systems (e.g. cardiac or respiratory)
- Issues with swallowing may also effect weight loss. Your nutritionist should work closely with speech-language pathologists to develop eating plans to help you to maintain or gain weight, develop diet changes that may be helpful for you during mealtimes, and decide when it may be necessary to evaluate your swallowing

SWALLOWING MANAGEMENT (FIGURE 12)

Weakness of the facial, jaw, and throat muscles can lead to swallowing problems (dysphagia), further accentuating nutritional issues. Dysphagia can also cause aspiration (bits of food or fluid going into the lungs) because of poor movement of the swallowing muscles, which can increase the risk of pneumonia. Dysphagia can often come on very gradually, meaning it can be difficult to spot. For this reason, swallowing symptoms need to be reviewed at every visit.

SYMPTOMS OF DYSPHAGIA:

- You may feel that there is food “stuck in the throat”
- You may have unintentional weight loss of 10 percent or more or unsatisfactory weight gain (if you are still growing)
- Your meal times may be prolonged (taking longer than 30 minutes) and/or mealtimes accompanied by fatigue, drooling, coughing, or choking
- An unexplained decline in pulmonary function or a fever of unknown origin may be signs of aspiration pneumonia or pneumonia caused by fluid going down into the lungs

DYSPHAGIA INTERVENTIONS:

- Clinical and X-ray tests of swallowing are necessary when these symptoms are seen
- In case of swallowing problems, a speech language pathologist (SLP) should be involved to help you to develop an individualized treatment plan with the goal of preserving good swallowing function
- Gastric tube placement may be discussed if efforts to maintain your weight and fluid intake by mouth seem insufficient
  - The potential risks and benefits of placing a G-tube should be discussed in detail
  - A gastrostomy tube may be placed several ways. You should discuss the surgical and anesthesia risks, as well as your personal preference, when making a decision

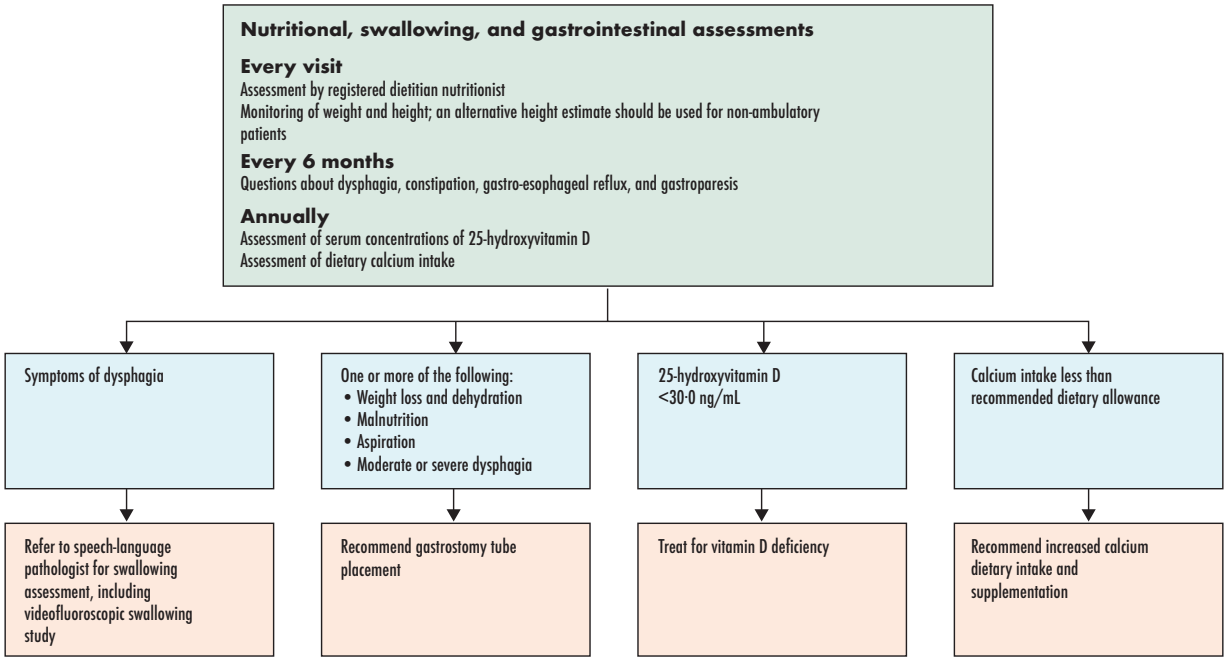


Figure 12[1] Nutritional, Swallowing, and Gastrointestinal Assessment and Management

- A G-tube provided at the right time can relieve the pressure of trying to eat enough food to maintain your calories
- If your swallowing muscles are strong, having a feeding tube does NOT mean you can't still eat the food you want to! It just takes away the stress of consuming enough calories and the other nutrients you need, as you can supplement nutrition with your G-tube

CONSTIPATION AND GASTROESOPHAGEAL REFLUX DISEASE (GERD)

Constipation and gastroesophageal reflux (acid coming from the stomach up into the throat, which causes heartburn) are the two most common gastrointestinal conditions seen in people living with Duchenne. Because constipation is a frequent complaint, and is often underreported, it is important to discuss bowel habits with your care team. Management of constipation can help avoid future complications that impact the bowel because of long-standing constipation.

- Laxatives and other medicines can be useful. Ask your primary care provider or neuromuscular team which laxatives are most appropriate for you and how long you should take them. All laxatives are not the same
- It is important that you are drinking enough fluid every day. Increasing fiber may make symptoms worse especially if fluids are not increased, so make sure that you review your dietary and fluid intake with a dietician at each visit, especially if you are having constipation
- Gastroesophageal reflux is typically treated with medicines that suppress gastric acids; these are commonly prescribed for people on steroid therapy or oral bisphosphonates
- Oral care is an important area for everyone, especially in those using bisphosphonates for bone loss. Expert recommendations for oral care are outlined in Box 5
- With jaw weakness, there may be fatigue with chewing that can result in decreased caloric intake

BOX 5. ORAL CARE RECOMMENDATIONS

- People living with Duchenne should, starting at a young age, see a dentist with extensive experience and detailed knowledge of the disease. The dentist's mission should be to strive for high-quality treatment, oral health, and wellbeing, and to function as a resource in your home community. This dentist should be aware of the specific differences in dental and skeletal development in people with Duchenne and collaborate with a well-informed and experienced orthodontist
- Oral and dental care are based on prophylactic measures with a view to maintaining good oral and dental hygiene
- Teaching parents and other caregivers how to brush teeth of another person is important, especially in Duchenne, where the large tongue and sometimes limited mouth opening makes it more difficult
- Individually adapted assistive devices and technical aids for oral hygiene are of particular importance when the muscular strength of the hands, arms, jaw, mouth, and neck begin to decrease or if contractures in the jaw are present

BOX 6. SPEECH AND LANGUAGE MANAGEMENT – THE DETAILS:

- There are well-documented patterns of speech and language deficit in Duchenne, including problems with language development, short-term verbal memory, and phonological processing, as well as a risk for impaired IQ and specific learning disorders
- These do not affect all people living with Duchenne but should be considered and interventions should be implemented if they are present
- Referral to a speech language pathologist (SLP) or therapist for speech and language evaluation and treatment is necessary if problems with speech and language are suspected
- Exercises for the muscles involved in speech and articulation may be appropriate and necessary for children with speech and language difficulties, as well as for older individuals who have weakening oral muscle strength and/or impaired speech intelligibility
- Compensatory strategies, voice exercises, and speech amplifications are appropriate if it becomes difficult to understand the person living with Duchenne due to problems with respiratory support
- Voice output communication aid (VOCA) assessment may be appropriate at any age if speech output is limited
- Language problems may lead to difficulties in school but can be helped with proper assessment and intervention

14. PSYCHOSOCIAL MANAGEMENT

Navigating the path of living with Duchenne can be complex, and psychosocial and emotional support are critical for both the person living with Duchenne and their families (box 7). Psychosocial issues can arise at any time. It is important that you let your neuromuscular team know if you are having issues with any of the things listed below.

- Difficulty with social interactions and/or making friendships (i.e., social immaturity, poor social skills, withdrawal, or isolation from peers)
- Learning problems
- Excessive or constant anxiety/worry
- Frequent arguing and behavioral outbursts; difficulty controlling your anger or sadness
- Increased risk of neurobehavioral and neurodevelopmental disorders, including autism-spectrum disorders, attention-deficit/hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD)
- Problems with emotional adjustment and anxiety and/or depression

Psychosocial and emotional issues are an important part of your health and should not be ignored. If you are having worries, concerns, or questions about your diagnosis, or anything else, it is important to get answers. You should be asked, formally or informally, about anxiety and depression at every neuromuscular visit and, if there are issues, you should be referred for evaluation and treatment as quickly as possible.

BOX 7. FOR FAMILIES

Parents who are open and willing to answer questions will make it easier for children to ask. It is important parents answer questions openly but in an age-appropriate manner, and answer just the question being asked (without elaborating). We realize that this can be a very difficult conversation to have. Advocacy groups and the staff at your clinic can offer help with information, guidance, and resources. The neuromuscuar team should know that children are reaching out and that support would be appreciated. They can help connect families with a medical provider most appropriate to help with delicate conversations.

While it is important for the individual with Duchenne to receive psychosocial and emotional support, this diagnosis affects the entire family. Parents and siblings may also be at risk for social isolation and depression. It is important that you tell your neuromuscular teams how your family is doing at each visit and, if you feel you could benefit from counseling, be sure to get referrals.

Several well-known interventions exist to help in various areas of psychotherapy. These include training for parents in trying to cope with behavior and conflicts, individual or family therapy, and behavioral interventions. Applied behavior analysis may help with certain behaviors related to autism.

ASSESSMENTS (FIGURE 13)

Your yearly psychosocial assessment should cover cognitive and language development, emotional adjustment, behavioral regulation, social skills, and all other areas of concern. While not every clinic will have direct access to all of the assessments and interventions listed, these recommendations can serve as a guide to your psychosocial care.

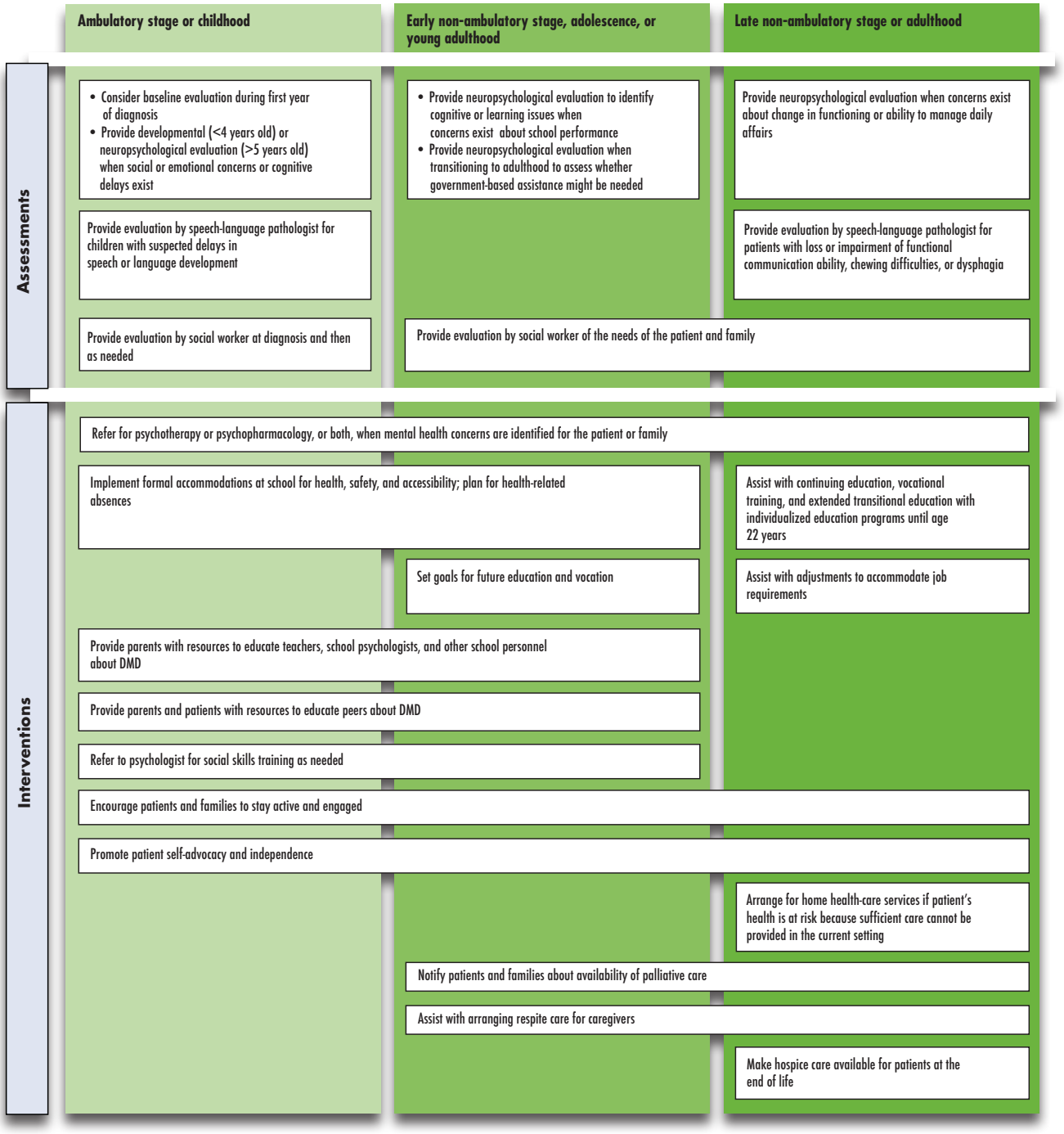


Figure 13[3] Psychosocial Assessment and Management

CARE & SUPPORT INTERVENTIONS

- A **neuromuscular care coordinator** is a crucial member of the team and can facilitate referrals to behavioral health clinicians, social workers, counselors, and palliative care specialists. If your team does not include a NM care coordinator, ask who you should contact for questions/concerns/emergencies between appointments
- It is important for you to help educate your school personnel about Duchenne so that they can be informed about your diagnosis and help to facilitate your access to everything that you need for your education, social participation, and future education and employment
- A special individualized plan for education (IEP) should be developed to address any potential learning problems that you may have and to modify activities that might otherwise prove harmful to your muscles (e.g. physical education), further reduce your energy or increase your fatigue (e.g. walking long distances to/from lunch), impair your safety (e.g. playground activities), and address your accessibility issues
- Promoting self-advocacy, independence, and involvement in decision making (in particular, as decisions relate to medical care) and getting used to assistants (other than parents) providing your care is necessary and of significant importance to promote autonomy (see Section 17)
- Developing social and learning skills will make it easier for you to find a job and be part of daily life in adulthood
- In addition to pain management (Box 4), palliative care teams may also be able to provide you with emotional and spiritual support, assist your family in arranging respite care if needed, clarifying treatment goals in making difficult medical decisions, facilitate communication between you and your medical team, and address issues related to grief, loss, and bereavement

PSYCHOTHERAPY AND DRUG INTERVENTIONS

If you are having issues related to anxiety or depression, you may benefit from the use of prescribed antidepressants. These medicines can be prescribed and monitored closely when these issues for which they are appropriate have been specifically diagnosed.

15. CONSIDERATIONS FOR SURGERY

There will be a variety of situations, both related to Duchenne (e.g. muscle biopsy, joint contracture surgery, spinal surgery, or gastrostomy) and unrelated to Duchenne (e.g. acute surgical events) when surgery and/or general anesthesia may be needed. If you are having surgery, there are a number of condition-specific issues that need to be taken into account for your safety.

Surgery should be done in a hospital where personnel involved in the operation and after care are familiar with Duchenne and willing to work together to be sure everything goes smoothly. **Stress dosing of steroids should be considered.** Guidelines for stress dosing can be found in the PJ Nicholoff Steroid Protocol at www.parentprojectmd.org/PJ.

All people living with Duchenne are at risk of rhabdomyolysis. Rhabdomyolysis occurs when there is a massive amount of muscle breakdown. This muscle breakdown releases myoglobin and potassium into the blood stream. Myoglobin is dangerous to the kidneys and can cause kidney failure; potassium can be dangerous to the heart. Because of the risk of rhabdomyolysis, there are specific concerns with anesthesia and Duchenne.

- **Succinycholate will cause rhabdomyolysis and should never be used**
- **Avoid inhaled anesthesia;** there is an increased risk of rhabdomyolysis using inhaled anesthesia
- IV anesthesias agents are usually safe
- Take caution using any anesthesia agents in Duchenne
- A list of anesthesias that are considered to be safe and unsafe can be found on the PPMD website at www.parentprojectmd.org/Surgery
- Remind your medical team that oxygen should be used with caution (see Section 11)
- Care in the use of opiates, other sedating medication, and muscle relaxants is essential – they may affect your breathing rate and depth, making breathing shallower and slower

Cardiac care

A cardiologist should be consulted before all surgical procedures
Anesthetists should be aware that patients with DMD are at risk of cardiac decompensation during surgery

Major surgical procedures
- Patients with DMD are at particular risk of cardiac compromise during major procedures
- Echocardiogram and electrocardiogram should be done in close proximity to any planned surgery

Minor surgical procedures
- In patients with normal cardiac function, a cardiac assessment is suggested if last investigation was >1 year before

Respiratory care

Preoperative training in and postoperative use of assisted cough techniques
- Cough techniques are necessary for patients with baseline peak cough flow <270 L/min or baseline maximum expiratory pressure <60 cm H_2O*

Preoperative training in and postoperative use of non-invasive ventilation
- Non-invasive ventilation is necessary for patients with baseline FVC <30% predicted
- Non-invasive ventilation is strongly recommended for patients with FVC <50% predicted

Extubation to supplemental oxygen alone without concomitant use of non-invasive ventilation should be avoided

Incentive spirometry is not indicated because it is potentially ineffective in patients with respiratory muscle weakness, and preferred alternatives are available

Anesthesia

Total intravenous anesthesia is strongly recommended
Depolarizing muscle relaxants, such as suxamethonium chloride, are absolutely contraindicated because of risk of fatal reactions

Risk of rhabdomyolysis and hyperkalaemia
- Patients with DMD are at risk of developing rhabdomyolysis with inhalational anesthetics or when given suxamethonium chloride
- Rhabdomyolysis complications are frequently confused with malignant hyperthermia

Blood loss

Hypotensive anesthetics to minimize blood loss are not recommended because of hemodynamic risk with cardiomyopathy in patients with DMD

Cell-saver technology, along with use of aminocarpoic acid or tanexamic acid, can be considered to help manage intraoperative blood loss

Postoperative anticoagulation with heparin or aspirin is not appropriate for patients with DMD

Compression stockings of sequential compression might be indicated for prevention of deep-vein thrombosis

Figure 14[2] Surgical Considerations in Duchenne

16. EMERGENCY CARE CONSIDERATIONS

If you find yourself needing to go to the hospital in an emergency situation, there are a range of factors that should be taken into account.

- Your primary care provider or NMS should call the hospital before you arrive. This will allow the hospital staff to receive, and appropriately care for you
- If you find yourself in the emergency room, be sure to call your NMS or neuromuscular team
- Your diagnosis of Duchenne, current medications, presence of any respiratory and cardiac complications, and the people who are your normal key medical team should be made clear to the admitting unit
- As many health professionals are not aware of the potential management strategies available for Duchenne, the current life expectancy and expected good quality of life should also be explained

EMERGENCY INFORMATION

Ideally, you should always carry an emergency card and have access to a brief medical summary provided by your NMS that includes your:

- Diagnosis
- List of medications
- Baseline medical status including the results of recent pulmonary and heart function studies
- Any past history of recurring medical problems (i.e. pneumonia, heart failure, kidney stones, gastroparesis [delayed stomach emptying])
- Brief discussion of initial assessment and management

There is also information about what to do during an emergency on the PPMD mobile app for smartphones (www.parentprojectmd.org/App), and may be available in other countries through local advocacy groups.

STEROIDS

Chronic daily steroid use needs to be made clear to the emergency room (ER) providers. Tell the ER staff how long you have been using daily steroids and if a dose(s) has been missed. It is also important to let the ER staff know if you have used steroids in the past, even if you aren't taking them now.

BOX 8. MAJOR POINTS OF EMERGENCY CARE:

1. Bring your emergency information card or download the PPMD App (www.parentprojectmd.org/App) or app available in your country, to use when talking to doctors, nurses, and hospital administration
2. Contact your NMS after the initial assessment to discuss disease management
3. Advise the emergency staff if you are taking steroids
4. If you can, bring copies of your most recent heart and pulmonary test results, such as FVC, ECG, and LVEF
5. If you have a cough assist device and/or breathing equipment (i.e. BiPAP), bring them with you to the hospital
6. If your oxygen level drops, the staff must be very careful giving oxygen without breathing support (ventilator). This can cause a situation where the urge to breathe is taken away (see Box 8)
7. If you have a broken bone, insist that they speak with your NMS or physical therapist. Watch for signs and symptoms of fat embolism syndrome (FES) (Section 9)

This may be important because:

- Steroids can decrease the body's response to stress, so extra stress doses of steroids may be needed in the ER
- Steroids can increase the risk of stomach ulceration; this should be considered by the ER staff
- Rarely, other steroid-related complications can present acutely and should be considered by the ER staff

HEART FUNCTION

- Recent test results about your heart function can be helpful (e.g. ECG, echo, or MRI results); bring those if you can
- Remind the ER staff that, for patients with Duchenne, the ECG is typically abnormal at all ages; bring a copy of your ECG with you if you can
- During acute illness, continuous cardiac monitoring may be needed to be sure there is not an issue with your heart rate or rhythm

BREATHING FUNCTION

- Recent test results about your respiratory function can be helpful (e.g., forced vital capacity or FVC); bring those if you can
- It is important to bring any equipment that you use (cough assist, BiPAP, etc.) with you to the hospital in case they do not have equipment for you to use. Insist that the ER staff use your equipment to assist in your care
- If you use a ventilator at home, the hospital's respiratory care team should be involved as soon as possible
- Care in the use of opiates, other sedating medication, and muscle relaxants is essential – they may affect your breathing rate and depth, making breathing shallower and slower (see Section 15)
- If anesthesia is needed, IV anesthesia should be used and inhaled anesthesia should be avoided; succinylcholine is strictly contraindiciated in Duchenne and should not be given (see Section 15)

Breathing and coughing muscles are further weakened when you are ill, and the risk of these complications dramatically increases. Thus, if you have significantly weak breathing muscles:

- Antibiotics may be needed for chest infections
- Breathing support with a non-invasive ventilator is likely to be needed or needed for longer than usual
- If oxygen is needed, use caution (see Box 9)
- Continuous use of non-invasive ventilation while awake, interrupted as necessary for frequent assisted cough, should be a standard approach to respiratory illnesses in the emergency room

BOX 9. OXYGEN – CAUTION!

- We all breathe to inhale oxygen (O2) AND exhale carbon dioxide (CO2)
- If you have reduced pulmonary function, giving oxygen may reduce the body's drive to breathe and lead to high levels of carbon dioxide (called "CO2 retention" or "respiratory acidosis"). This can be dangerous, and may even be life threatening. Giving supplemental oxygen should be done with extreme caution and carbon dioxide should be monitored
- Blood levels of carbon dioxide should be checked if oxygen saturation in the blood (measured by finger pulse oximetry) has decreased to <95 percent. If the carbon dioxide in the blood is elevated, manual and mechanically assisted cough and non-invasive breathing support are necessary
- If oxygen is needed, it should be given with non-invasive ventilation (bi-level positive pressure ventilation) and with blood CO2 carefully monitored

BROKEN BONES

People living with Duchenne are at risk of broken bones. Breaking a leg bone may make it difficult to walk again, especially if walking was becoming more difficult before the break. Let your neuromuscular team, especially your physical therapist, know if there is a fracture so they can talk to the surgeons if necessary.

- Surgical fixation, if it is appropriate for your fracture, is often a better option than a cast for a broken leg if someone is still walking (weight bearing is often sooner with surgical fixation than casting)
- Input from a physical therapist is crucial to make sure you get back on your feet as soon as possible
- If the broken bone is one of the vertebrae (backbones) and there is pain in your back, input from your bone doctor or endocrinologist is needed to provide the right treatment (see Section 9)

Fat embolism syndrome (FES) is a risk in Duchenne and presents a medical emergency (see Section 9). **Immediately let the emergency staff know that you suspect a fat embolism**. Symptoms of FES include:

- Confusion and/or disorientation
- "Not acting like yourself"
- Rapid breathing and heart rate
- Shortness of breath

17. TRANSITION OF CARE

As you prepare for greater independence, your health and care needs must be considered. Typically, the ability to achieve your desired level of independence requires careful and ongoing planning.

TIMING OF TRANSITION PLANNING

Beginning in early childhood, providers, educators, and parents should start to include you in your health care and future planning. In many cases, aging into

adulthood may require that you transition some – or all – of your medical providers. You and your family should start to consider plans for your health care transition (from pediatric to adult neuromuscular care) by age 12, with initiation of transition discussions and planning by at least age 13 to 14.

- Your plan should include what services need to be provided, who will provide them, and how they will be financed
- Your transition plan should be based on the needs, wants, and values that you and your family feel are important
- Your plan should include the outcomes that you feel are important in four areas: employment/education (what you want to do), independent living (where you would most like to live and with whom), health (based on your personal priorities), and social inclusion (how you would like to stay active with your friends and in your community)
- Financial planning should include a long-term financial plan
- Legal planning for when you are 18 and older should be included. This may differ by country, but in the US includes a discussion of legal guardianship or conservatorship (someone else would be your "guardian" or "conservator" and would make legal decisions for you) and healthcare power of attorney (you would give someone the power to make decisions about your health care if you could not)

CARE COORDINATION (FIGURE 15)

A care coordinator and/or social worker can serve as a central resource for any questions you may have about managing health and caregiving related to Duchenne. Care coordinators help to facilitate communication between your neuromuscular team, primary care providers, family, and community, and can help anticipate your health care needs and connect you to resources to meet those needs. Often, they can assist with navigating benefits and acquiring equipment and resources. Without care coordination and social work involvement, care can become fragmented, recommendations unheeded, and needs unmet.

HEALTH CARE

Transition planning should include a plan for continuity of care with pediatric providers until adult care is established. The transition coordinator should help facilitate your own self-management of your health care, facilitate referrals to appropriate adult providers, and ensure that there is a transfer of medical records.

- From an early age, you should be encouraged to participate in discussions about your health and eventually (~age 14 years old) have alone time with providers
- As you begin to show an interest and ability to advocate for yourself about care and needs, then you are ready to begin to move from family-centered pediatric to patient-centered adult interactions
- Sensitive topics are more common in your adolescent and young adult years and may include discomfort, anxiety, coping, and loss, and should be assessed and addressed with professionals. Discussing these topics out in the open with your neuromuscular team will allow your team to work with you to access additional medical or supportive services that you may need
- It is important for you to communicate your personal values and preferences about health with your neuromuscular team. Parents and providers can help you in advance care planning as you begin to consider critical medical care choices into adult life

EDUCATION, EMPLOYMENT, AND PERSUIT OF VOCATIONS

Education and vocation planning following high school takes detailed attention. School personnel, vocation counseling services, and formal transition clinics may be able to offer you additional guidance. Not everyone seeks additional education beyond high school. Your particular strengths and talents should be cataloged to create a program of daily activities that are meaningful and rewarding for you.

- Education planning meetings should occur at least annually starting around age 13 and include assessment of your personal strengths and interests with focus on your needs and goals
- Establishing a plan that balances your medical needs and a time for rest with practical issues involving school attendance and academic standards/work demands is important
- It is important to identify resources for access of necessary equipment and technology that you will need, as well as methods of transportation
- Empowering you to lead a productive, rewarding, and meaningful life, in whatever capacity possible, is critical

HOUSING AND ASSISTANCE WITH ACTIVITIES OF DAILY LIVING

As you move from adolescence into young adulthood, you should explore desired levels of independent living, as well as the resources and supports needed to facilitate optimal independence. Activities of daily living are supported by family members when you are younger, but as you mature, it is more common for you to begin to enlist caregivers from outside the family. Hired attendants or para-educators at school can provide assistance with hygiene, meals, transfers, as well as health care interventions. Home care agencies can often provide licensed services for more advanced health care needs. Please ask your neuromuscular team what services are available for teens/adults living in your country.

As a result of the complex and often fragmented nature of disability benefits systems, you may require financial counseling and understanding that is above and beyond that required of those without disabilities. Your neuromuscular team, particularly social workers, will help educate you and your family about private insurance, state or regional programs, and national social support systems.

If you are thinking about living independently, there are some options you may wish to consider:

- A residential setting may include living in a family home, living on campus during academic studies, in group home or organized facility, or in a home or apartment with or without a roommate
- Home modifications and accommodations may be needed for accessibility (consult with experts, understand laws and rights, financial resources, assistive technology options)
- You may need assistance with personal care and activities of daily living (hired PCAs vs family care providers, availability of providers, funding resources, management and training of care providers)

TRANSPORTATION

Transportation issues may affect your autonomy and independence, your opportunities for employment and education, and your involvement in social activities. Your neuromuscular team should discuss your options for safe transportation including:

- Independent driving with vehicle modifications
- Modifications to family-owned vehicles
- Public transportation

PERSONAL RELATIONSHIPS

- Social connections are critically important for ensuring health, well-being, and quality of life
- Sometimes opportunities for personal contact and social engagement happen less naturally and require more of an intentional effort to foster and facilitate social connections. Many social groups exist for teens and adults with Duchenne and can be found through contacting major advocacy organizations. Your social worker may have a list of social groups that you may be interested in as well
- Dating, intimacy, and sexuality are high-priority topics among some people living with Duchenne. Try starting these discussions around relationships, dating, sexual orientation, and marriage with a trusted friend or family member. They may also be able to talk to you about troubleshooting barriers to developing social relationships and participating in social events. Talking with someone on your neuromuscular team may be helpful as well
- During routine primary care and specialty appointments, you should have someone on your neuromuscular team that you feel comfortable asking about masturbation, having sex with a partner, parenting children, or other intimate topics. When appropriate, getting guidance, together with your partner, from a marriage or relationship therapist may be helpful

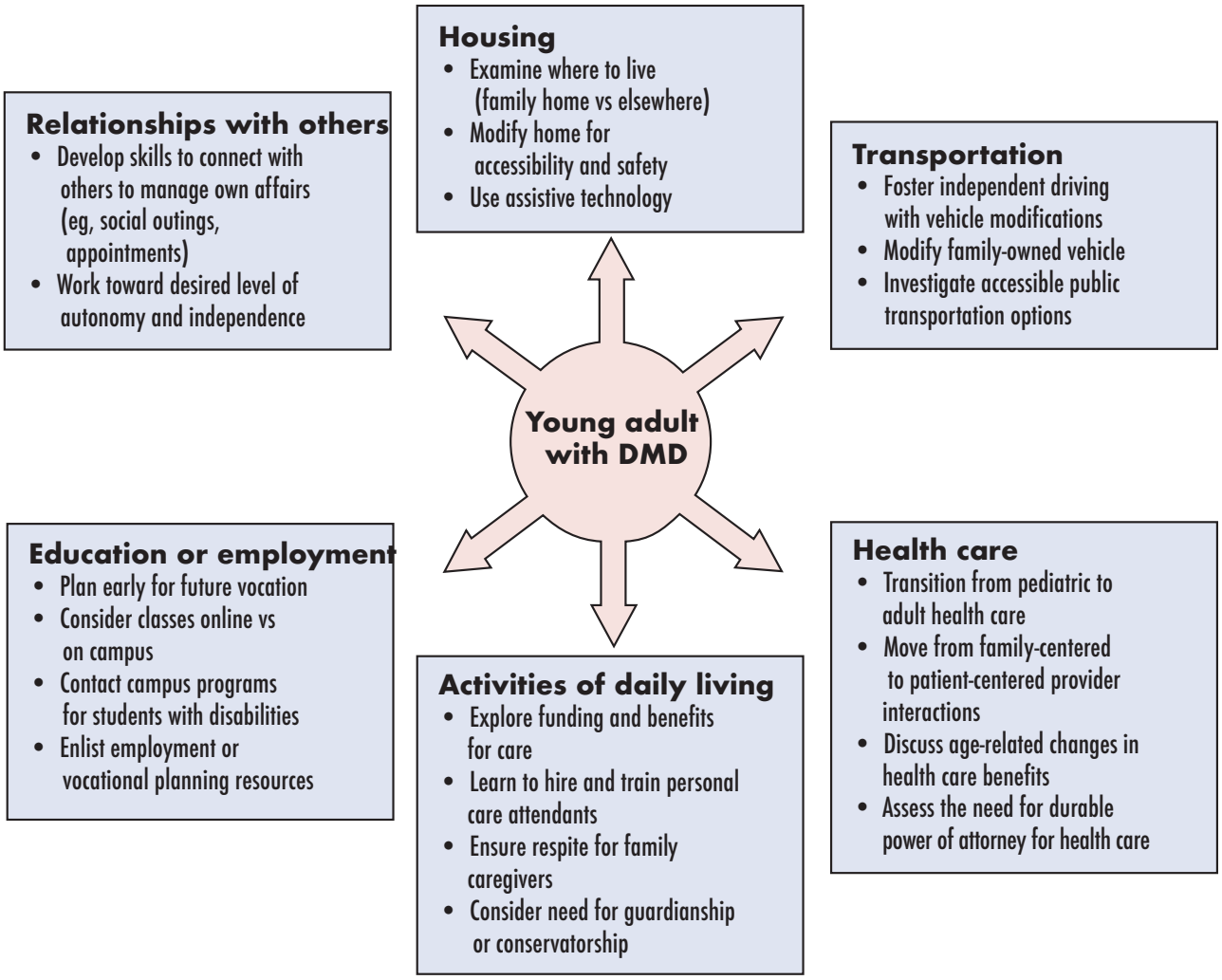


Figure 15[3] Considerations for Adults Living with Duchenne

CONCLUSION

We hope that this guide is helpful as you move through your journey of living with Duchenne. Always remember that there are advocacy groups, neuromuscular centers and teams, families, and friends who are here to support you every step of the way. Reaching out is always the hardest, but the first, step. You are not alone in this journey.

www.mda.org

www.parentprojectmd.org

www.treat-nmd.eu

www.worldduchenne.org

Photos provided by Parent Project Muscular Dystrophy. Photo credit: Rick Guidotti, Positive Exposure.

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