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## Using an Online Modified-Delphi Approach to Engage Patients and Caregivers in Determining the Patient-Centeredness of Duchenne Muscular Dystrophy Care Considerations

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### Abstract

**Purpose.**—To determine the patient-centeredness of endocrine and bone health Duchenne muscular dystrophy (DMD) care considerations using the RAND/PPMD Patient-Centeredness Method (RPM), which is a novel, online, modified-Delphi approach to engaging patients and caregivers in clinical guideline development.

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#### Authors' Contributions

All authors were responsible for designing the study. Authors DK, SG, BD, and AM were directly involved in the data collection. Authors DK, MB, CA, BD, MB, ED, and CC analyzed the data. Authors DK and SG drafted the initial manuscript. All authors critically reviewed both the draft and revised version of the manuscript and approved the final version for submission.

#### Publisher's Disclaimer: Disclaimer

**Publisher's Disclaimer:** This work was presented at G-I-N and PPMD conferences and as part of G-I-N NA and PPMD webinar series.

#### Ethics Approval and Consent to Participate

The study was reviewed and considered to be exempt by the RAND's Human Subjects' Protection Committee (ID 2016-0518). All participants were consented when they logged into the ExpertLens system for the first time.

#### Transparency Statement

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any relevant discrepancies from the study as planned and registered have been explained.

#### Data Sharing

The data analyzed during this study are available from the corresponding authors on reasonable request.

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: DK and SG are members of the ExpertLens team at RAND. SG's spouse is a salaried employee of Eli Lilly and Company and owns stock. SG has accompanied his spouse on company-sponsored travel. All other coauthors report no conflicts of interest.

#### Supplemental Material

Supplementary material for this article is available on the *Medical Decision Making* Web site at <http://journals.sagepub.com/home/mdm>.

**Methods.**—We solicited input on the patient-centeredness of care considerations from 28 individuals with DMD and 94 caregivers, randomly assigned to 1 of 2 mixed panels. During a 3-round online modified-Delphi process, participants rated the importance and acceptability of 19 DMD care considerations (round 1), reviewed and discussed the initial results (round 2), and revised their original ratings (round 3). Patient-centeredness was operationalized as importance and acceptability of recommendations. We considered a care consideration to be patient-centered if both panels deemed it important and acceptable.

**Results.**—Ninety-five panelists (78%) participated in this study. Of these, 88 (93%) participated in round 1, 74 (78%) in round 2, and 56 (59%) in round 3. Panelists deemed 12 care considerations to be patient-centered: 3 weight management, 3 bone health, 4 vertical growth, and 2 puberty recommendations. Seven care considerations did not meet patient-centeredness criteria. Common reasons were lack of evidence specific to DMD and concerns about insurance coverage, access to treatment, and patient safety.

**Conclusions.**—Using the RPM, Duchenne families considered most care considerations to be patient-centered. Besides being clinically appropriate, these considerations are likely to be consistent with the preferences, needs, and values of Duchenne families. While all relevant care considerations should be discussed during patient-provider encounters, those that did not meet patient-centeredness criteria in particular should be carefully considered as part of joint decision making between Duchenne families and their providers.

**Study Registration:** HSRProj 20163126.

## Keywords

clinical practice guidelines; DMD care considerations; duchenne muscular dystrophy; online modified-delphi; patient engagement; RAND/PPMD patient-centeredness method rhGH stands for recombinant human growth hormone

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In 2010, the US Centers for Disease Control and Prevention (CDC) supported the development of the Duchenne muscular dystrophy (DMD) care considerations to help health care providers, affected individuals, and their families better manage this rare disorder.<sup>1,2</sup> DMD is a progressive, fatal neuromuscular disorder caused by mutations in the dystrophin gene. DMD affects approximately 1 in 5000 males,<sup>3</sup> typically manifesting itself between ages 3 and 5.<sup>4</sup> It is a multisystem disorder in which affected individuals experience progressive loss of functional muscle fibers, which results in weakness, loss of mobility, and premature death. About half of males with DMD survive into their 20s and some live into their 30s and 40s.<sup>5</sup> As the condition runs its course, caregiving, financial, emotional, and physical demands increase and affect the entire family.<sup>6–8</sup>

The DMD care considerations, or care guidelines, as they are commonly called in the Duchenne community,<sup>9</sup> were revised in 2018 to incorporate new evidence and guidance on primary and emergency care, transition of care/adult care, and endocrine and bone health management.<sup>10–12</sup> (In this article, we use the terms *guidance* and *care considerations* when referring to the 2018 DMD care considerations. When referring to the development of clinical guidelines in general, we use the terms *guidelines* and *recommendations* interchangeably.) Clinical experts achieved consensus through reviewing the existing

evidence and using the RAND/UCLA Appropriateness Method (RAM)<sup>13</sup> to rate the clinical appropriateness and necessity of different approaches to providing care. Because RAM does not require patient involvement when rating evidence or inclusion of evidence about patient preferences, individuals with DMD and their families did not directly participate in developing most sections of the care considerations.

Although there are commonly accepted practices for synthesizing research, clinical, and economic evidence for clinical guideline development purposes,<sup>14,15</sup> there is less clarity on how best to integrate patient-based evidence or information generated by patients about different aspects of care, patient preferences, and care experiences.<sup>16–18</sup> Doing so is important because patient involvement in developing care guidelines enhances their quality and legitimacy<sup>17</sup> by ensuring that guidelines focus on topics and outcomes important to patients, identify risks and benefits of different recommendations, and address the feasibility and acceptability of recommended care standards.<sup>19,20</sup> Involving patients at what Concannon et al.<sup>21</sup> call the “dissemination and application” stage of patient-centered outcomes research can also facilitate the use of guidelines in practice. There is no consensus on whether patients should be equal members of guideline groups or if patient input and preferences should just be shared with clinicians on guideline groups.<sup>17</sup> This lack of consensus may reflect the challenges of engaging patients at the population level.<sup>22</sup> It may also reflect the lack of systematic, low-burden approaches to engagement that can solicit patient-based evidence in a way that is consistent with how clinicians develop guidelines but does not require travel and extensive training and support.<sup>19,23</sup>

The main objective of this study is to use a new scalable online approach for engaging patients and caregivers in guideline development called the RAND/PPMD Patient-Centeredness Method (RPM)<sup>24</sup> to determine what individuals with DMD and their caregivers think about the patient-centeredness of the 2018 DMD care considerations. We consider patient-centeredness, operationalized as perceived importance and acceptability of a recommendation for a typical family, to be a form of patient-based evidence, which serves as a “bridge between individual and population approaches”<sup>25</sup> to providing care. Systematically incorporating patient-centeredness into clinical guideline development before recommendations are finalized can help align evidence-based medicine with patient needs, values, concerns, and preferences by facilitating shared decision making.<sup>26</sup>

## Methods

A month after the 2018 DMD care considerations were published,<sup>10–12</sup> we conducted 2 online modified-Delphi panels that solicited the perspectives of individuals with DMD and their caregivers on the patient-centeredness of care considerations for endocrine and bone health management following a prespecified study design.<sup>27</sup> We chose to focus on endocrine and bone health care because this guidance was added only in 2018. It was also developed without direct patient or caregiver involvement. Both panels were conducted using the RPM<sup>24</sup> (see below) that closely mirrors a 3-round modified-Delphi rating process of appropriateness and necessity that clinicians used to develop the DMD care considerations. We also used the guidance for conducting and reporting Delphi studies (CREDES) in

preparing this article.<sup>28</sup> The RAND institutional review board reviewed and determined our study to be exempt.

## Participants

We used the Parent Project Muscular Dystrophy's (PPMD) "Duchenne Registry"—the largest patient and caregiver registry in the United States for Duchenne and Becker muscular dystrophy<sup>29</sup>—to recruit individuals with Duchenne and their caregivers. We considered them key stakeholders. We sent invitation emails describing the study to 719 potential participants who had logged into their registry account at least once during the previous 8 months, asking those interested in participating to answer basic demographic questions. We assembled a diverse sample of 122 participants (28 individuals with DMD and 94 caregivers) from 153 individuals who expressed an interest in this study. By design, we included only individuals with DMD 18 years and older and their caregivers because some care considerations focused on pubertal development, and we wanted to ensure that all individuals with DMD in our panels have gone through puberty. We excluded those who participated in a previous pilot study, parents and children providing the same email address, and caregivers from the same household.

Because 40 to 60 participants is a recommended size for online panels,<sup>30</sup> we randomly assigned selected participants to 1 of 2 panels. We balanced the panel composition in terms of the number of individuals with DMD and caregivers, caregiver educational attainment, ambulatory status of the individual with DMD, and the distance to the closest PPMD Certified Duchenne Care Center.<sup>31</sup>

## Design

Our study uses an embedded mixed-methods design, in which quantitative data are used to determine patient-centeredness and qualitative data are used to explain the factors that might have affected participants' ratings of patient-centeredness.<sup>32</sup> Based on the RAM,<sup>13</sup> the RPM<sup>24</sup> consists of 2 rating rounds interspersed with a discussion round. We solicited input from Duchenne families using ExpertLens™, a previously evaluated online modified-Delphi platform.<sup>30,33</sup> We tested our approach to data collection and face validity of our measure of patient-centeredness during a pilot test in which a group of 8 individuals with DMD and caregivers completed all 3 modified-Delphi rounds and shared their feedback by participating in a telephone interview. Participants were consented when they logged into ExpertLens for the first time.

## The RAND/PPMD Patient-Centeredness Method

In round 1, participants reviewed, rated, and commented on 19 statements summarizing guidance on endocrine and bone health management from the 2018 care considerations, covering delayed vertical growth, weight management, bone health, and delayed puberty (see online Appendix A for care statements). Because this was the first time the RPM was used, we did not include all care considerations covering these topics. We used plain language to describe each care consideration, having solicited input from our advisory board and Duchenne families about how to increase readability. We included the clinical rationale

for each care consideration, what the process of following the guidance may entail, and any relevant additional information, including treatment burden (Figure 1).

Participants used 9-point Likert scales to rate patient-centeredness, operationalized as the importance and acceptability, of each care consideration. We defined importance as the extent to which a consideration is likely to be consistent with the preferences, needs, and values of Duchenne families in general. We defined acceptability as the extent to which the process of following a given care consideration is likely to be consistent with available resources (e.g., time and finances) and with the ethical standards of Duchenne families. Focusing on the experiences of Duchenne families in general is consistent with what clinicians are asked to do when they rate appropriateness and necessity in the RAM. We developed these scales based on the GRADE Evidence to Decision Framework<sup>20</sup> and with input from the study advisory board. We instructed participants to explain their ratings and list factors that most powerfully influenced their responses. To help participants comment about Duchenne families in general, we gave them results of a previous survey we conducted with Duchenne families about their main reasons (as well as barriers and facilitators) for seeking care for each aspect of DMD care included in our study.<sup>34</sup> Round 1 was open from March 12, 2018, to March 21, 2018.

In round 2, participants reviewed bar charts showing their own responses in relation to the group's distribution of round 1 responses (Figure 2). Below each chart, we displayed simple, color-coded statements describing whether agreement was reached and whether the panel judged each care consideration as important/acceptable, of uncertain importance/acceptability, or not important/not acceptable. We analyzed ratings using the RAM's approach to calculating consensus.<sup>13</sup> We also thematically analyzed round 1 rationale comments and displayed comment summaries in round 2 (see below). Finally, participants discussed round 1 results using asynchronous and moderated discussion boards; comments were partially anonymous, as we used IDs that only revealed whether a participant was an individual with DMD or a caregiver. Round 2 was open from March 26, 2018, to April 4, 2018.

In round 3, participants revised their original ratings based on round 2 feedback and discussion of round 1 results. Round 3 was open from April 4, 2018, to April 24, 2018.

## Data Analysis

To determine the patient-centeredness of the care considerations, we used a 2-step analytic approach developed in previous ExpertLens studies<sup>35,36</sup> (Figure 3). We first used round 3 ratings and RAM to determine if participants in each panel agreed on the importance and acceptability of each care consideration. We then looked at the ratings across panels and considered a care consideration to be patient-centered if it was deemed important and acceptable by both panels. To assess the reliability of importance and acceptability determinations between panels, we calculated the pairwise agreement and kappa coefficients. We prespecified that at least a 70% agreement level and a moderate level of kappa (.41–.60) would indicate an acceptable reliability level between panels.<sup>37</sup>

To better explain perceived patient-centeredness of the care considerations, we thematically analyzed rationale and discussion comments. As in previous ExpertLens panels,<sup>27</sup> we grouped all rationale comments for a given rating criteria and care consideration based on the numeric ratings to which they referred; we also grouped all discussion comments based on the relevant care consideration. Five researchers (SG, CA, RG, ED, CC) trained by the principal investigator (DK) reviewed and coded all qualitative comments inductively to identify emergent themes that could be used to explain why a certain care consideration was considered important and/or acceptable. All coding results were reviewed by DK to ensure consistency in the way that the codebook was applied, as well as by a clinician (KK), a genetic counselor and Duchenne Registry director (AM), and a caregiver (BD) to ensure the correct interpretation of comments. Disagreements were discussed until consensus was achieved. In the Results section, we describe main themes and provide illustrative quotations, indicating whether a quotation came from an individual with DMD or a caregiver and noting which panel (A or B) a particular participant was part of. Online Appendix B provides additional illustrative quotations describing main themes.

## Results

Out of 122 invited participants, 95 (78%) participated in at least 1 panel round. Of these 95 participants, 54 (57%; 13 patients, 41 caregivers) participated in all 3 rounds, 15 (16%; 2 patients, 13 caregivers) in any 2 rounds (2 patients, 13 caregivers), and 26 (27%; 9 patients, 17 care givers) in only 1 round. Of 95 participants, 88 (93%) participated in round 1; 74 (78%) reviewed round 2 discussions and, of these, 55 (74%) posted a total of 1201 comments (mean [SD], 21.8 [34.2]; range, 1–209); and 56 (59%) participated in round 3.

By design, the majority of our 95 participants were caregivers (75%); of those, most were female (83%) and white (92%) (Table 1). Slightly over two-fifths of study participants reported living within a 50-mile radius from a clinic where individuals with DMD receive neuromuscular care. While almost all males with Duchenne (96%) who participated in our panel reported no longer being able to walk, 59% of participating parents/caregivers reported providing care to a child who is still ambulatory. The difference in the ambulatory status between these 2 groups was statistically significant ( $\chi^2 = 19.7$ ,  $df = 1$ ,  $P < 0.001$ )

There were no statistically significant differences in the demographic characteristics of participants and nonparticipants, including sex, ethnicity, child's ambulatory status, and distance traveled to receive neuromuscular care. Participants, however, were more likely than nonparticipants to have higher educational attainment. While a little over 50% of participants had at least a bachelor's degree, just over 25% of nonparticipants had similar educational levels ( $\chi^2 = 4.049$ ,  $df = 1$ ,  $P = 0.044$ ; data not shown).

### Ratings of Patient-Centeredness

There was no disagreement within each panel about the importance and acceptability of any care consideration.



Both panels reached identical decisions on 34 of 38 rating questions (either importance or acceptability) (Table 2), yielding a kappa of .69, which indicates a substantial level of agreement.

Moreover, both panels agreed that 12 (63%) recommendations were both important and acceptable and 3 (16%) were of uncertain importance and acceptability. Panels reached different decisions on either importance or acceptability of 4 care considerations. These results yield a kappa coefficient of .49, indicating moderate agreement across panels on the ratings of importance *and* acceptability taken together.

Of the 15 care considerations that both panels rated similarly, 12 (80%) met our definition of patient-centeredness (i.e., both panels considered them important and acceptable) (Table 2). Of 12 patient-centered care considerations, 4 were about vertical growth, 3 were about weight management, 3 others were about bone health, and 2 were about puberty. The remaining 3 care considerations that both panels agreed on but considered of uncertain importance and acceptability focused on treating impaired vertical growth with hormone therapy.

Although no care consideration was deemed unimportant or infeasible, we have less confidence in the patient-centeredness of 3 care considerations about puberty and 1 care consideration about delayed vertical growth because of disagreement between 2 panels. While panel A deemed them important and acceptable, panel B considered them either of uncertain importance or uncertain acceptability.

### Comments about Patient-Centeredness

In general, participants' ratings of patient-centeredness seemed to be most influenced by quality of life considerations and the nuances of daily lives and functional limitations of individuals with DMD. The importance ratings were often affected by concerns related to the presence/absence of scientific evidence specific to DMD, considerations of self-esteem, tradeoffs of dealing with other effects of the disease, and subjective risk-benefit calculations. The ratings of acceptability were generally affected by participants' concerns about insurance coverage, access to treatment, pain caused by tests/treatments, and treatment safety for pediatric patients. Individuals with DMD and caregivers sometimes cited different factors that affected their ratings the most, with the former focusing on self-esteem and psychological well-being and the latter stressing insurance coverage and medication side effects.

All 3 weight management care considerations were deemed patient-centered. Both panels agreed that it is important and acceptable to maintain healthy weight and to exercise, especially while taking glucocorticoids: "This is an important aspect of maintaining a healthy weight while taking Prednisone or Emflaza," said an individual with DMD B07. Participants also discussed issues related to being overweight and underweight, which can negatively affect quality of life. "Increased weight can greatly shorten the patient's life and also makes care difficult and can cause further social ostracism," said individual with DMD A12. Regardless of the patient-centeredness of all weight management care considerations, panel A participants still raised concerns about the lack of nutritional guidance developed

specifically for Duchenne. To use the words of caregiver A19, “Being given a nutritional plan would be a good guide to follow to know what is acceptable to eat.” Panel B participants discussed how disease progression and different treatments can negatively affect the ability to feed oneself, exercise, and attend school full-time. In addition, participants raised concerns about insurance coverage for physical therapy and noted the need for more specific guidance on which type of exercise to pursue and which to stop or avoid. (Although included in other sections of the 2018 DMD care considerations, we did not include this more specific guidance into our protocol due to concerns about participation burden.) As individual with DMD A10 put it, “Exercise can be risky, especially when falls happen, which . . . can lead to fractured bones. So even . . . with the safeguards, these risks will be there, but the process is still acceptable because the reward of increased quality of life is greater in my experience.”

All 3 bone health care considerations were deemed patient-centered. Participants stressed the importance of obtaining baseline bone health information even in the absence of visible signs of bone loss for monitoring disease progression: “Spinal imaging should be monitored for scoliosis and compression fractures. A baseline is needed for future comparison,” said caregiver B07. Participants generally viewed assessments as important for early detection of bone thinning and for identifying the right time to start taking vitamins and supplements, adjusting their dosage, or initiating bisphosphonate treatment. X-rays and dual-energy X-ray absorptiometry (DEXA) scans used to assess bone health were generally considered safe and minimally invasive. Nonetheless, some raised concerns about difficulties in transferring individuals with DMD to an X-ray table, the ability to lie flat on a table during procedures due to discomfort caused by joint contractures, and DEXA scan costs that are not always covered by insurance. While treatment of vertebral fractures and bone loss with intravenous (IV) bisphosphonates was deemed patient-centered, some participants worried about off-label use of this drug for children, high costs of medication, and potential side effects. As caregiver A38 said, “It’s off label for children . . . cost, insurance coverage, safety. . . . I don’t feel this is something for the typical DMD family.”

Four of 8 vertical growth care considerations were deemed patient-centered, including guidance to periodically assess growth until puberty is complete and to work with an endocrinologist to identify reasons for growth delays. Both panels felt that it is important to identify growth delays before age 13 and that X-rays of the hand and wrist are simple procedures with limited risks: “a very easy and tolerable process that the boys go through each year. If this helps with their quality of care, it should be done in all clinics,” said caregiver B44. Panel B participants, however, were less optimistic about the importance of identifying growth delays in boys 13 and older because “you have little time to promote growth through treatments,” said caregiver B31. Nonetheless, as individual with DMD A10 noted, identifying growth delays might be more acceptable after age 13 because “the older you get, the less stressful X-rays or other scans are.” Finally, both panels were uncertain about the importance and acceptability of treating growth delays in boys of different age groups with abnormal growth hormone stimulation tests using hormone replacement therapy, citing the need for daily injections, concerns about side effects, and the lack of evidence that this treatment works. This result, however, is consistent with the guidance in



the 2018 care considerations that does not recommend routine use of growth hormones to treat DMD-related growth delay.

While 2 of the 5 puberty-related care considerations were deemed patient-centered, participants generally had somewhat different opinions about assessing and treating pubertal delays. Panel B's ratings were generally lower than panel A's. Some caregivers argued that there are more important concerns than pubertal delays that Duchenne families worry about and that such assessments are invasive and require additional doctor visits. "It seems unnecessarily invasive, especially to boys who already have extra medical attention," said caregiver B22. Nonetheless, individuals with DMD stressed the importance of self-esteem for boys. To use the words of individual with DMD A38, assessments "would detect delays, which would help the boys keep up with peers." Indeed, testosterone treatment discussions highlighted the tension between the importance of addressing emotional and social isolation that may be exacerbated by delayed puberty with the potential of negative side effects (e.g., mood swings) from what may be a medically unnecessary therapy. The following quotation from caregiver B34 summarizes the dilemma: using testosterone replacement therapy "is important, as long as the testosterone is monitored and does not make the boys more aggressive." Participants also stressed the importance of allowing each boy to develop at his own pace. "Let each individual unfold uniquely, steroids destroy children's lives for the hope of maintaining strength and destroys their immune system," said individual with DMD B05 in support of his low rating of the care consideration that focused on using testosterone therapy while taking glucocorticoids. The decision to initiate testosterone replacement therapy seemed to be largely dependent on the choice of a child or a family. Both panels, however, viewed as patient-centered the care consideration to slowly increase testosterone dosing to mimic normal pubertal development after the decision to start this therapy was made. Panelists cited strong scientific evidence behind dosing and the importance of starting with low doses to ensure patient safety.

## Discussion

Using the RPM, our study showed that most care considerations our participants rated were deemed patient-centered. That is, patients and their caregivers identified these care considerations as likely to be consistent with the preferences, needs, and values—and aligning with available resources and ethical standards—of Duchenne families in general. Patient-centered care considerations include guidance about weight management and bone health, assessment and identification of impaired vertical growth, assessment of pubertal delays, and guidance about testosterone dosing for treating pubertal delays.

Our study provided somewhat less certainty about the patient-centeredness of 7 care considerations. The care considerations not meeting our patient-centeredness criteria, however, should not be automatically treated as not patient-centered. Because such care considerations might be highly preference sensitive, conditional, and context specific, individuals with DMD and their caregivers may want to discuss them with clinicians to assess the reasons why these care considerations were not deemed patient-centered in our study. Reviewing a list of potential concerns raised by our study participants can inform the development of patient decision aids<sup>38,39</sup> and can help providers who do not see many

patients with DMD initiate discussions that focus on the aspects of care that may be potentially problematic to Duchenne families. Such discussions can bring patient-based evidence into clinical decision making<sup>40</sup> and bridge the gap between evidence-based clinical care and patient values and preferences that patient-centered care seeks to achieve.<sup>25,26</sup> Because patient-centered care “is a quality of personal, professional, and organizational relationships,”<sup>41</sup> it is created through a “give-and-take” during a patient-provider encounter. Knowing what Duchenne families think about the importance and acceptability of different care considerations already deemed clinically appropriate and necessary can help providers and families engage in shared decision making<sup>42,43</sup> informed by clinical, research, and patient-based evidence, as well as local context.<sup>44</sup>

The 3 care considerations that both panels agreed were of uncertain importance and acceptability all related to treating impaired growth with growth hormone therapy. The actual statement we used in the study was to reserve recombinant human growth hormone (rhGH) only for treating children if they had abnormal growth hormone stimulation tests, which is consistent with the clinical guidance not to use this treatment routinely.<sup>10</sup> Although such “conditional” guidance to use the therapy only under certain circumstances further reinforces the need for shared decision making, it may have been confusing to participants. On the one hand, the lower ratings of importance and acceptability may suggest that Duchenne families may be less supportive of this treatment. On the other hand, they may suggest that participants may have misunderstood that these care considerations are conditional. This finding highlights the need to interpret patient-centeredness ratings in the context of a particular care consideration and shows the importance of explaining conditional recommendations more clearly to participants.

Finally, only 1 panel viewed care considerations about using testosterone replacement therapy to treat delays in pubertal development as important and acceptable, suggesting that Duchenne families might have highly varying perspectives on this treatment depending on their values, needs, and life circumstances. In discussing the goals that individuals with DMD and their families want to achieve, clinicians may want to start a conversation about concerns raised about testosterone replacement therapy so that Duchenne families are more informed before initiating or refusing this therapy.

We note several limitations of our study. First, we asked participants to provide their input on already finalized care considerations. Ideally, patients and caregivers should provide their input on draft recommendations to allow guideline developers to account for patient-centeredness determinations before finalizing the recommendations. Second, we used a purposive sample of individuals with DMD and their caregivers that may not be representative of the experiences of Duchenne families in general. We note, however, that the purposive sampling approach is a best practice for Delphi panels<sup>45</sup> because their goal is to explore consensus among key stakeholders rather than make statistical inferences about a population. Moreover, our panels included a much larger number of participants with diverse experiences than previous efforts to solicit patient input on guide lines.<sup>46</sup> Third, not all panelists participated in round 3, which could have biased our results. Attrition, however, is common for Delphi studies.<sup>47</sup> Fourth, because of the nature of Duchenne, we invited more caregivers than adult individuals with DMD and excluded children. We could not apply the

RAM to determine consensus within each panel for each participant type separately because there were fewer than 9 responses to round 3 questions from individuals with DMD in 1 panel. RAM requires responses from at least 9 participants.<sup>13</sup> To highlight the difference that existed in their perspectives on patient-centeredness, we used the qualitative analyses. Fifth, although our measure of patient-centeredness was developed based on best practices for rating appropriateness and necessity, is consistent with the GRADE Evidence to Decision Framework,<sup>20</sup> and was pilot-tested, it has not been formally validated. Finally, we used a conditional wording of care considerations related to treating delayed vertical growth with growth hormones, which may have confused some participants.

Based on the results of this study, we identified 3 topics for future research. First, if feasible, future studies should recruit more patients and balance the number of patients and caregivers to be able to better understand the difference in their perspectives. Second, to further explore the difference between patient and caregiver perspectives, future projects should include individuals with DMD younger than 18 as their perspectives may be different from older individuals with DMD and their caregivers. Third, although we used the RPM to explore the relevance of care considerations to patients and caregivers, future work can focus on adapting the RPM to determining 3 core components of content validity of patient-reported outcome measures as defined in the COSMIN framework, including relevance, comprehensiveness, and comprehensibility.<sup>48</sup>

## Conclusions

In summary, we used the RPM, a novel approach to large-scale patient and caregiver involvement in the process of developing clinical guidelines, to determine the patient-centeredness of 2018 DMD care considerations. Instead of asking participants to comment on clinical appropriateness and necessity of different care considerations—the 2 areas where they may not have enough expertise—we asked individuals with DMD and their caregivers to rate the extent to which specific care considerations are important and acceptable. Treatment acceptability/burden is not always considered by guideline developers, but including this information can help patients make informed decisions about their care<sup>49</sup> and ultimately improve guideline adherence.<sup>50</sup>

Although we found that most DMD care considerations met the patient-centeredness criteria, our findings highlight the need to engage both patients and caregivers because they may have different views, especially on questions around sensitive issues (i.e., pubertal development). As individuals with DMD grow older, their input in the decisions about their own care becomes particularly crucial. Parents of younger boys with DMD noted the importance of seeing the perspectives of men with DMD who have already gone through certain stages of disease progression, arguing that their opinion is helpful not only for making final determinations of patient-centeredness but also for initiating treatment discussions with clinicians. Engaging families in guideline development, however, should happen before guidelines are finalized.<sup>51</sup> Doing so may improve the quality of recommendations and increase their use in practice. By incorporating patient and caregiver perspectives, guideline developers can preemptively draw clinicians' attention to certain aspects of the recommendations that might be of concern to patients and their caregivers.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Recommendation 1: Assessment of growth**  
Height and length measurements for patients with Duchenne should be assessed every 6 months until puberty is complete and final height is reached.  
*Clinical reason for recommendation: To identify any growth delays early on by comparing individual's height to the height of children of similar age.*  
*Process: Track height/length on a standard growth chart twice a year until puberty.*  
*Additional information: Height and length measurements are typically taken during a routine health visit, and should be tracked every 6 months until puberty/final adult height is reached.*

How important is the clinical reason for recommendation 1 for a typical individual/family with Duchenne?

1 2 3 4 5 6 7 8 9

Not very important          Very important

Please briefly explain your response. What factor(s) affected your response the most?

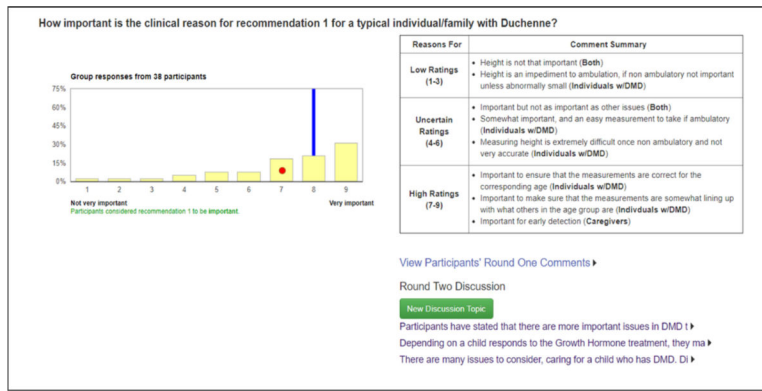
How acceptable is the process of following recommendation 1 to a typical individual/family with Duchenne?

1 2 3 4 5 6 7 8 9

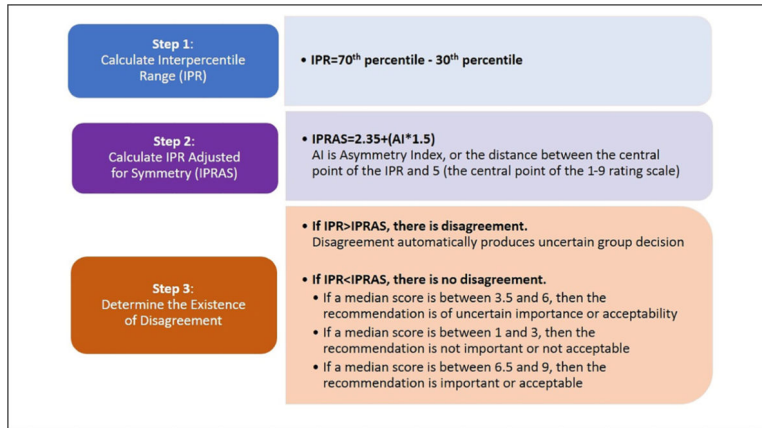
Not very acceptable         Very acceptable

Please briefly explain your response. What factor(s) affected your response the most?

**Figure 1.** Round 1 questions. Participants are presented with a brief description of a care consideration, clinical reasons for and process involved in following the care consideration, and any additional relevant information that can help them rate its importance and acceptability. Participants are then asked to use 9-point Likert scales to rate the importance and acceptability of each care consideration and explain the factors that affected their responses the most using open text boxes below each rating scale.



**Figure 2.** Round 2 feedback and discussion. The bar chart represents a distribution of participants’ responses. The blue line indicates a group median. The red dot indicates a participant’s own response. The statement presented below the chart informs participants about the group decision. In this particular chart, participants considered recommendation 1 to be important. The median was 8 on a 9-point scale. However, the participant’s own response was 7, which is below the median value. The table presents a summary of participants’ rationale comments from round 1. It lists the main reasons for providing low ratings (1–3), uncertain ratings (4–6), and high ratings (7–9). It also indicates whether a given reason was provided by individuals with Duchenne muscular dystrophy (DMD), caregivers, or both stakeholder groups. At the bottom of the figure are links to the discussion threads with comments posted in round 2 about the importance of this recommendation.



**Figure 3.** Statistical approach to determining final group decisions about the importance and acceptability of care considerations. Final group decisions are determined using the RAND/UCLA Appropriateness Method (RAM) approach.

**Table 1**

Participant Characteristics<sup>a</sup>

| Characteristic                               | Overall (n = 95),<br>n (%) | Individuals with<br>Duchenne (n = 24), n (%) | Parents/Caregivers<br>(n = 71), n (%) | P Value |
|--|----------------------------|--|---------------------------------------|---------|
| <b>Sex</b>                                   |                            |  |                                       |         |
| Female                                       | 59 (62.1)                  | 0 (0)  | 59 (83.1)                             | <.001   |
| Male   | 36 (37.9)                  | 24 (100)                                     | 12 (16.9)                             |         |
| <b>Region</b>                                |                            |  |                                       |         |
| Northeast                                    | 23 (24.2)                  | 8 (33.3)                                     | 15 (21.1)                             | .257    |
| Midwest                                      | 23 (24.2)                  | 5 (20.8)                                     | 18 (25.4)                             |         |
| South  | 24 (25.3)                  | 3 (12.5)                                     | 21 (29.6)                             |         |
| West   | 25 (26.3)                  | 8 (33.3)                                     | 17 (23.9)                             |         |
| <b>Hispanic/Latino/Spanish<sup>b</sup></b>   |                            |  |                                       |         |
| Yes  | 4 (4.3)                    | 0 (0)  | 4 (5.7)                               | .569    |
| No   | 90 (95.7)                  | 24 (100)                                     | 66 (94.3)                             |         |
| <b>Race</b>                                  |                            |  |                                       |         |
| White  | 86 (90.5)                  | 21 (87.5)                                    | 65 (91.5)                             | .559    |
| Black/African American                       | 1 (1.1)                    | 0 (0)  | 1 (1.4)                               |         |
| Asian  | 4 (4.2)                    | 1 (4.2)                                      | 3 (4.2)                               |         |
| Multirace                                    | 1 (1.1)                    | 0 (0)  | 1 (1.4)                               |         |
| Other  | 3 (3.2)                    | 2 (8.3)                                      | 1 (1.4)                               |         |
| <b>Highest education level</b>               |                            |  |                                       |         |
| High school or equivalent                    | 10 (10.5)                  | 4 (16.7)                                     | 6 (8.5)                               | .127    |
| Some college                                 | 21 (22.1)                  | 7 (29.2)                                     | 14 (19.7)                             |         |
| Associate degree                             | 15 (15.8)                  | 5 (20.8)                                     | 10 (14.1)                             |         |
| Bachelor degree                              | 24 (25.3)                  | 6 (25)                                       | 18 (25.4)                             |         |
| Graduate degree                              | 25 (26.3)                  | 2 (8.3)                                      | 23 (32.4)                             |         |
| <b>Status of an individual with Duchenne</b> |                            |  |                                       |         |
| Ambulatory                                   | 43 (45.3)                  | 1 (4.2)                                      | 42 (59.2)                             | <.001   |
| Nonambulatory                                | 52 (54.7)                  | 23 (95.8)                                    | 29 (40.8)                             |         |

How far do you usually travel to receive neuromuscular care?<sup>b</sup>

| Characteristic | Overall ( <i>n</i> = 95),<br><i>n</i> (%) | Individuals with<br>Duchenne ( <i>n</i> = 24), <i>n</i> (%) | Parents/Caregivers<br>( <i>n</i> = 71), <i>n</i> (%) | <i>P</i> Value |
|----------------|---|---|--|----------------|
| <50 miles      | 38 (41.3)                                 | 10 (43.5)   | 28 (40.6)  | .087           |
| 50–99 miles    | 22 (23.9)                                 | 9 (39.1)  | 13 (18.8)  |                |
| 100–249 miles  | 17 (18.5)                                 | 1 (4.3)   | 16 (23.2)  |                |
| 250 miles      | 15 (16.3)                                 | 3 (13)  | 12 (17.4)  |                |

<sup>a</sup>. *P* values of the Fisher exact test measuring the difference between the demographic characteristics of individuals with Duchenne muscular dystrophy and caregivers participating in our study are presented in the last column.

<sup>b</sup>. Not all participants answered this question.

**Table 2**

Ratings of Importance and Acceptability of Endocrine Care Considerations<sup>a</sup>

| Characteristic   | Panel A (n = 27) |          |               |          |            |          | Panel B (n = 27) |          |            |          |               |          | Patient-Centered <sup>b</sup> |
|--|------------------|----------|---------------|----------|------------|----------|------------------|----------|------------|----------|---------------|----------|-------------------------------|
|  | Importance       |          | Acceptability |          | Importance |          | Acceptability    |          | Importance |          | Acceptability |          |                               |
|  | Median           | Decision | Median        | Decision | Median     | Decision | Median           | Decision | Median     | Decision | Median        | Decision |                               |
|  |                  |          |               |          |            |          |                  |          |            |          |               |          |                               |
| Vertical growth  | 8                | +        | 8             | +        | 7          | +        | 9                | +        | 7          | +        | 9             | +        | Yes                           |
| Assessment of growth   | 7                | +        | 7             | +        | 7          | +        | 8                | +        | 7          | +        | 8             | +        | Yes                           |
| Identification of impaired growth (7 years of age and younger)                           | 8                | +        | 8             | +        | 7          | +        | 8                | +        | 7          | +        | 8             | +        | Yes                           |
| Identification of impaired growth (between 8 and 12 years of age)                        | 8                | +        | 8             | +        | 6          | u        | 7                | +        | 6          | u        | 7             | +        | No                            |
| Identification of impaired growth (between 13 and 18 years of age)                       | 8                | +        | 8             | +        | 7          | +        | 8                | +        | 7          | +        | 8             | +        | Yes                           |
| Identification of reasons for impaired growth and development of a treatment plan        | 5                | u        | 5             | u        | 5          | u        | 5                | u        | 5          | u        | 5             | u        | No                            |
| Treatment of impaired growth with growth hormone therapy (7 years of age and younger)    | 6                | u        | 5             | u        | 6          | u        | 5                | u        | 6          | u        | 5             | u        | No                            |
| Treatment of impaired growth with growth hormone therapy (between 8 and 12 years of age) | 6                | u        | 5             | u        | 5.5        | u        | 5                | u        | 5.5        | u        | 5             | u        | No                            |
| Treatment of impaired growth with growth hormone therapy(between 13 and 18 years of age) |                  |          |               |          |            |          |                  |          |            |          |               |          |                               |
| Weight management  |                  |          |               |          |            |          |                  |          |            |          |               |          |                               |
| Maintaining healthy weight (diet)  | 9                | +        | 8             | +        | 9          | +        | 9                | +        | 9          | +        | 9             | +        | Yes                           |
| Maintaining healthy weight (nutrition)   | 9                | +        | 8             | +        | 9          | +        | 7.5              | +        | 9          | +        | 7.5           | +        | Yes                           |
| Maintaining healthy weight (exercise)  | 8                | +        | 7             | +        | 8          | +        | 8                | +        | 8          | +        | 8             | +        | Yes                           |
| Bone health  |                  |          |               |          |            |          |                  |          |            |          |               |          |                               |
| Assessment of spinal health and detection of vertebral compression fractures             | 9                | +        | 8             | +        | 9          | +        | 8.5              | +        | 9          | +        | 8.5           | +        | Yes                           |
| Assessment of bone health/mineralization using dual-energy X-rayabsorptiometry scans     | 9                | +        | 8             | +        | 9          | +        | 8                | +        | 9          | +        | 8             | +        | Yes                           |
| Treatment of vertebral fractures and bone loss with intravenous bisphosphonates          | 8                | +        | 7             | +        | 8          | +        | 7                | +        | 8          | +        | 7             | +        | Yes                           |
| Puberty  |                  |          |               |          |            |          |                  |          |            |          |               |          |                               |
| Assessment of puberty  | 7.5              | +        | 7             | +        | 6          | u        | 7                | +        | 6          | u        | 7             | +        | No                            |
| Assessment and treatment of delays in puberty  | 8                | +        | 8             | +        | 8          | +        | 8                | +        | 8          | +        | 8             | +        | Yes                           |
| Use of testosterone replacement therapy to treat delays in puberty                       | 7.5              | +        | 7             | +        | 6.5        | +        | 6                | u        | 6.5        | +        | 6             | u        | No                            |
| Use of testosterone therapy while taking glucocorticoids                                 | 7                | +        | 7             | +        | 6          | u        | 7                | +        | 6          | u        | 7             | +        | No                            |
| Testosterone dosing to mimic normal pubertal development                                 | 8                | +        | 7             | +        | 7          | +        | 6.5              | +        | 7          | +        | 6.5           | +        | Yes                           |



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$p$  . +: a positive decision, meaning that participants within a given panel considered a given care consideration to be important or feasible (a median score of 6.5–9, without disagreement). u: an uncertain decision without disagreement, meaning that participants within a given panel considered a given care consideration to be of uncertain importance or feasibility (a median score of 3.5–6, without disagreement).

$q$  . A care consideration is patient-centered if both panels deemed it important and acceptable.