General

Guideline Title


Bibliographic Source(s)


Guideline Status

This is the current release of the guideline.


This guideline meets NGC’s 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions of the levels of the recommendations (A, B, C, U) and classification of the evidence (Class I-IV) are provided at the end of the "Major Recommendations" field.

Practice Recommendations

Clinical Context

Prednisone 0.75 mg/kg/d has significant benefit in Duchenne muscular dystrophy (DMD) management and should be considered the optimal prednisone dose. Prednisone 10 mg/kg/weekend is equally effective over a 12-month period, although long-term outcomes of this alternate regimen remain to be seen. Because of the expectation of significant adverse events (AEs) with corticosteroids, proper informed consent is required, and AEs should be discussed with patients and their families prior to therapy initiation and should be managed proactively. The American College of Rheumatology Task Force osteoporosis guideline recommends calcium and vitamin D supplementation for patients taking corticosteroids (any dose with an anticipated duration of ≥3 months) in order to maintain a total calcium intake of 1,200 mg/d and vitamin D intake...
of 800 IU/d through dietary sources and supplementation.

If a significant number of AEs develop, reducing the prednisone dose to 0.3 mg/kg/d may reduce the AE burden, albeit with less efficacy.

The AE profiles of deflazacort and prednisone vary slightly. Weight gain and cushingoid appearance may occur more frequently with prednisone than deflazacort, but cataracts are more frequently reported with deflazacort.

Recommendations

Prednisone, offered as an intervention for patients with DMD:

- Should be used to improve strength (Level B) and may be used to improve timed motor function (Level C)
- Should be used to improve pulmonary function (Level B)
- May be used to reduce the need for scoliosis surgery (Level C)
- May be used to delay the onset of cardiomyopathy by 18 years of age (Level C)

Deflazacort, offered as an intervention for patients with DMD, may be used to:

- Improve strength and timed motor function and delay the age at loss of ambulation by 1.4–2.5 years (Level C)
- Improve pulmonary function (Level C)
- Reduce the need for scoliosis surgery (Level C)
- Delay the onset of cardiomyopathy by 18 years of age (Level C)
- Increase survival at 5 and 15 years of follow-up (Level C)

Deflazacort and prednisone may be equivalent in improving motor function (Level C). There is insufficient evidence to establish a difference in effect on cardiac function (Level U). Prednisone may be associated with increased weight gain in the first years of treatment compared with deflazacort (Level C). Deflazacort may be associated with increased risk of cataracts compared with prednisone (Level C).

If patients with DMD are treated with prednisone, prednisone 0.75 mg/kg/d should be the preferred dosing regimen (Level B). Prednisone 10 mg/kg/weekend is equally effective over 12 months, but long-term outcome is not yet established. Prednisone 0.75 mg/kg/d is probably associated with significant risk of weight gain, hirsutism, and cushingoid appearance (Level B), with equal side effect profile seen over 12 months with the 10 mg/kg/weekend dosing.

Prednisone 0.3 mg/kg/d may be used as an alternative dosing regimen with lesser efficacy and fewer AEs (Level C). Prednisone 1.5 mg/kg/d is another alternative regimen; it may be equivalent to 0.75 mg/kg/d but may be associated with more AEs (Level C).

Data are insufficient to support or refute the following (all Level U):

- The addition of calcifediol and bisphosphonates (alendronate) as significant interventions for improving bone health in patients with DMD taking prednisone
- A benefit of bisphosphonates for improving survival in patients with DMD taking corticosteroids
- A benefit of prednisone for survival
- A significant difference in efficacy or AE rates among daily, alternate day, and intermittent regimens for prednisone or prednisolone dosing
- A preferred dose of deflazacort
- An effect of corticosteroids on quality of life (QoL)

Suggestions for Counseling

The following suggestions for counseling are the opinion of the authors and extend from logical conclusions of the recommendations.

Patients with DMD and their families should:

- Have a voice in the choice of the corticosteroid used, noting that the various corticosteroids differ in evidence supporting use, cost, availability, and AE profiles. When a corticosteroid has been agreed upon, a focused discussion of the risks particular to that corticosteroid should take place.
- Be informed of the risks and benefits of adding a bisphosphonate to corticosteroid treatment.

Definitions

American Academy of Neurology (AAN) Classification of Evidence Scheme for Therapeutic Studies
Class I

- Randomized, controlled clinical trial (RCT) in a representative population
- Masked or objective outcome assessment
- Relevant baseline characteristics are presented and substantially equivalent between treatment groups, or there is appropriate statistical adjustment for differences
- Also required:
  a. Concealed allocation
  b. Primary outcome(s) clearly defined
  c. Exclusion/inclusion criteria clearly defined
  d. Adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias
  e. For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*:
     1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority
     2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose, and dosage adjustments are similar to those previously shown to be effective)
     3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment
     4. The interpretation of the study results is based on a per-protocol analysis that accounts for dropouts or crossovers

Class II

- Cohort study meeting criteria a-e above or an RCT that lacks one or two criteria b-e
- All relevant baseline characteristics are presented and substantially equivalent among treatment groups, or there is appropriate statistical adjustment for differences
- Masked or objective outcome assessment

Class III

- Controlled studies (including studies with external controls such as well-defined natural history controls)
- A description of major confounding differences between treatment groups that could affect outcome**
- Outcome assessment masked, objective, or performed by someone who is not a member of the treatment team

Class IV

- Did not include patients with the disease
- Did not include patients receiving different interventions
- Undefined or unaccepted interventions or outcome measures
- No measures of effectiveness or statistical precision presented or calculable

* Numbers 1–3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III

** Objective outcome measurement: An outcome measure that is unlikely to be affected by an observer’s (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data)

Classification of Recommendations

A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)*

B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)
U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

Clinical Algorithm(s)
None provided

Scope

Disease/Condition(s)
Duchenne muscular dystrophy (DMD)

Guideline Category
Management
Treatment

Clinical Specialty
Neurology
Pediatrics

Intended Users
Physicians

Guideline Objective(s)
To update the 2005 American Academy of Neurology (AAN) guideline on corticosteroid treatment of Duchenne muscular dystrophy (DMD)

Target Population
Children with Duchenne muscular dystrophy (DMD)

Interventions and Practices Considered
1. Corticosteroids
   - Prednisone
   - Deflazacort
2. Addition of calcifediol and bisphosphonates (alendronate) to corticosteroids (insufficient evidence to recommend)

Major Outcomes Considered
- Survival
Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The panel searched MEDLINE for articles published from January 2004 through June 2012 (see appendix e-3 in the full guideline [see the "Availability of Companion Documents" field] for the search strategy). They performed update searches covering July 2012 through April 2013 and May 2013 through July 2014. The panel searched the Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Clinical Trials, Database of Abstracts of Reviews of Effects, and Science Citation Index, and references of selected articles and review articles.

The panel reviewed the titles and abstracts of the identified citations for relevance to the clinical questions and retrieved the full text of potentially relevant articles. They also included the Class I–III trials from the original guideline. The panel excluded trials with fewer than 10 patients.

The searches identified 757 citations. The panel reviewed the full text of 121 potentially relevant articles.

Please see the full guideline for further information about the literature search.

Number of Source Documents

Sixty-three articles fulfilled the inclusion criteria, of which 24 were graded Class I–III. Table e-1 in the full guideline (see the "Availability of Companion Documents" field) describes the selected studies on corticosteroids, and table e-2 lists the selected studies on bone health interventions in patients taking corticosteroids.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

American Academy of Neurology (AAN) Classification of Evidence Scheme for Therapeutic Studies

Class I

- Randomized, controlled clinical trial (RCT) in a representative population
- Masked or objective outcome assessment
- Relevant baseline characteristics are presented and substantially equivalent between treatment groups, or there is appropriate statistical adjustment for differences
- Also required:
  a. Concealed allocation
b. Primary outcome(s) clearly defined
c. Exclusion/inclusion criteria clearly defined
d. Adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias
e. For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*:
   1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority
   2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose, and dosage adjustments are similar to those previously shown to be effective)
   3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment
   4. The interpretation of the study results is based on a per-protocol analysis that accounts for dropouts or crossovers

Class II
- Cohort study meeting criteria a-e above or an RCT that lacks one or two criteria b-e
- All relevant baseline characteristics are presented and substantially equivalent among treatment groups, or there is appropriate statistical adjustment for differences
- Masked or objective outcome assessment

Class III
- Controlled studies (including studies with external controls such as well-defined natural history controls)
- A description of major confounding differences between treatment groups that could affect outcome**
- Outcome assessment masked, objective, or performed by someone who is not a member of the treatment team

Class IV
- Did not include patients with the disease
- Did not include patients receiving different interventions
- Undefined or unaccepted interventions or outcome measures
- No measures of effectiveness or statistical precision presented or calculable

*Numbers 1–3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III

**Objective outcome measurement: An outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data)

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Two authors reviewed articles and completed data abstraction independently. Discrepancies were resolved through discussion. The panel rated studies for their risk of bias using the American Academy of Neurology (AAN) 4-tiered classification of evidence scheme for therapeutic studies (see the "Rating Scheme for the Strength of the Evidence" field).

Methods Used to Formulate the Recommendations

Expert Consensus
Description of Methods Used to Formulate the Recommendations

The American Academy of Neurology (AAN) Guideline Development Subcommittee convened a panel of experts on the treatment of Duchenne muscular dystrophy (DMD) to develop this guideline update (see appendices e-1 and e-2 in the full guideline [see the "Availability of Companion Documents"] following the AAN's 2004 process manual (see the "Availability of Companion Documents" field).

The panel addressed the following questions with regard to patients with Duchenne muscular dystrophy (DMD):

1. What is the efficacy of corticosteroids, specifically their effect on survival, quality of life (QoL), motor function, scoliosis, pulmonary function, and cardiac function?
2. What are the side effects of corticosteroid treatment?
3. How do prednisone and deflazacort compare in efficacy or side effect profile?
4. What is the optimal dosing regimen for corticosteroids?
5. Are there any useful interventions for maximizing bone health?

The panel linked the strength of practice recommendations to the strength of evidence (see the "Rating Scheme for the Strength of the Recommendations" field).

Rating Scheme for the Strength of the Recommendations

Classification of Recommendations

A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)*

B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Drafts of the guideline have been reviewed by at least 3 American Academy of Neurology (AAN) committees, a network of neurologists, Neurology peer reviewers, and representatives from related fields.

The guideline was approved by the Guideline Development Subcommittee on March 20, 2013; by the Practice Committee on December 8, 2014; and by the American Academy of Neurology Institute (AANI) Board of Directors on October 6, 2015.

This guideline was endorsed by the American Academy of Pediatrics on September 30, 2015; by the American Association of Neuromuscular & Electrodiagnostic Medicine on August 11, 2015; and by the Child Neurology Society on August 25, 2015.
Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of corticosteroid treatment for patients with Duchenne muscular dystrophy (DMD)

Potential Harms

- In patients with Duchenne muscular dystrophy (DMD), corticosteroids probably have adverse events (AEs) of short stature, behavioral changes, fractures, and cataracts.
- Prednisone 0.75 mg/kg/d is probably associated with significant risk of weight gain, hirsutism, and cushingoid appearance.
- Deflazacort is associated with an increase in the risk of cataracts compared with prednisone.

Qualifying Statements

Qualifying Statements

Clinical practice guidelines, practice advisories, systematic reviews, and other guidance published by the American Academy of Neurology (AAN) and its affiliates are assessments of current scientific and clinical information provided as an educational service. The information (1) should not be considered inclusive of all proper treatments, methods of care, or as a statement of the standard of care; (2) is not continually updated and may not reflect the most recent evidence (new evidence may emerge between the time information is developed and when it is published or read); (3) addresses only the question(s) specifically identified; (4) does not mandate any particular course of medical care; and (5) is not intended to substitute for the independent professional judgment of the treating provider, as the information does not account for individual variation among patients. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. The AAN provides this information on an "as is" basis and makes no warranty, expressed or implied, regarding the information. The AAN specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. The AAN assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information or for any errors or omissions.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources

Quick Reference Guides/Physician Guides

Slide Presentation
Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need
- Getting Better
- Living with Illness

IOM Domain
- Effectiveness
- Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)


Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Feb 2

Guideline Developer(s)

American Academy of Neurology - Medical Specialty Society

Source(s) of Funding

This guideline was developed with financial support from the American Academy of Neurology (AAN). Authors who serve as AAN subcommittee members or methodologists were reimbursed by the AAN for expenses related to travel to subcommittee meetings where drafts of manuscripts were reviewed.

Guideline Committee

Guideline Development Subcommittee of the American Academy of Neurology
Composition of Group That Authored the Guideline

*Guideline Authors:* David Gloss, MD, MPH&TM; Richard T. Moxley III MD; Stephen Ashwal, MD; Maryam Oskoui, MD

*Guideline Development Subcommittee Members:* Cynthia Harden, MD (*Chair*); Steven R. Messé, MD (*Co-Vice-Chair*); Melissa Armstrong, MD; Eric J. Ashman, MD; Misha-Miroslav Backonja, MD; Richard L. Barbano, MD, PhD; Diane Donley, MD; Terry Fife, MD; David Gloss, MD; John J. Halperin, MD; Cheryl Jaigobin, MD; Andres M. Kaner, MD; Jason Lazarou, MD; David Michelson, MD; Pushpa Narayanaswami, MBBS, DM; Anne Louise Oakkinder, MD, PhD; Tamra Pringsheim, MD; Alexander Rae-Grant, MD; Michael Shevell, MD; Kelly Sullivan, PhD; Theresa A Zesiewicz, MD; Jonathan P. Hosey, MD (*Ex-Officio*); Stephen Ashwal, MD (*Ex-Officio*); Deborah Hirtz, MD (*Ex-Officio*); Jacqueline French, MD (*AAN Guideline Historian, Ex-Officio, Voting*)

Financial Disclosures/Conflicts of Interest

**Conflict of Interest**

The American Academy of Neurology (AAN) is committed to producing independent, critical, and truthful clinical practice guidelines (CPGs). Significant efforts are made to minimize the potential for conflicts of interest to influence the recommendations of this CPG. To the extent possible, the AAN keeps separate those who have a financial stake in the success or failure of the products appraised in the CPGs and the developers of the guidelines. Conflict of interest forms were obtained from all authors and reviewed by an oversight committee prior to project initiation. The AAN limits the participation of authors with substantial conflicts of interest. The AAN forbids commercial participation in, or funding of, guideline projects. Drafts of the guideline have been reviewed by at least 3 AAN committees, a network of neurologists, Neurology peer reviewers, and representatives from related fields. The AAN Guideline Author Conflict of Interest Policy can be viewed at [www.aan.com](http://www.aan.com). For complete information on this process, access the 2004 AAN process manual.

**Disclosure**

D. Gloss serves as a paid evidence-based medicine consultant for the American AAN. R. Moxley III has served as an editorial advisory board member of the *Journal of the American Medical Association* Clinical Trials Board; has received $2,500 in honoraria for an Isis Pharmaceuticals meeting (honoraria donated to the Abrams Family Fund for myotonic dystrophy research at the University of Rochester in Rochester, NY); and was awarded a 5-year National Institute of Neurological Disorders and Stroke grant 2U54NS048843 (totaling $7,013,097), a 4-year US Food and Drug Administration grant 1R01FD003716 (totaling $1,510,125), and a National Cancer Institute contract HHSN261201200318P (totaling $40,000). S. Ashwal has served on a medical advisory board for the Tuberous Sclerosis Association; has served as an associate editor for *Pediatric Neurology*; has a patent pending for use of HRS for imaging in stroke; is a coeditor of and has received royalties for *Pediatric Neurology: Principles and Practice*, 6th edition; has received grant funding from the National Institute of Neurological Disorders and Stroke for use of advanced imaging for detecting neural stem cell migration after neonatal HII in a rat pup model; works in the Department of Pediatrics at Loma Linda University School of Medicine; and is called once yearly to act as a witness in legal proceedings as a treating physician for children with nonaccidental trauma. M. Oskoui has received travel funding from the AAN and Isis Pharmaceuticals and has received research support from Isis Pharmaceuticals, Fonds de Recherché Santé (Québec, Canada), NeuroDevNet, the Canadian Institutes of Health Research (Canada), and McGill University Research Institute.

Go to [Neurology.org](http://neurology.org) for full disclosures.

Guideline Endorser(s)

American Academy of Pediatrics - Medical Specialty Society

American Association of Neuromuscular and Electrodiagnostic Medicine - Medical Specialty Society

Child Neurology Society - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Moxley RT 3rd, Ashwal S, Pandya S, Connolly A, Florence J, Mathews K, Baumbach L, McDonald

This guideline meets NGC’s 2013 (revised) inclusion criteria.

Guideline Availability

A list of American Academy of Neurology (AAN) guidelines, along with a link to this guideline, are available from the AAN Web site.

Availability of Companion Documents

The following are available:


Patient Resources

The following is available:


Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline’s content.

NGC Status

This NGC summary was completed by ECRI on February 11, 2005. The information was verified by the guideline developer on March 8, 2005. This information was reaffirmed by the guideline developer on February 8, 2008 and this summary updated by ECRI Institute on December 17, 2010. This summary was updated again by ECRI Institute on March 18, 2016. The updated information was not verified by the guideline developer.

Copyright Statement
This NGC summary is based on the original guideline, which is copyrighted by the American Academy of Neurology.

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouseâ“¢ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion-criteria.aspx.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.