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Management of DMD patients

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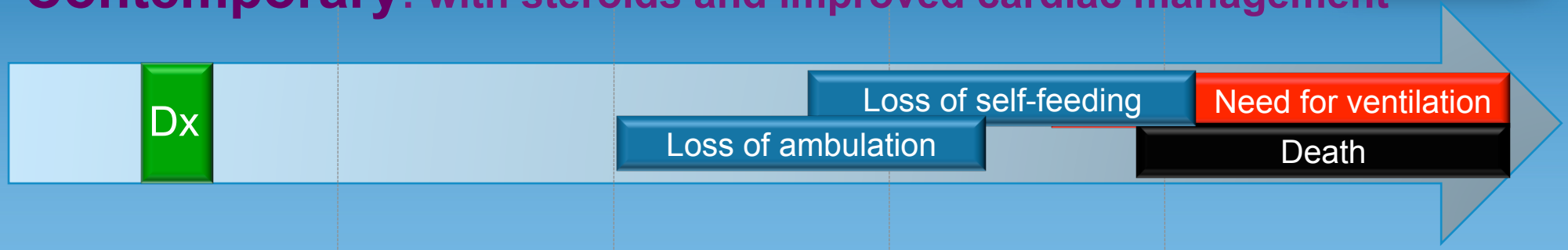
DMD in 2018

#stoconNEMO

New natural history of DMD

5 years 9 years 14 years 20 years

Contemporary: with steroids and improved cardiac management



Functional gains

Functional decline of upper limb function

Functional decline of ambulation

Novel clinical endpoints in DMD

- **6MWT**
- **Northstar ambulatory assessment**
- **9-hole peg test**
- **Patient-reported outcomes: NeuroQOL and neuromuscular module of PedsQL**

Very young Ambulant DMD Non ambulant

DMD in 2018

- Late survivors (psychosocial, mental, independence..)
- Long-term effects of glucocorticoids
- Earlier diagnosis
- New treatment options

DMD SOC 2018

Why?

What's new?

Implementation challenges

DMD care considerations 2018

Birnkrant DJ et al. Lancet Neurol 2018; 17: 251–67, 347–61, 445–55

Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management

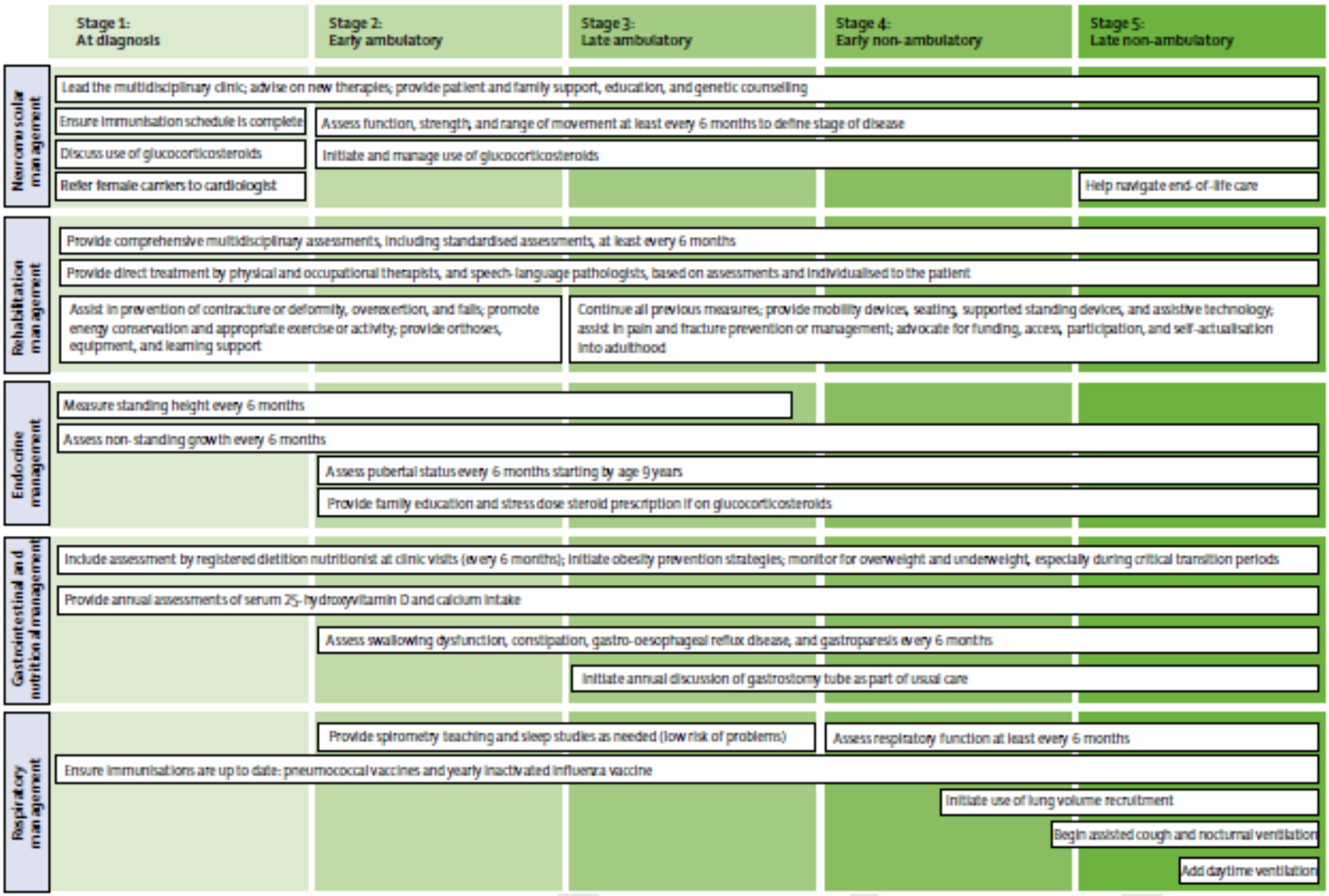
*David J Birnkrant, Katharine Bushby, Carla M Bann, Susan D Apkon, Angela Blackwell, David Brumbaugh, Laura E Case, Paula R Clemens, Stasia Hadjiyannakis, Shree Pandya, Natalie Street, Jean Tomezsko, Kathryn R Wagner, Leanne M Ward, David R Weber, for the DMD Care Considerations Working Group**

Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management

Diagnosis and management of Duchenne muscular dystrophy, part 3: primary care, emergency management, psychosocial care, and transitions of care across the lifespan

DMD care considerations 2018

- 11 topics (8 in 2010) + 3 new topics
  1. primary care and emergency
  2. endocrine management
  3. transitions of care
- Not EBM but expert opinion and consensus


Stage 1: At diagnosis
Stage 2: Early ambulatory
Stage 3: Late ambulatory
Stage 4: Early non-ambulatory
Stage 5: Late non-ambulatory
Neuromuscular management
Lead the multidisciplinary clinic; advise on new therapies; provide patient and family support, education, and genetic counselling
Ensure immunisation schedule is complete
Assess function, strength, and range of movement at least every 6 months to define stage of disease
Discuss use of glucocorticosteroids
Initiate and manage use of glucocorticosteroids
Refer female carriers to cardiologist
Help navigate end-of-life care
Rehabilitation management
Provide comprehensive multidisciplinary assessments, including standardised assessments, at least every 6 months
Provide direct treatment by physical and occupational therapists, and speech-language pathologists, based on assessments and individualised to the patient
Assist in prevention of contracture or deformity, overexertion, and falls; promote energy conservation and appropriate exercise or activity; provide orthoses, equipment, and learning support
Continue all previous measures; provide mobility devices, seating, supported standing devices, and assistive technology; assist in pain and fracture prevention or management; advocate for funding, access, participation, and self-actualisation into adulthood
Endocrine management
Measure standing height every 6 months
Assess non-standing growth every 6 months
Assess pubertal status every 6 months starting by age 9 years
Provide family education and stress dose steroid prescription if on glucocorticosteroids
Gastrointestinal and nutritional management
Include assessment by registered dietitian nutritionist at clinic visits (every 6 months); initiate obesity prevention strategies; monitor for overweight and underweight, especially during critical transition periods
Provide annual assessments of serum 25-hydroxyvitamin D and calcium intake
Assess swallowing dysfunction, constipation, gastro-oesophageal reflux disease, and gastroparesis every 6 months
Initiate annual discussion of gastrostomy tube as part of usual care
Respiratory management
Provide spirometry teaching and sleep studies as needed (low risk of problems)
Assess respiratory function at least every 6 months
Ensure immunisations are up to date: pneumococcal vaccines and yearly inactivated influenza vaccine
Initiate use of lung volume recruitment
Begin assisted cough and nocturnal ventilation
Add daytime ventilation

	Stage 1: At diagnosis	Stage 2: Early ambulatory	Stage 3: Late ambulatory	Stage 4: Early non-ambulatory	Stage 5: Late non-ambulatory
Cardiac management	Consult cardiologist; assess with electrocardiogram and echocardiogram* or cardiac MRI†	Assess cardiac function annually; initiate ACE inhibitors or angiotensin receptor blockers by age 10 years	Assess cardiac function at least annually, more often if symptoms or abnormal imaging are present; monitor for rhythm abnormalities Use standard heart failure interventions with deterioration of function		
Bone health management		Assess with lateral spine x-rays (patients on glucocorticosteroids: every 1–2 years; patients not on glucocorticosteroids: every 2–3 years) Refer to bone health expert at the earliest sign of fracture (Genant grade 1 or higher vertebral fracture or first long-bone fracture)			
Orthopaedic management	Assess range of motion at least every 6 months Refer for orthopaedic surgery if needed (rarely necessary)	Monitor for scoliosis annually Refer for surgery on foot and Achilles tendon to improve gait in selected situations		Monitor for scoliosis every 6 months Consider intervention for foot position for wheelchair positioning; initiate intervention with posterior spinal fusion in defined situations	
Psychosocial management	Assess mental health of patient and family at every clinic visit and provide ongoing support Provide neuropsychological evaluation/interventions for learning, emotional, and behavioural problems	Assess educational needs and available resources (individualised education programme, 504 plan); assess vocational support needs for adults Promote age-appropriate independence and social development			
Transitions	Engage in optimistic discussions about the future, expecting life into adulthood	Foster goal setting and future expectations for adult life; assess readiness for transition (by age 12 years)	Initiate transition planning for health care, education, employment, and adult living (by age 13–14 years); monitor progress at least annually; enlist care coordinator or social worker for guidance and monitoring Provide transition support and anticipatory guidance about health changes		

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DIAGNOSIS & MANAGEMENT: Part 1

- Diagnosis
- Neuromuscular
- Rehabilitation
- Endocrine
- GI

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DMD: the diagnosis

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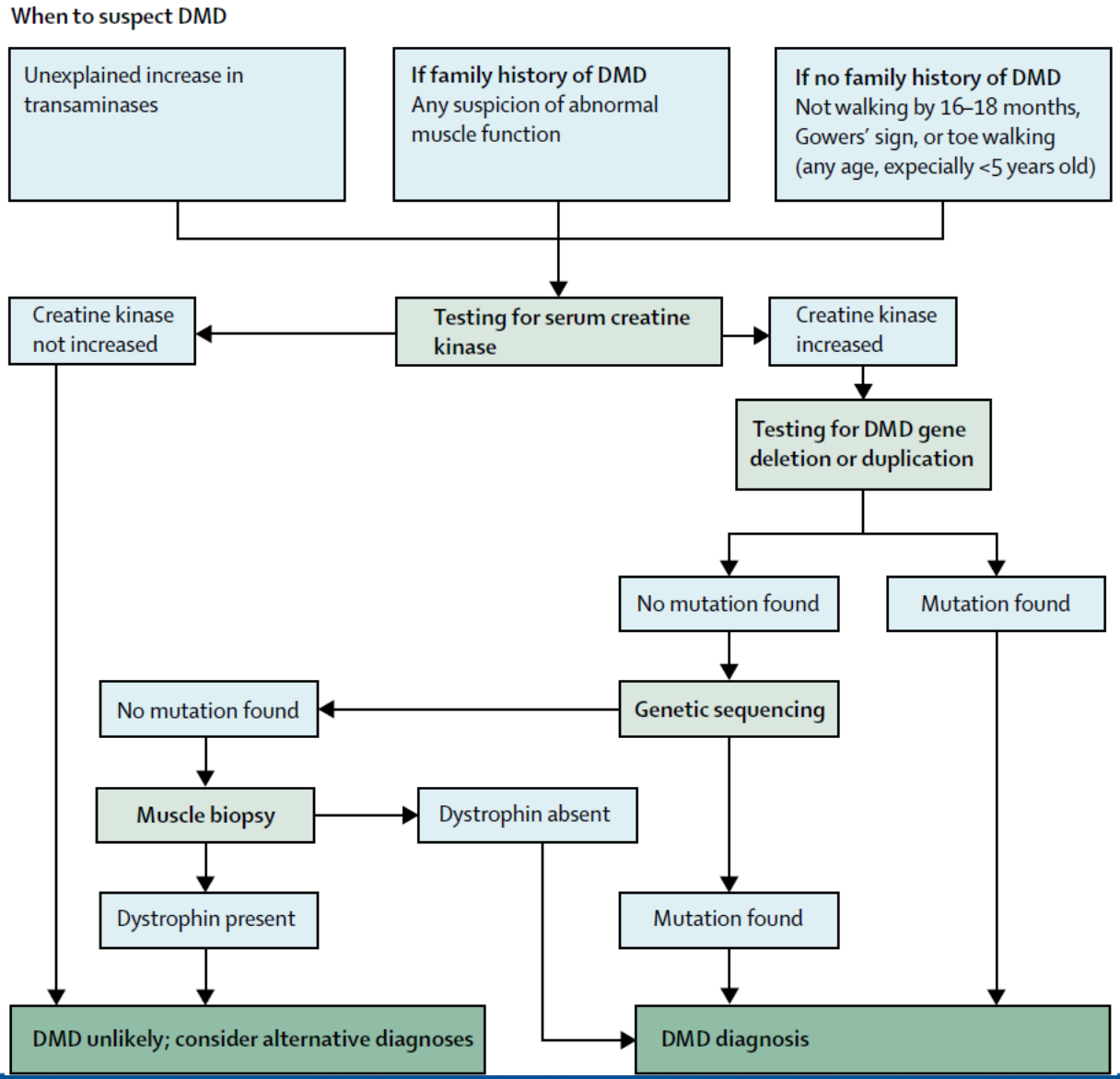

Most commonly observed early signs and symptoms in patients with DMD

Motor

- Abnormal gait
- Calf pseudohypertrophy
- Inability to jump
- Decreased endurance
- Decreased head control when pulled to sit
- Difficulty climbing stairs
- Flat feet
- Frequent falling or clumsiness
- Gowers' sign on rising from floor
- Gross motor delay
- Hypotonia
- Inability to keep up with peers
- Loss of motor skills
- Muscle pain or cramping
- Toe walking
- Difficulty running or climbing

Non-motor

- Behavioural issues
- Cognitive delay
- Failure to thrive or poor weight gain
- Learning and attentional issues
- Speech delay or articulation difficulties

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Rehabilitation assessments and interventions

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

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

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)

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.

Care considerations for glucocorticoid (steroid) initiation and use for patients with DMD

Timeline and dosing

Initial discussion
Discuss use of steroids with family

Begin steroid regimen
- Before substantial physical decline
- After discussion of side-effects
- After nutrition consultation

Recommended starting dose
- Prednisone or prednisolone 0·75 mg/kg per day
  OR
- Deflazacort 0·9 mg/kg per day

Dosing changes
If side-effects unmanageable or intolerable
- Reduce steriods by 25–33%
- Reassess in 1 month

If functional decline
- Increase steroids to target dose per weight on the basis of starting dose
- Reassess in 2–3 months

Use in non-ambulatory stage
- Continue steroid use but reduce dose as necessary to manage side-effects
- Older steroid-naive patients might benefit from initiation of a steroid regimen

Cautions

Adrenal insufficiency
Patient and family education
- Educate on signs, symptoms, and management of adrenal crisis

Prescribe intramuscular hydrocortisone for administration at home
- 50 mg for children aged <2 years old
- 100 mg for children aged ≥2 years old and adults

Stress dosing for patients taking >12 mg/m² per day of prednisone/deflazacort daily
- Might be required in the case of severe illness, major trauma, or surgery
- Administer hydrocortisone at 50–100 mg/m² per day

Do not stop steroids abruptly
- Implement PJ Nicholoff steroid-tapering protocol
- Decrease dose by 20–25% every 2 weeks
- Once physiological dose is achieved (3 mg/m² per day of prednisone or deflazacort) switch to hydrocortisone 12 mg/m² per day divided into three equal doses
- Continue to wean dose by 20–25% every week until dose of 2·5 mg hydrocortisone every other day is achieved
- After 2 weeks of dosing every other day, discontinue hydrocortisone
- Periodically check morning CRH-stimulated or ACTH-stimulated cortisol concentration until HPA axis is normal
- Continue stress dosage until HPA axis has recovered (might take 12 months or longer)

Adrenal insufficiency
Patient and family education
• Educate on signs, symptoms, and management of
adrenal crisis
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PLOS | CURRENTS MUSCULAR DYSTROPHY

The PJ Nicholoff Steroid Protocol for Duchenne and Becker Muscular Dystrophy and Adrenal Suppression

June 27, 2017 · *Advanced Diagnostics and Biomarkers*

Medical/Surgical Stress	Corticosteroid Dosage DOS*	Postoperative Taper Regimen
Minor (local anesthesia, < 1 hour) (e.g. inguinal hernia, single tooth extraction, colonoscopy), mild febrile illness, mild, nausea/vomiting, mild diarrhea)	25mg or 30-50 mg/m2 po (if able to take po) or IV hydrocortisone (HC) or equivalent	None Resume maintenance physiologic dose of hydrocortisone when illness, pain or fever subsides
Moderate (e.g. multiple teeth extraction, fracture, pneumonia)	50mg or 50-75 mg/m2 IV hydrocortisone or equivalent	25 mg Q 8 or 50-75 mg/m2/day ÷ q 6 hours X 24 hour. Taper to baseline over 1-2 days.
Major (e.g. Septic shock, multiple trauma/fractures or severe burns, severe systemic infections, major surgery, pancreatitis, orthopedic surgery including open reduction, spinal fusion, etc.)	100mg or 100 mg/m2/dose IV hydrocortisone or equivalent	50 mg IV Q 8 or 100 mg/m2/day ÷ q 6 hours X 24-48hours. Taper to baseline over 1-3 days (continue stress dose if the physical stress (fever or pain) continues).

Table 2: Corticosteroid Stress Dosing

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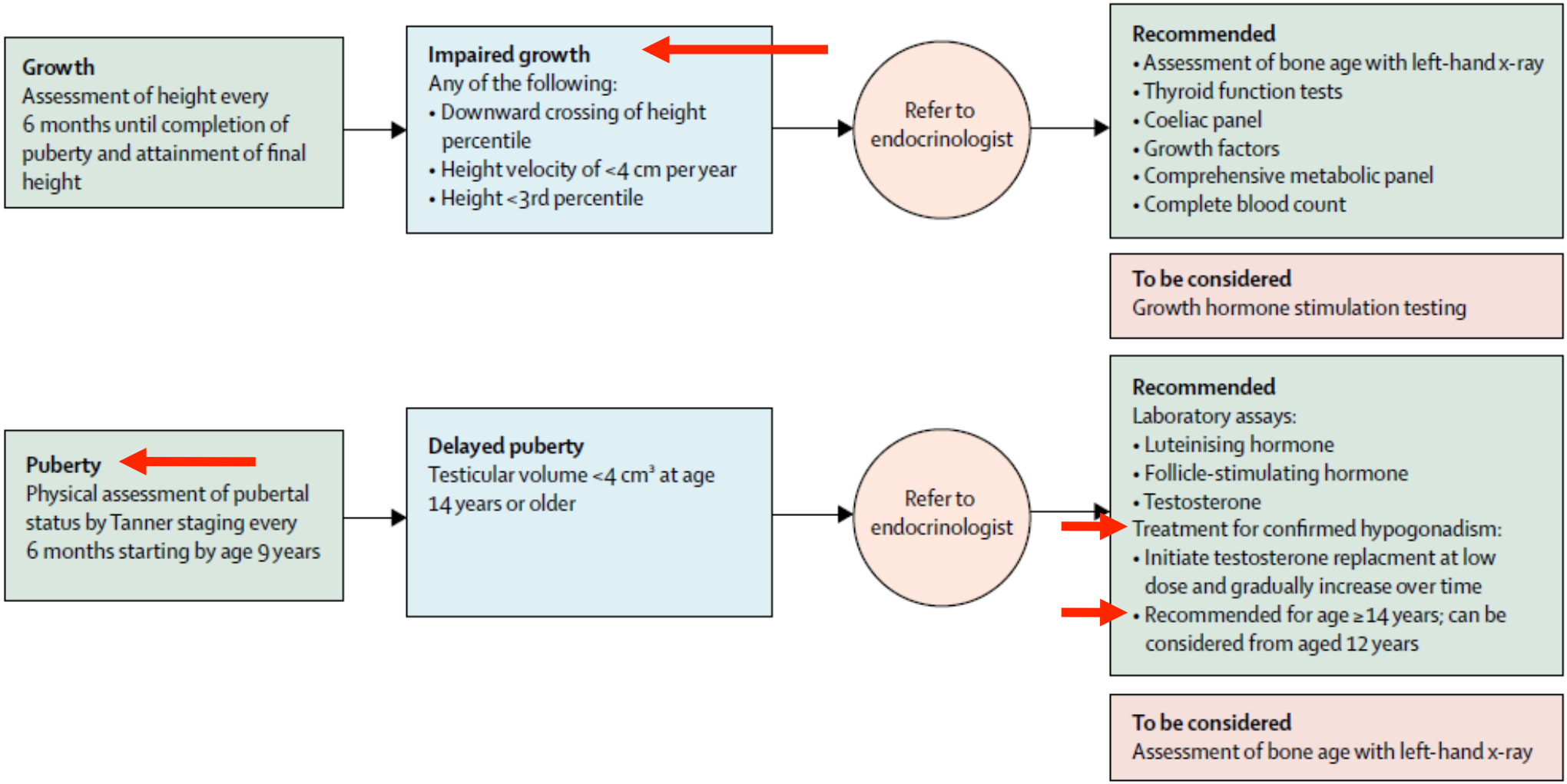
Interventions for impaired growth and delayed puberty in MD

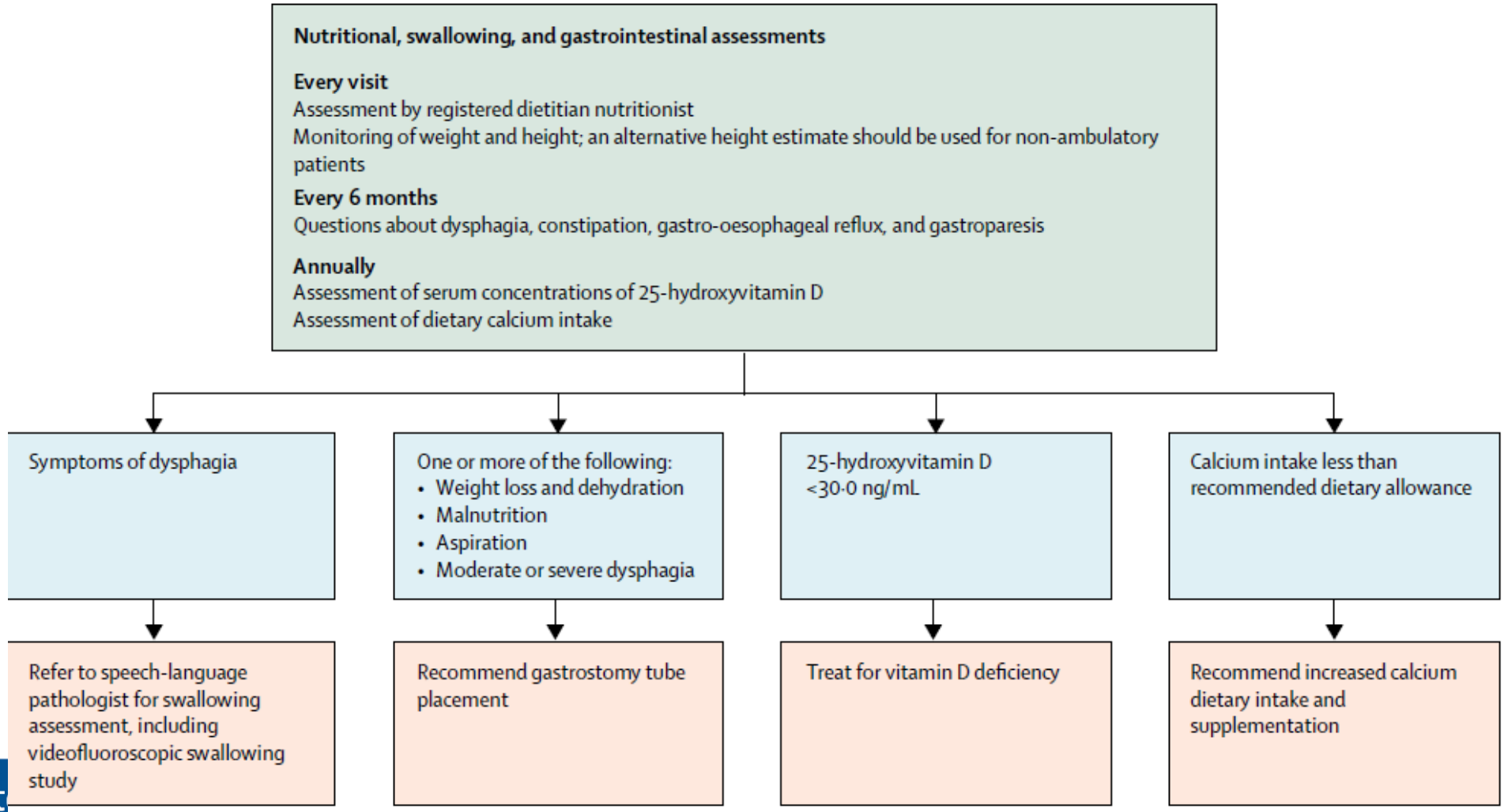


Interventions for delayed puberty in MD

- Delayed puberty due to hypogonadism complication of glucocorticoid therapy
- **Absence of pubertal development by age 14 years -prompt referral to an endocrinologist**
- Biochemical testing - diagnosis of hypogonadism

- **Testosterone replacement therapy** is recommended
  - to treat confirmed hypogonadism in patients older than 14 years
  - can be considered in boys older than 12 years on glucocorticoids with absent pubertal development.

Assessments and interventions for nutritional, swallowing, & GI in DMD



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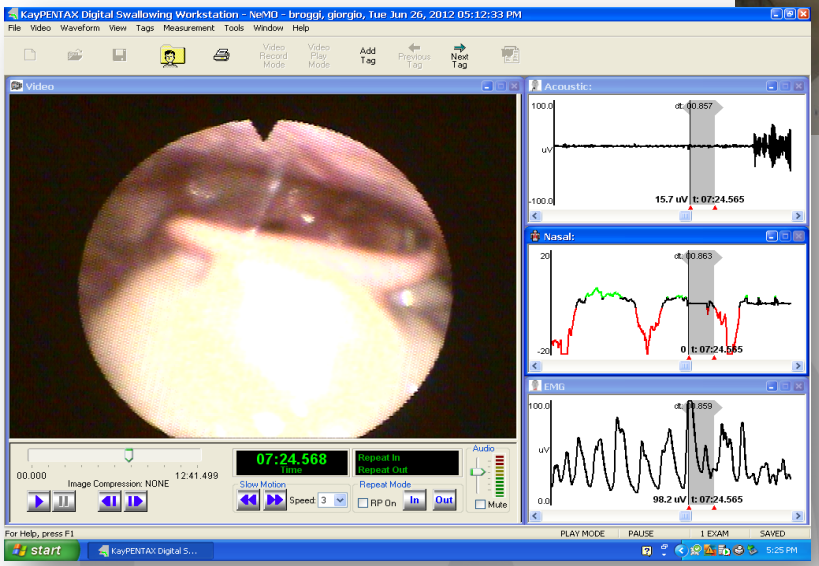

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DIAGNOSIS & MANAGEMENT: Part 2

- Heart
- Lungs
- bone

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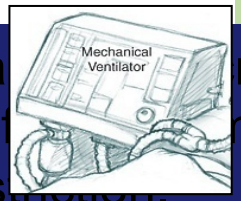
Respiratory care in DMD

	Ambulatory stage	Early non-ambulatory stage	Late non-ambulatory stage
Assessments	Once yearly: FVC	Twice yearly: FVC, MIP/MEP, PCF, SpO_2, $p_{et}CO_2/p_{tc}CO_2$	
	Sleep study* with capnography for signs and symptoms of obstructive sleep apnoea or sleep-disordered breathing		
Interventions	Immunisation with pneumococcal vaccines and yearly inactivated influenza vaccine		
		Lung volume recruitment when FVC ≤60% predicted	
		Assisted coughing when FVC <50% predicted, PCF <270 L/min, or MEP <60 cm H_2O†	
		Nocturnal assisted ventilation with back-up rate of breathing (non-invasive preferred) when there are signs or symptoms of sleep hypoventilation or other sleep-disordered breathing,‡ abnormal sleep study,* FVC <50% predicted, MIP <60 cm H_2O, or awake baseline SpO_2 <95% or pCO_2 >45 mm Hg	
			Addition of assisted daytime ventilation when, despite nocturnal ventilation,§ daytime SpO_2 <95%, pCO_2 >45 mm Hg, or symptoms of awake dyspnoea are present



"A a r tients with DMD de ti n st walls and lung volume restriction.

To preserve lung compliance, **lung volume recruitment is indicated when FVC is 60% predicted or less**, achieved with a self-inflating manual ventilation bag or mechanical insufflation– exsufflation device to provide deep lung inflation once or twice daily"

suffla

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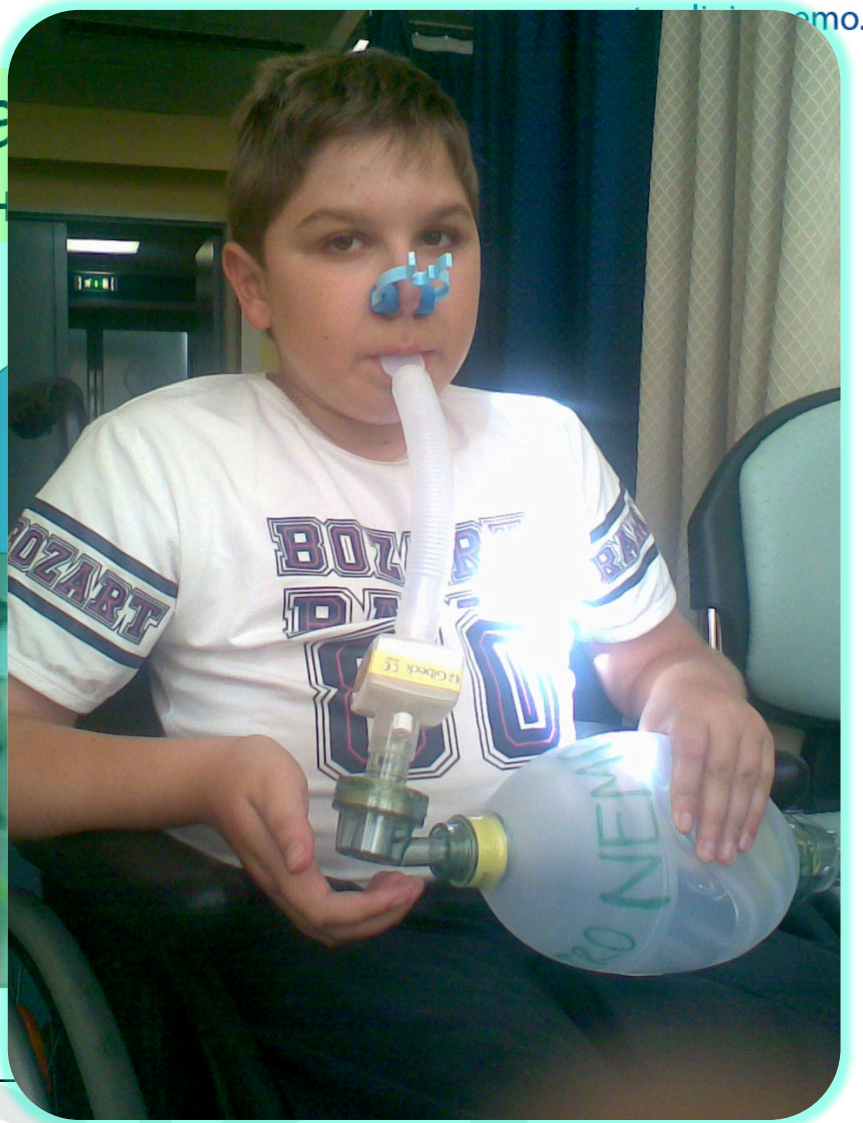


Respiratory care in DMD

Late non-ambulatory stage

weak cough - risk of atelectasis, pneumonia, ventilation–perfusion mismatch, and progression to respiratory failure, especially during respiratory tract infections.

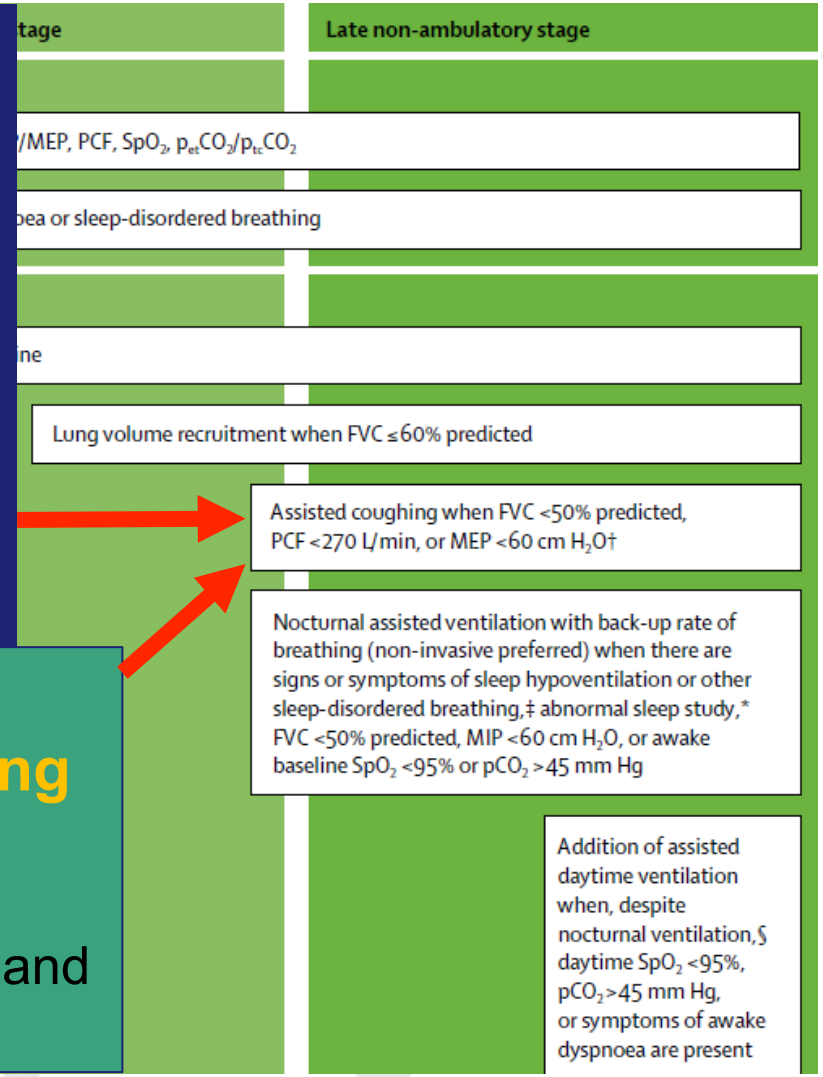
Treatment - **manual and mechanically assisted coughing indicated when:**

•FVC is less than 50% predicted,

•peak cough flow <270 L/min,

•maximum expiratory pressure < 60 cm H2O

- Advise having a **home pulse oximeter for individuals treated with assisted coughing** during respiratory infections.
- When SpO2 < 95% on room air, the frequency of assisted coughing should be increased to prevent and treat mucus plugging, atelectasis, and pneumonia



Ventilation via tracheostomy or non-invasively (NIV) ?

Clinical experience supports the use of NIV for up to 24 h/day

Strongly endorse the use of NIV in most clinical situations.

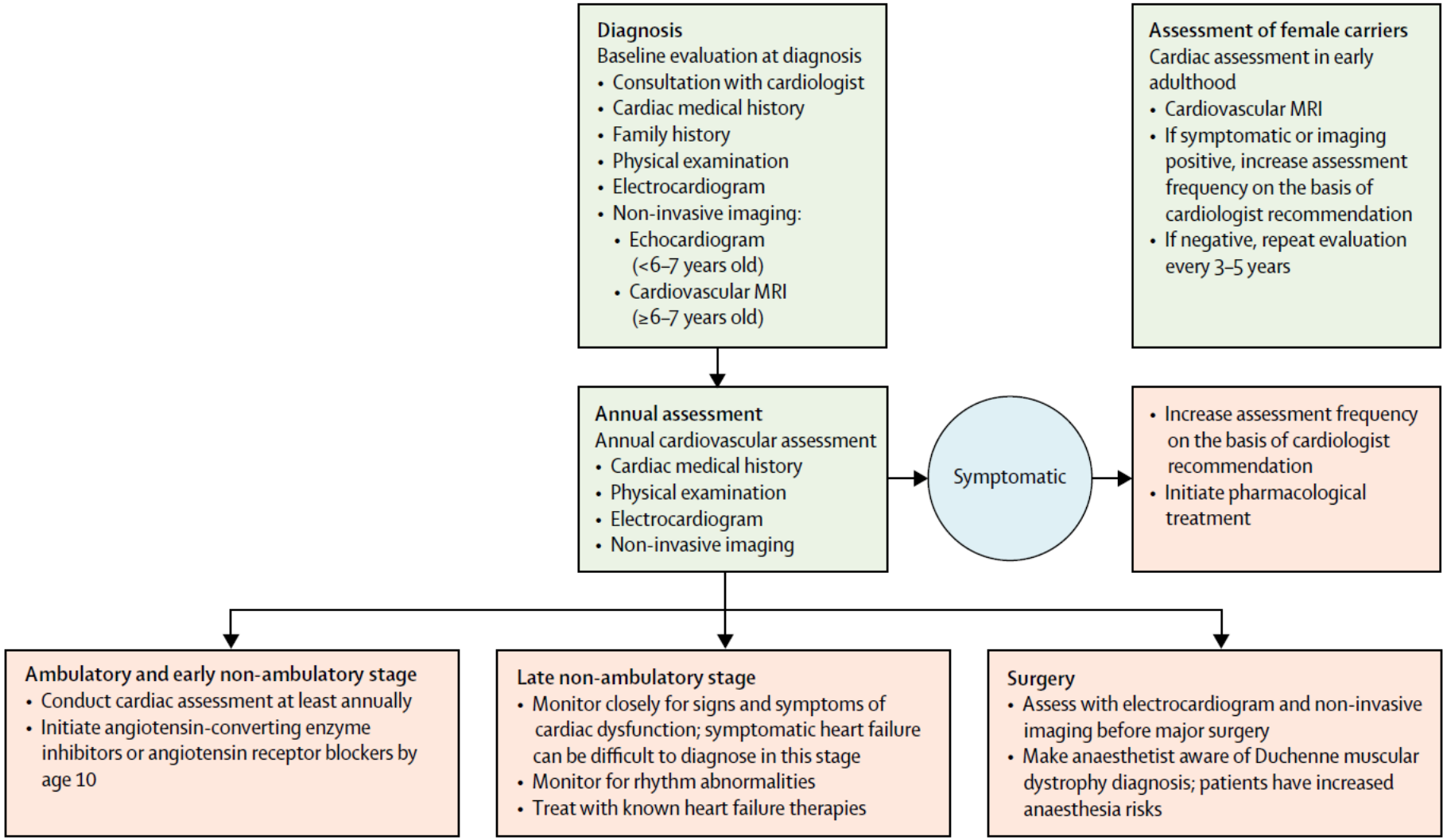
Indications for tracheostomy:

- patient preference,
- inability to use non-invasive ventilation,
- 3 failed extubation attempts during a critical illness despite optimum use of NIV & mechanically assisted coughing

The decision is highly dependent on

- each individual's preference and clinical course,
- skills and usual practices of the individual's clinicians
- local standard of care,
- availability of home resources such as overnight nursing

Cardiac monitoring, diagnosis, and treatment algorithm



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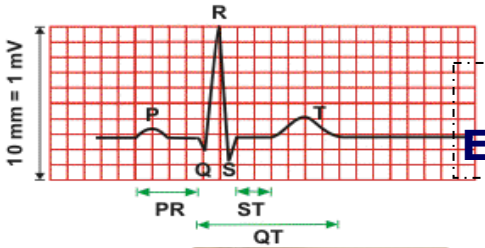
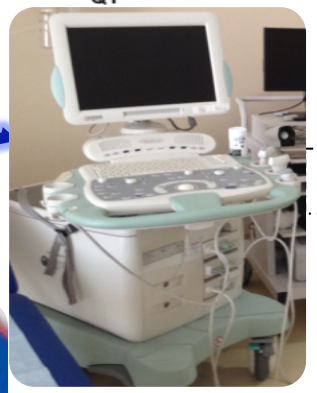
MONITORING
TREATMENT
PREVENTION

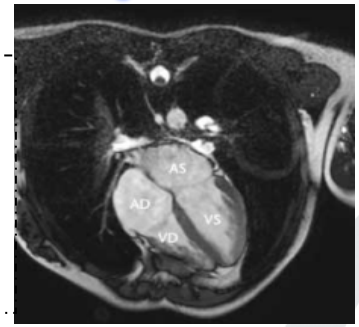


EKG

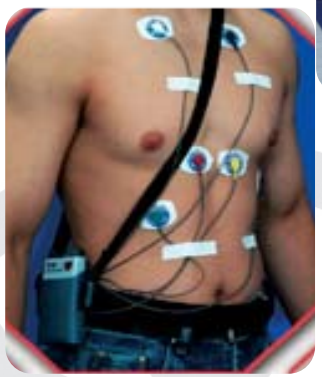


Ecocardiography

Pharmacological treatments
- **ACE inhibitors**
- **β blockers**
- **Diuretics**



CARDIAC MRI



24 hrs Holter ECG

Bone health: Observations in children with chronic, glucocorticoid-treated illnesses

Vertebral fractures – are **frequent manifestation of osteoporosis in children** with chronic illness, including those with glucocorticoid-treated.

Vertebral fractures **can be relatively asymptomatic** – rationale for -regular spine imaging.

Vertebral fractures at any time point in a patient's clinical course are predictive of future spine fractures - **vertebral fracture cascade**

Vertebral fractures can occur in children who have BMD Z scores higher than −2 SD

BMD Z score above −2 SD does not preclude the diagnosis of osteoporosis

Bone health monitoring and diagnosis of osteoporosis

Important development that distinguishes the current guidance from the 2010 care considerations is that

Bone health monitoring and diagnosis in children no longer focus on bone mineral density (BMD)

Now - BMD serves as an adjuvant in an approach that focuses on identification of the earliest signs of bone fragility

"Although BMD Z scores are no longer at the forefront of diagnosis, they remain useful to determine the overall trajectory of bone health in an individual child and thereby guide frequency of lateral spine radiographs during the monitoring phase."

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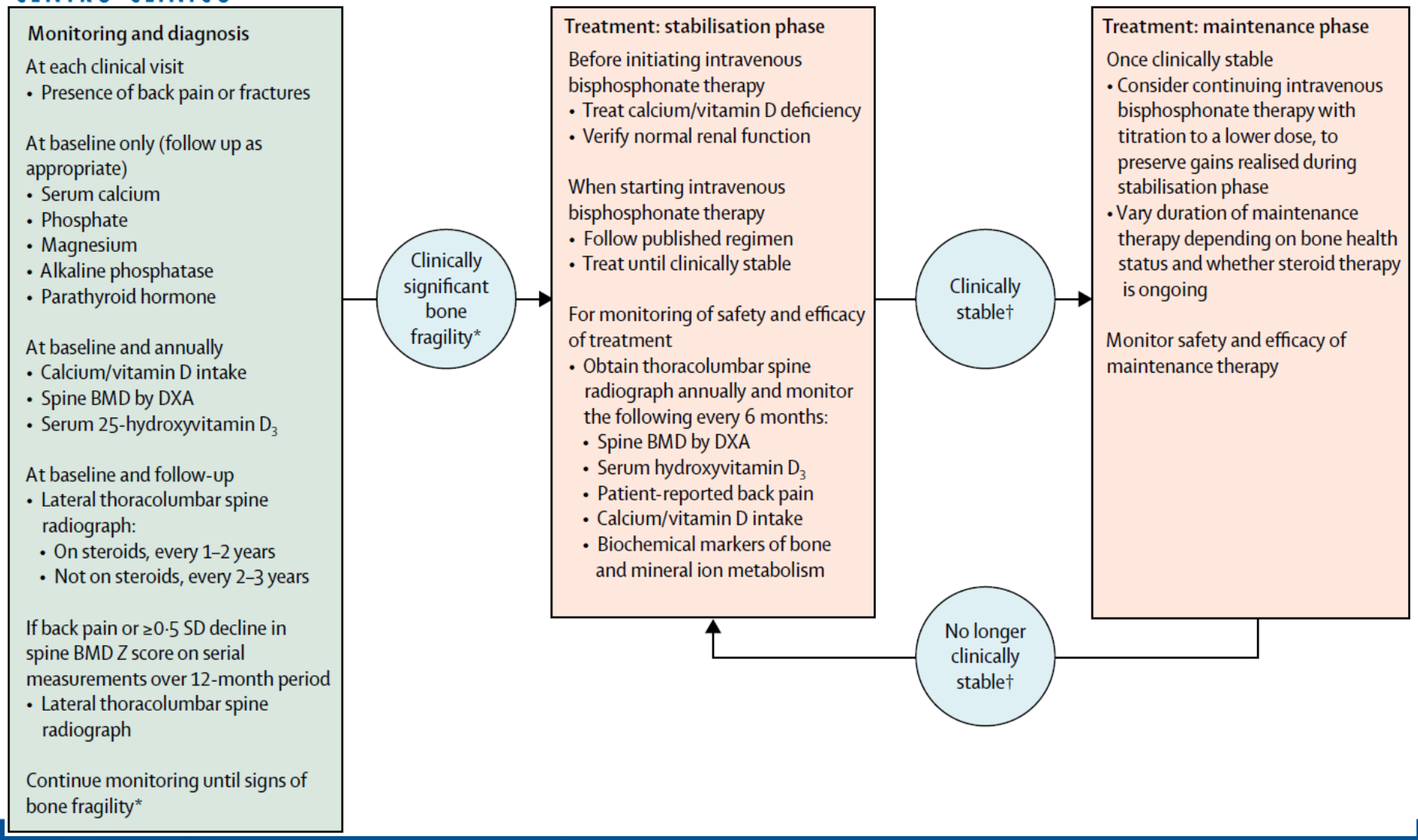
Osteoporosis monitoring, diagnosis & treatment algorithm



Treatment of osteoporosis

Indications for treatment with intravenous bisphosphonate presence of low-trauma vertebral fractures or long-bone fractures generally remain unchanged

notable difference 2018

in the timing of treatment initiation.

Previously - back pain or spine deformity prompted a radiograph to identify vertebral fractures necessitating bisphosphonate therapy.

The current call for routine spine radiographs for all patients with DMD will lead to diagnosis of symptomatic vertebral fractures (mild, moderate, and severe) and asymptomatic moderate and severe vertebral fractures, all of which should prompt referral to an osteoporosis expert for treatment

General guidance on fracture prevention in DMD

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

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Orthopaedic and surgical care in DMD

Ambulatory stage	Early non-ambulatory stage	Late non-ambulatory stage
With physical therapy guidance, implement home stretching programme focusing on ankles, knees, and hips		
	With occupational therapy guidance, add focus on upper extremities	
When passive dorsiflexion <10°, use custom-molded nighttime ankle-foot orthoses set in neutral position	Use custom-molded daytime ankle-foot orthoses to delay worsening of equinovarus contracture	Continue use of lower-extremity braces; fabrication of custom wrist and hand splints may be appropriate
	Initiate standing programme using standing device or wheelchair with upright positioning	Use standing programmes with caution
Refer for surgery on foot and Achilles tendon to improve gait if substantial ankle contracture with good quadriceps and hip extensor strength	Refer for foot and ankle surgery to improve foot positioning only if advocated by patient	
Avoid use of spinal orthoses		
Provide anticipatory fracture prevention guidance to families		
Consult with cardiology and respiratory specialists before any surgical intervention		
Refer for physical therapy after surgery	Refer for posterior spinal instrumentation and fusion if spinal curve >20–30° in prepubertal individuals who are not on corticosteroids; provide preoperative and postoperative evaluation with physical therapy	Refer for posterior spinal instrumentation and fusion if curve is progressive
Ensure families and medical team are aware of fat embolism syndrome		

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Surgical considerations for patients with DMD

Cardiac care

A cardiologist should be consulted before all surgical procedures
Anaesthetists 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

Anaesthesia

Total intravenous anaesthesia is strongly recommended
Depolarising 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 anaesthetics or when given suxamethonium chloride
- Rhabdomyolysis complications are frequently confused with malignant hyperthermia

Blood loss

Hypotensive anaesthetics to minimise blood loss are not recommended because of haemodynamic 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

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DIAGNOSIS & MANAGEMENT: Part 3

- Primary care
- Emergency
- Psychosocial
- Transition

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Considerations for primary care of individuals with DMD

Immunisation

- Administer all non-live-virus vaccinations recommended by the US Centers for Disease Control and Prevention (CDC)[7]
- Aim to give live-virus vaccines before the initiation of steroid treatment; live-virus vaccines are contraindicated in individuals with Duchenne muscular dystrophy (DMD) on high-dose daily corticosteroids (>20 mg per day or >2 mg/kg per day prednisone or equivalent)
- Annually administer injectable influenza vaccine to individuals with DMD and all close contacts (do not give the live-virus nasal vaccine, which is contraindicated)
- Follow the CDC pneumococcal vaccination schedule,[8] integrating PCV13 with PPSV23

Nutrition (see part 1 of this Review)

- Ensure that individuals with DMD receive nutritional counselling to prevent obesity and malnutrition
- Encourage adequate nutrient intake (especially calcium and vitamin D)
- Refer to registered dieticians for nutritional counselling

Dental care

- Ensure that individuals with DMD have regular dental care
- Ensure that the primary care provider or dentist applies varnish as per protocol[9]
- Ensure that fluoride is supplemented for patients with unfluoridated water

Safety counselling

- Raise awareness that individuals with DMD are prone to falls as muscle weakness progresses, especially when they begin to lose ambulation
- Consult the multidisciplinary clinical team (including occupational or physical therapist) for appropriate safety practices (eg, use of wheelchair and advice on safety devices) to minimise risk of falls
- Emphasise that seatbelts should be worn in motor vehicles at all times; individuals with DMD with poor trunk control might require special positioning devices
- Ensure that individuals with DMD who sit in their wheelchairs in motor vehicles are aware that they should secure the wheelchair according to manufacturer guidelines

Monitoring for adrenal insufficiency (see part 1 of this Review)

- For individuals with DMD taking corticosteroids:
  - Educate the family not to miss any doses of prescribed corticosteroid and to be vigilant for signs of adrenal insufficiency (such as lethargy) in association with febrile illnesses, vomiting, surgeries, and other physiological stresses
  - Supply the patient or family with a stress dose of steroids at home for symptoms of adrenal insufficiency and ensure that they seek immediate medical attention when a stress dose is needed

Psychosocial care for patients and family members

- Monitor physical and developmental milestones and be aware of DMD-specific neurodevelopmental and neuropsychological issues, such as the increased prevalence of intellectual disability, attention-deficit hyperactivity disorder, and autism spectrum disorder
- Refer to a psychologist for psychological and neuropsychological assessments and interventions when appropriate (see main text)
- Refer to a speech-language pathologist for suspected delays
- Help the family with special educational needs (eg, in the USA, plans include the Individualized Education Programs and 504 plans)
- Identify community resources that might enhance individual and family functioning and coping, such as local social service agencies and patient advocacy organisations
- Help to initiate discussions about transitions of care
- Ensure that adults with DMD have completed advance directives, when appropriate, and that they have appointed a health-care power of attorney

Other screening

- Do standardised screenings such as hearing and vision screening, and screening for mood disorders and substance abuse, on the usual schedule
- Screen for cardiovascular risk factors, such as hypertension and hypercholesterolaemia

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Key issues related to emergency care in DMD

Advance directives, history, and contacts

- Determine whether there are restrictions on resuscitation
- Ask for the patient's emergency card and baseline test results, including electrocardiogram results
- Obtain a brief history with a focus on baseline respiratory and cardiac status, including use of relevant devices and medications
- Determine whether the patient is treated with chronic steroid therapy
- Contact the patient's neuromuscular specialist

Breathing problems

- Ask about respiratory symptoms and home equipment
- Monitor blood oxygen saturation (SpO_2) levels via pulse oximetry; even mild hypoxaemia (SpO_2 <95% in room air) is a concern; do a blood gas analysis if necessary
- Treat with non-invasive ventilation and frequent application of a cough assistance device (or manual assisted coughing if device is unavailable); use the patient's home equipment when available
- Obtain a portable chest radiograph
- Obtain early consultation with a respiratory therapist and respiratory physician

Cardiac problems

- Ask about cardiac symptoms
- Monitor heart rate and rhythm
- Obtain an electrocardiogram (this is typically abnormal and Q waves might be expected) and portable chest radiograph
- Measure blood levels of B-type natriuretic peptide or troponin I, or both, as indicated
- Consider worsening cardiomyopathy, congestive heart failure, and arrhythmias
- Obtain an echocardiogram when necessary
- Obtain early consultation with a cardiologist

Endocrine problems

- Determine whether stress steroid dosing is necessary
- For critical adrenal insufficiency, administer intravenous or intramuscular hydrocortisone: 50 mg for children <2 years old; 100 mg for children ≥2 years and adults
- In less critical situations, consult the PJ Nicholoff Steroid Protocol[10]
- Obtain early consultation with an endocrinologist

Orthopaedic problems

- Assess for long-bone or vertebral fractures as indicated
- Review critical precautions related to sedation and anaesthesia if applicable (see text)
- Consider fat embolism syndrome if individual has dyspnoea or altered mental status
- Obtain consultation with an orthopaedic specialist early in the process

Disposition after discharge from emergency care

- Be aware that most patients will need hospital admission (eg, to initiate or intensify respiratory or cardiac therapy or to manage fractures)
- Early in the process, initiate emergency transport by skilled personnel to a centre specialising in the care of patients with Duchenne muscular dystrophy, in cooperation with the individual's neuromuscular specialist

*See appendix for more details.

Components of clinic-based psychosocial care in DMD

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Routine mental health screening

Appropriate tools

•Paediatric patients – Strengths and Difficulties Questionnaire

•Adult patients - Patient Health Questionnaire 9-item depression scale - (PHQ-9) Generalized Anxiety Disorder 7-item scale

•Parents of patients aged 5–17 years - Personal Adjustment and Role Skills Scale (PARSIII)

Care coordination

- The care coordinator is a point of contact for patients with Duchenne muscular dystrophy (DMD) and families; they should be health professionals with sufficient training or experience in the clinical care of patients with DMD
- The role of the care coordinator is to provide information, coordinate (and possibly schedule) appointments, and facilitate communication with clinicians across disciplines

Routine mental health screening

- At each neuromuscular clinic visit, mental health and quality of life should be screened
- Screening can be informal and does not require comprehensive assessment
- An appropriate tool for paediatric patients is the Strengths and Difficulties Questionnaire;[26] for adult patients, the Patient Health Questionnaire 9-item depression scale (PHQ-9)[27] and the Generalized Anxiety Disorder 7-item scale (GAD-7)[28] are appropriate; for parents of patients aged 5–17 years, the Personal Adjustment and Role Skills Scale (PARSIII) is suitable[29,30] (scale and scoring programme is available on the Parent Project Muscular Dystrophy website)
- Screening can be conducted by a social worker or mental health professional or by other clinic staff with sufficient training or experience in this area (eg, a nurse or attending physician)
- If screening is positive, a referral should be made to a psychologist and psychiatrist for further assessment or treatment
- Every clinic should have a plan to assess and address suicidal ideation or other acute safety concerns
- Caregiver emotional adjustment should be monitored and intervention or support offered as needed
- Siblings of a person with DMD should be provided with opportunities to connect with other siblings of patients with DMD and with access to mental health services as needed

Psychological care

- All individuals with DMD should be expected to live rich, fulfilling lives, and those without additional neurodevelopmental or psychological disorders may achieve a high level of independence in managing their disease; however, all patients and their families might need psychosocial support
- The neuromuscular care team should include a mental health professional (ie, psychologist or psychiatrist) with training and experience in assessing and treating psychiatric conditions in the context of chronic medical or neurodevelopmental conditions
- When mental health concerns are identified, the mental health professional should provide further evaluation of individuals with DMD and their family members, and provide cognitive or behavioural interventions to treat psychiatric conditions
- Standard, evidence-based practices should be used for those who need more formal mental health treatment
- Neuropsychological evaluations should be done when cognitive delays, difficulties with emotional and behavioural regulation, or concerns about social skills exist; re-evaluations should be done every 2–3 years to monitor developmental progress and response to interventions
- Neuropsychological evaluations should be considered within the first year of diagnosis to establish a baseline, or when transitioning to adulthood if government-based assistance might be necessary to promote functional independence

Pharmacological interventions

- The neuromuscular team should include a psychiatrist or other physician with training and experience in providing medication to treat behavioural or emotional disorders in the context of chronic medical or neurodevelopmental conditions
- Standard prescribing practices should be followed
- Selective serotonin-reuptake inhibitors should be prescribed for depression, anxiety, and obsessive–compulsive disorder
- α-Adrenoceptor agonists (first choice) or atypical antipsychotics (second choice) should be prescribed for aggression and anger or emotional dysregulation
- Stimulants or α-adrenoceptor agonists should be prescribed for attention-deficit hyperactivity disorder

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Considerations for psychosocial care in DMD

	Ambulatory stage or childhood	Early non-ambulatory stage, adolescence, or young adulthood	Late non-ambulatory stage or adulthood
Assessments	• Consider baseline evaluation during first year of diagnosis • Provide developmental (<4 years old) or neuropsychological evaluation (>5 years old) when social or emotional concerns or cognitive delays exist	• Provide neuropsychological evaluation to identify cognitive or learning issues when concerns exist about school performance • Provide neuropsychological evaluation when transitioning to adulthood to assess whether government-based assistance might be needed	Provide neuropsychological evaluation when concerns exist about change in functioning or ability to manage daily affairs
	Provide evaluation by speech-language pathologist for children with suspected delays in speech or language development		Provide evaluation by speech-language pathologist for patients with loss or impairment of functional communication ability, chewing difficulties, or dysphagia
	Provide evaluation by social worker at diagnosis and then as needed	Provide evaluation by social worker of the needs of the patient and family	

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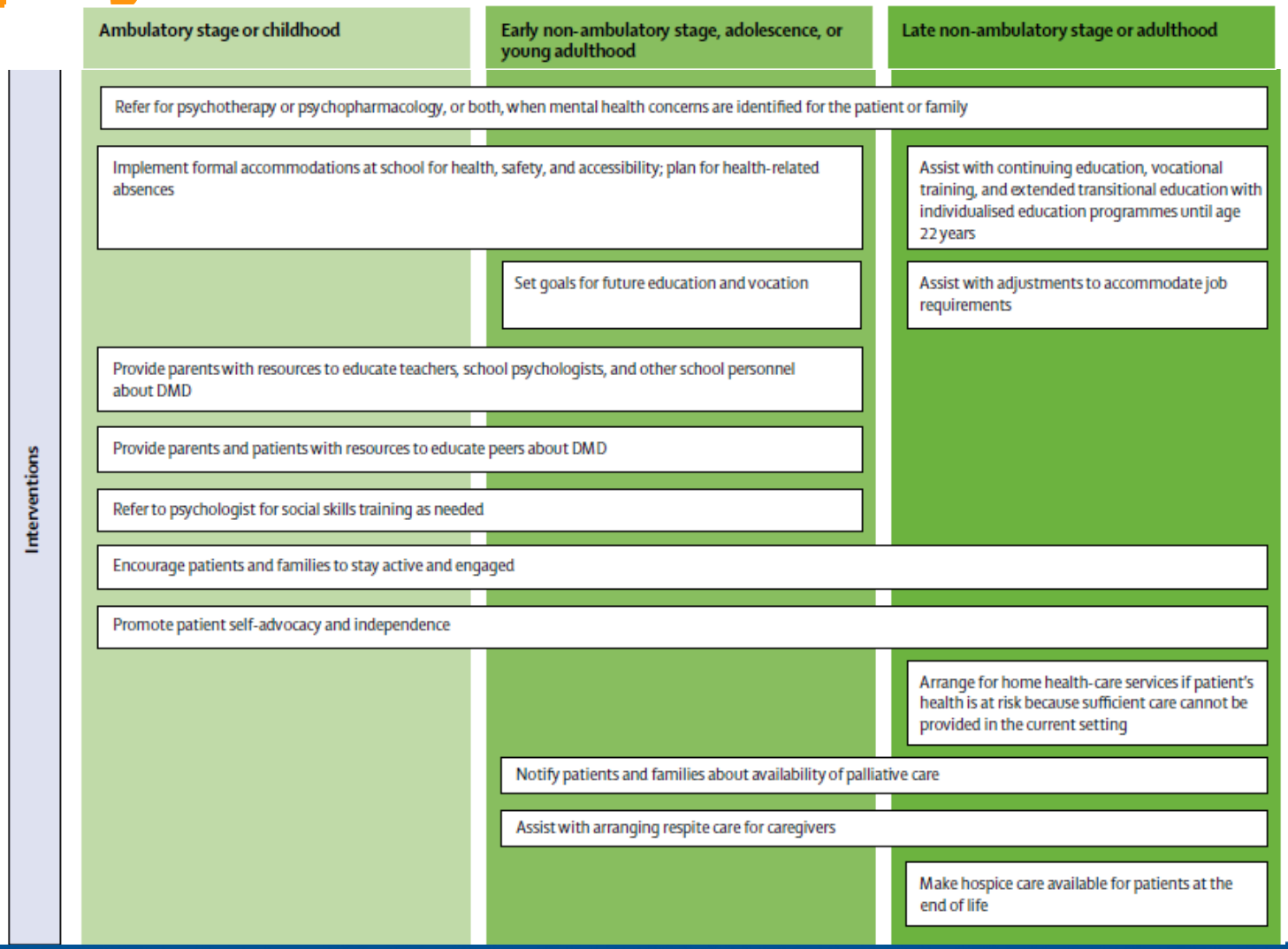
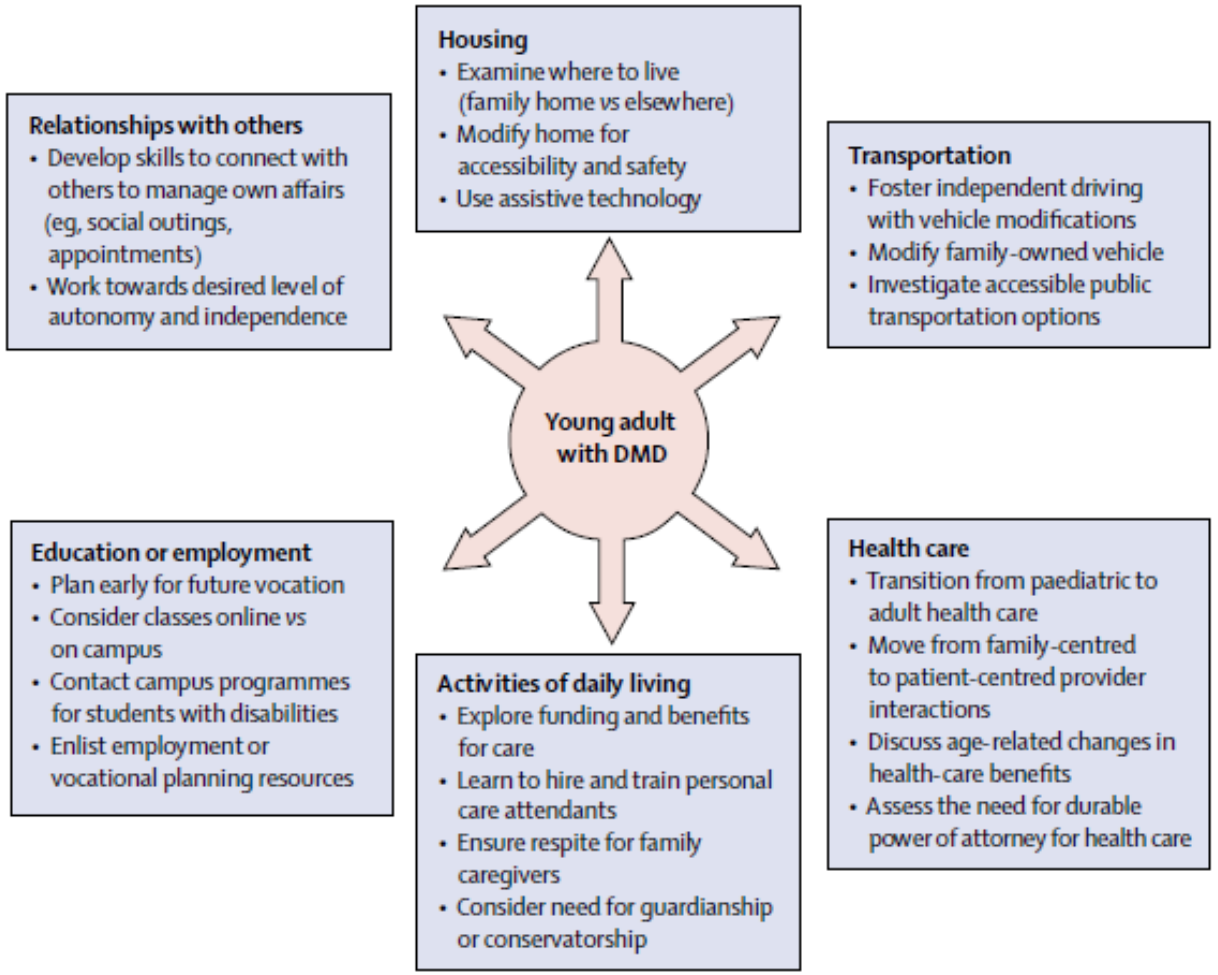
Considerations for psychosocial care in DMD



Components of young adulthood to be addressed during transition planning for individuals with DMD



Adult DMD want to maintain their independence and their relationships

LEDHA was contacted by 31 patients with DMD/BMD in 2018

Average age: 30 years ± 13 years

6 between 14-18 yrs and 25 > 18

-to live on their own

-to have their personal caregiver (not their parents)

Only 10% of DMD are working

None are married or have a family life

LEDHA. Available from: http://www.ledha.it/index.asp. Accessed June 2018.

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Challenges with implementation

Challenge #1:
Diagnostic delay

- Usually diagnosis within year 5
- Still cases > 10 years of age
- The earlier the better for rehab & pharma

Challenge #2:
Implementation of SoC

- Important for patients
- Important for physicians
- Important for clinical trials

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Challenge #3:
access to treatment

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COOPERATIVE INTERNATIONAL NEUROMUSCULAR RESEARCH GROUP DUCHENNE NATURAL HISTORY STUDY DEMONSTRATES INSUFFICIENT DIAGNOSIS AND TREATMENT OF CARDIOMYOPATHY IN DUCHENNE MUSCULAR DYSTROPHY

CHRISTOPHER SPURNEY, MD,[1] REIKO SHIMIZU, MD,[2] LAUREN P. MORGENROTH, MS,[1] HANNA KOLSKI, MD,[3] HEATHER GORDISH-DRESSMAN, PhD,[1] PAULA R. CLEMENS, MD,[2,4] and the CINRG INVESTIGATORS

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[4] Neurology Service, Department of Veterans Affairs Medical Center, Pittsburgh, Pennsylvania, USA

Muscle Nerve **50**: 250–256, 2014

340 DMD patients, aged 2–28 years.

231 participants reported echocardiogram

174 had data for SF or EF.

Prevalence of cardiomyopathy was 27% (47 of 174)

Patients with cardiomyopathy - 57% (27 of 47) reported not taking any cardiac medications.

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Take-home messages

Take-home message#1

- **2018 CARE RECOMMENDATIONS FOR DMD ARE AVAILABLE**

Birnkrant DJ et al. Lancet Neurol 2018; 17: 251–67, 347–61, 445–55

Take-home message #2

Neurologists

NMD nurses

Orthopedics

Child Neurologists

Cardiologists

Pulmonologists and respiratory physiotherapists

Nutrizionists

ENT

Physiatrists, physiotherapists, occupational therapists

Psychologists

Take-home message#3

- **PHARMACOLOGICAL TREATMENTS ARE AN ADD ON TO THE PATHWAY OF CARE**

Thank you from Rome….

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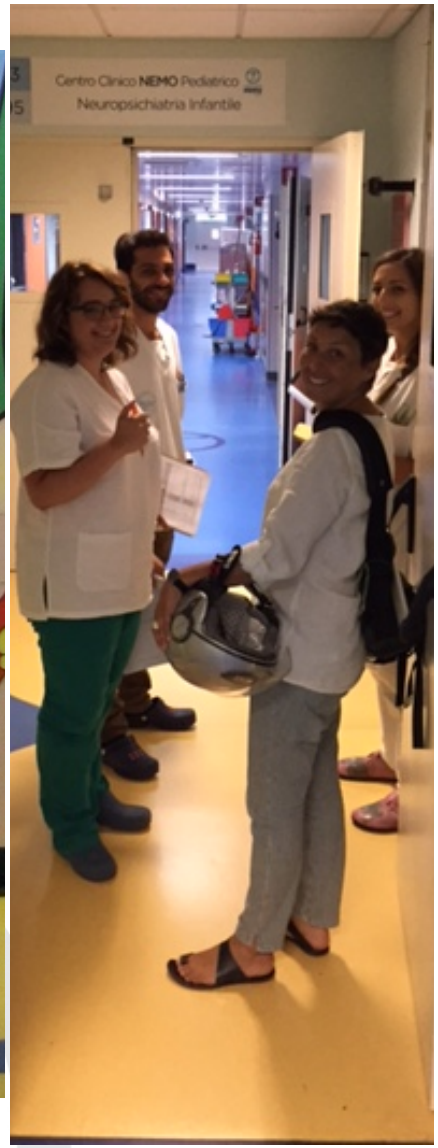

…and from Milan!