Reduction in the aMMO (<40 mm) was found in 26% of the total patient group. LNAS patients had significantly smaller mandibular movements compared to AS and ENAS ($P < 0.05$). Multiple linear regression analysis for aMMO revealed a positive correlation with the body height and disease progression, with MFM total score as the strongest independent risk factor ($R^2 = 0.71$). Mandibular movements in DMD are significantly reduced and become more hampered with loss of motor function, including the sitting position, arm function, and neck and head control. We suggest that measurement of the aMMO becomes a part of routine care of patients with DMD.

**Keywords:** Duchenne muscular dystrophy, masticatory system, mandibular range of motion, quantitative ultrasound, masticatory muscles, motor function measure

Accepted for publication 22 December 2014
The most important influencing factors upon the mandibular ROM in healthy subjects are the length of the mandible, functional capacity of the mandibular opening and closing muscles, morphology and status of the temporomandibular joint (TMJ), and pain conditions in the masticatory system (9, 10).

Ultrasound measurements in patients with DMD of the masseter muscles and the suprahyoid muscles showed structural changes in these muscles indicating muscular dystrophy (4, 11). Hypothetically, the structural changes may lead to decreased strength of the muscles involved in mandibular movement and contribute to a limited mandibular ROM.

Factors beyond the masticatory system may contribute to a reduction in the mandibular range of motion as well. Recent observations suggest a functional relationship between the cranio-cervical and the masticatory system (12, 13). As a consequence, gross motor function measurement, which includes assessment of posture, neck function and head control, might be predictive for the mandibular range of motion.

The aim of our investigation was to determine whether the mandibular range of motion in DMD is impaired compared to that in healthy subjects and to explore predictive factors for the active maximum mouth opening (aMMO) in DMD.

Material and methods

Participants

Twenty-four patients with DMD aged from 6 to 38 years, participating in a swallowing study on DMD (11), and 24 age-matched healthy males were examined between May 2010 and February 2012.

Patients were recruited by announcements of patient organisations. Only patients with an established diagnosis of DMD older than 5 years were eligible. Duchenne muscular dystrophy patients who were entirely dependent on tube feeding were excluded.

The control group was recruited at a primary and a secondary school located in the western part of the Netherlands. Healthy students above 18 years were recruited at the College of Dental Sciences, Nijmegen, the Netherlands. Exclusion criteria for controls were the following: a history of neuromuscular disease, temporomandibular disorder, orthodontic treatment and morphologic dental malocclusion such as cross-bite and a tendency to cross-bite.

Protocol

The participants in both the patient and the control group completed a questionnaire and underwent a clinical examination of the masticatory system including measurement of the mandibular range of motion.

Additionally, the patients underwent quantitative muscle ultrasound imaging (QMUS) of the anterior belly of the digastic muscle and the geniohyoid muscle (14), and an assessment of their general physical abilities using the Motor Function Measure (MFM) (15).

Questionnaire

All subjects completed the questionnaire Screen, which was developed to assess pain in the head and neck region, mandibular function and related issues (16, 17).

Clinical examination of the masticatory system

All participants in this study were clinically examined following the validated procedure as described by Lobbezoo-Scholte et al. (18–21). This clinical examination included, among others, measurement of the mandibular range of motion, palpation of the masticatory muscles and the temporomandibular joints. All patients and controls were examined in the upright position with their heads supported in a neutral position.

The following mandibular movements were assessed: active maximum mouth opening (aMMO), passive maximum mouth opening (pMMO), protrusion, and left and right lateral range of motion. The overbite and overjet were also measured. The aMMO was the distance measured between the incisal edges of the upper and lower central incisors plus the overbite. All measurements were recorded with a metal ruler (mm). We considered mandibular movements to be reduced: <40 mm for aMMO, <8 mm for active lateral excursion and <5 mm for protrusion. The mobility of the temporomandibular joint was assessed by palpation of the lateral pole of the mandibular condyle during MMO with the index finger. Sliding of the mandibular condyle was assessed on a two-point scale: reduced meaning no or hardly any sliding of the lateral pole of the mandibular condyle and normal meaning sliding of the condyle to the
crest of the articular eminence or beyond the crest of the articular eminence.

The masseter and temporalis muscles were palpated to assess pain on palpation. The temporalis muscles were palpated bilaterally using the index and/or middle finger, applying firm pressure along the anterior, middle and posterior parts for 2–3 s. Then, the origin, the body and the insertion of the masseter are individually palpated for 2–3 s. Finally, the temporomandibular joints were palpated for 2–3 s. The left and right condyles were palpated in an open and closed mouth position. The lateral pole of each condyle was palpated anterior to the tragus of the ear and over the TMJ, and the posterior aspect of each condyle via the external acoustical meatus. Palpation pressure was firm (2–4 pounds) and was adjusted to the vulnerable patients, when appropriate (20, 22, 23).

All pain reports of the participants during examination were recorded on a five-point Likert scale: 0 = no pain, 1 = mild, 2 = moderate, 3 = severe and 4 = very severe.

Echo intensity imaging of the digastric and geniohyoid muscles

In the patient group, QMUS was used to measure echo intensity of the digastric and geniohyoid muscles (11). These two muscles were selected because of their anatomical location. The diagnostic value of muscle ultrasound and the test–retest reproducibility for the digastric muscle and the geniohyoid muscles was good (11).

The region of interest was quantified by grey-scale analysis and calculation of z-scores (i.e. the amount of standard deviations below or above the mean of norm values), a reliable method with which changes in muscle architecture are assessed and compared with normal values (24, 25). The grey value of the mean of the left and right digastrics muscles and of the left and right geniohyoid muscle was expressed as z-scores. Z-score of <-2 and >2 is considered abnormal. Quantitative muscle ultrasound imaging of the digastric and geniohyoid muscles proved to be feasible in healthy children and young adults and is used for the detection of structural changes in these muscles (14).

Medical information and general physical abilities

In the patient group, information was gathered, among others, on body height, and baseline physical abilities were assessed by a physical therapist with expertise in paediatrics using a selection of MFM items. The MFM items have been previously been described (15). The items 13–23 used in this study collect information about the sitting position, arm function, and neck and head control. The MFM items were scored on a four-point Likert scale and summed to comprise a total raw score (range 0–33), in which the maximum represents normal motor function.

Based on the ambulatory function and the MFM, the patients were divided into early and late ambulatory stage (AS), early non-ambulatory stage (ENAS) or late non-ambulatory stage (upper limb function and postural maintenance is increasingly limited) (LNAS) (26).

Statistical analysis

IBM SPSS version 20* was used to analyse the collected data. Mean and standard deviation were used to describe the average maximum mouth opening, the lateral excursions and the protrusion of the mandible in the patient and in control group. Paired Student’s t-test was used to compare between-group continuous variable outcomes, and for dichotomous variables, the chi-square test was used.

Patient data were further analysed using the three DMD stages. To compare test outcomes between the DMD stages, ANOVA was used for scale variables and chi-square test for dichotomous variables.

Univariate and multivariate regression analyses were performed to determine which factors possibly affect the aMMO within the patient group (dependent variable). The independent variables were age, body height, MFM total scores, MFM score item 13–14, ultrasound score of the digastric muscle and geniohyoid muscle.

Results

Participants

Twenty-four patients with DMD were approached for inclusion in the study. One of the patients was excluded from the study because DMD was not genetically confirmed, and the signs and symptoms did not fit into the

*IBM SPSS Statistics version 20, Inc., Chicago, IL, USA.
Table 1. Group comparison and descriptive statistics of the mandibular range of motion during clinical examination in the patient group (n = 23) and in the control group (n = 23)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patient group n = 23</th>
<th>Control group n = 23</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years, month (s.d.) range</td>
<td>16.7 (7.7) 16.3 (6.7)</td>
<td>0.851</td>
<td></td>
</tr>
<tr>
<td>aMMO (mm) (s.d.) range</td>
<td>43.5 (11.0) 54.6 (6.2)</td>
<td>&lt;0.0001*</td>
<td></td>
</tr>
<tr>
<td>pMMO (mm) (s.d.) range</td>
<td>44.3 (11.1) 55.4 (6.8)</td>
<td>&lt;0.0001*</td>
<td></td>
</tr>
<tr>
<td>Lateral ROM L/R (mm) (s.d.) range</td>
<td>6.4 (3.0) 9.3 (1.7)</td>
<td>&lt;0.0001*</td>
<td></td>
</tr>
<tr>
<td>Protrusion (mm) (s.d.)</td>
<td>4.7 (3.5) 9.3 (2.5)</td>
<td>&lt;0.0001*</td>
<td></td>
</tr>
</tbody>
</table>

aMMO: active maximum mouth opening, the maximum interciscal distance on opening as wide as possible plus the vertical overbite (limited MMO <40 mm).

pMMO: passive maximum mouth opening, the maximum interciscal distance on active opening, with a slight overpressure on the edges of the upper and lower front teeth by the examiner plus the vertical overbite.

Lateral ROM L/R: active mandibular lateral excursion, mean value between the left and right side.

Protrusion: active forward movement of the mandible. Statistically significant differences (*P < 0.05) between the patient group and control group, tested with paired Student’s t-tests.

For analysis, the data of 23 patients and 23 age-matched males were used (Table 1). Patient characteristics of the total DMD sample as well as of the three stage groups are indicated in Table 2.

Questionnaire

A limitation in the ability to open the mouth was noted in three patients (13%), and pain during opening the mouth was mentioned in four other patients (17-4%, Table 2). The maximum intensity of the recorded pain in these four patients was ‘mild’.

Clinical examination of the masticatory system

In six patients (26-1%), mild pain could be provoked during aMMO, passive mouth opening, or palpation of the masseter muscle, temporalis muscle or the lateral pole of the TMJ. Four of these six patients belonged to the LNAS (Table 2).

Active and passive maximum mouth opening, active mandibular lateral excursion and protrusion were significantly smaller in the patient group than in the control group (Table 1). In the patient group, 6 (26%) had a reduced aMMO (<40 mm). The difference between the aMMO and the pMMO in the patient and the control group was 1 mm. The LNAS had a statistically significant smaller aMMO than the ENAS (Table 2).

The active mandibular lateral excursion was reduced (<8 mm) in 16 patients (70%); all patients in the LNAS had a reduced lateral ROM. The LNAS had a statistically significant smaller lateral ROM than the ENAS (Table 2).

The active mandibular protrusion was reduced (<5 mm) in seven patients (30%). The ENAS had a statistically significant smaller protrusion than the AS (Table 2).

Clinical examination of the mobility of the temporomandibular joint revealed that 22 patients (96-0%) had a normal sliding of the mandibular condyle (Table 2). All controls had normal sliding of the mandibular condyle.

Echo intensity imaging

The echo intensity of the anterior belly of the digastric muscles, expressed as z-score, was found to be increased (z > 2) in 16-6% of the patients in the AS, 28-6% in ENAS and 50-0% in LNAS. The echo intensity of the geniohyoid muscles was increased in 50-0% of the patients in AS, 85-7% in ENAS and 90-0% in LNAS. There was a statistically significant difference between the AS and LNAS regarding the echo intensity of the geniohyoid muscles (Table 2).

General physical abilities

There was a significant difference in the MFM score between the ENAS and LNAS, and between AS and LNAS regarding the MFM total score (Table 2). There was a statistically significant difference between the ENAS and LNAS, and between AS and LNAS regarding the MFM items 13–14 score.

Predictive factors for the active maximum mouth opening

Univariate linear regression analysis outcomes of potential predictors of aMMO in patients with DMD are presented in Table 3. The univariate linear regres-
Table 2. Characteristics of patients with Duchenne muscular dystrophy (n = 23) presented by stages. Mean and standard deviation of the measurements referred to as x (s.d.) or number of patient as n/%

<table>
<thead>
<tr>
<th>Variable</th>
<th>DMD stage</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total (n = 23)</td>
<td>AS (1) (n = 6)</td>
</tr>
<tr>
<td>Age, years, month (s.d.) range</td>
<td>16.7 (7.7)</td>
<td>8.4 (1.5)</td>
</tr>
<tr>
<td>MFM, total raw score††</td>
<td>20.1 (12.6)</td>
<td>32.5 (0.8)</td>
</tr>
<tr>
<td>MFM item 13–14†</td>
<td>0–33</td>
<td>33–33</td>
</tr>
<tr>
<td>aMOMO (mm) range</td>
<td>43.5 (11.0)</td>
<td>47.5 (7.9)</td>
</tr>
<tr>
<td>pMOMO (mm) range (s.d.) range</td>
<td>44.3 (11.0)</td>
<td>48.3 (7.6)</td>
</tr>
<tr>
<td>Lateral ROM L/R (mm) (s.d.) range</td>
<td>6.4 (3.0)</td>
<td>7.3 (3.3)</td>
</tr>
<tr>
<td>Protrusion (mm) (s.d.) range</td>
<td>4.7 (3.5)</td>
<td>7.0 (1.8)</td>
</tr>
<tr>
<td>El digastri m., mean L/R‡‡</td>
<td>2.0 (3.1)</td>
<td>0.5 (1.4)</td>
</tr>
<tr>
<td>El geniohyoid (s.d.) range³ (z-score)</td>
<td>−1.3 to 10.6</td>
<td>−1.3 to 2.3</td>
</tr>
<tr>
<td>Body height (cm) (s.d.) range</td>
<td>158.7 (21.9)</td>
<td>130.8 (8.8)</td>
</tr>
<tr>
<td>MIMO reduced, subj†</td>
<td>3/13%</td>
<td>1/17%</td>
</tr>
<tr>
<td>Reduced TMJ sliding‡‡</td>
<td>1/4%</td>
<td>0/0%</td>
</tr>
<tr>
<td>Pain provocation‡‡</td>
<td>6/26%</td>
<td>1/17%</td>
</tr>
</tbody>
</table>

DMD, Duchenne muscular dystrophy; AS, Early and late ambulatory stage; ENAS, Early non-ambulatory stage; LNAS, Late non-ambulatory stage.

†Statistically significant difference between the DMD stages, tested with ANOVA for scale variables and with chi-square test for dichotomous outcome. The significance in the dichotomous outcomes relates to the variable being absent or present.

‡‡MFM: Motor Function Measure, domain 2, items 13–23 assessed axial en proximal motor capacities – 12 items (total raw score 33 points); MFM score per item: 0 = does not initiate movement or starting position cannot be maintained; 1 = partially completes the exercise; 2 = completes the exercise with compensations; slowness or obvious clumsiness; and 3 = completes the exercise with a standard pattern.

‡MFM items 13–14: item 13: seated on the chair without support of upper limbs or leaning against the back of the chair, maintains the sitting position, head and trunk in the axis; score 0–3; item14: seated on the chair or in their wheelchair. Head in flexion: from the fully flexed position, raises the head and maintains the raised position, head in the axis during the movement and when maintained; score 0–3.

El digastic L/R and geniohyoid muscles: echo intensity grey value (z-score) of the mean value of the left and right digastrics muscle and of the geniohyoid muscle; z-scores > 2.0; z-score < –2 and >2 is abnormal.

*Sliding of the temporomandibular joint was assessed by palpation: reduced = no or hardly any sliding of the lateral pole of the mandibular condyle and normal = sliding to and beyond the crest of the articular eminence.

††Pain provocation during active mouth opening, passive mouth opening, or palpation of the masseter muscle, temporalis muscle or the lateral pole of the TMJ.

Regression analysis revealed negative correlations between the aMOMO and age, body height, ultrasound score of the digastic muscle and geniohyoid muscle, and positive correlations for the MFM variables. Because of the small number of patients, only two variables are used in our multiple linear regression analysis. Age and MFM variables are strongly correlated (Pearson correlation 0.828; P = <0.001) via disease progression, making age less informative. Therefore, we entered body height in the model, which in combination with MFM total raw score improved the model (R² = 0.71).
Discussion

In this study, the impact of DMD on the mandibular movements was assessed by comparing the mandibular ROM of patients with those of a gender and age-matched healthy control group. Also, mandibular ROM per ambulatory stage (AS, ENAS or LNAS) in the DMD group was examined. Predictive factors were established for reduced aMMO in the patient group. This study shows that mandibular ROM was significantly lower in patients with DMD compared to controls. The decreased aMMO in patients with DMD was primarily related to body height and higher disease severity, expressed by the motor function.

Measurement of the mandibular movements is a standard procedure for evaluation of the musculoskeletal masticatory structures (18, 22). As an entity on itself, the active MMO is a parameter that can be established reliably, regardless of the severity of the limitation; the interobserver intra-class correlation coefficient (ICC) was 0.98, and the intra-observer ICC and inter-session ICC reliabilities both were 0.99 (27).

In view of the wide range of variation of individual mandibular movements, it is difficult to set normal ranges and uniformity regarding the maximum movements. Suggested cut-off values for the aMMO in healthy subjects vary between 40 and 44 mm for man; 38 and 42 mm for woman; and 35 and 40 for children (28–33). In accordance with the literature, we consider for our study <40 mm for aMMO, <8 mm for active lateral excursion and <5 mm for protrusion as restricted. These values do not seem to be in conflict with other findings from the literature.

In our study, we have incorporated the concept of the mandibular range of motion as an anatomical position (condyle in relation to the crest of the eminence next to the interincisal measurement of mandibular movements (34). Healthy individuals may perform normal opening with highly variable amounts of condylar translation, and variation in maximum incisor opening is largely explained by variation in the amount of mandibular rotation (35). It is mentioned in the literature that maximum incisor opening does not provide reliable information about condylar translation and its use as a diagnostic indicator of condylar movement is limited (35). A combination of the interincisal measurement of mandibular opening and assessment of the anatomical condylar position in relation to the crest of the eminence will improve establishing whether the impairment is intra-articular or not (34).

Regarding aMMO in patients with DMD compared to healthy controls, conflicting objective data can be found in the literature ranging from a reduced maximum mouth opening to a non-significant difference (3, 4). The mean reduction in the aMMO of our patient group compared to the age and gender matched controls was 11 mm, which is a clinically relevant difference. In another study, MMOs of 39-1 mm (DMD patients, mean age 11-7 years) and 54-2 (healthy controls, mean age 11-9 years) were found (4). However, in a Japanese population, no significant difference between the DMD group and the control group was found, although the MMO of the patients tended to be less compared to controls (mean age 21.5 vs. 21.3, MMO 36.9 vs. 41.0 mm) (3).

Despite the higher mean age in the latter study, the MMO was less than reported in the study of Botteron et al. (4) and our study. All studies included the vertical overbite in their measurements. Differences in ethnicity and instructions during the examination of the studied population in these studies may explain the variation of the aMMO values.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Effect</th>
<th>Lower bound</th>
<th>Upper bound</th>
<th>P-value</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>−0.52</td>
<td>−1.35</td>
<td>0.28</td>
<td>0.005*</td>
<td>0.13</td>
</tr>
<tr>
<td>Body height (cm)</td>
<td>−0.12</td>
<td>−0.33</td>
<td>0.10</td>
<td>0.27</td>
<td>0.06</td>
</tr>
<tr>
<td>MFM total raw score</td>
<td>0.64</td>
<td>0.39</td>
<td>0.90</td>
<td>&lt;0.001*</td>
<td>0.57</td>
</tr>
<tr>
<td>MFM item 13−14</td>
<td>2.65</td>
<td>1.06</td>
<td>4.23</td>
<td>0.002*</td>
<td>0.37</td>
</tr>
<tr>
<td>El digastric muscle (z-score)</td>
<td>−1.67</td>
<td>−3.07</td>
<td>−0.27</td>
<td>0.022*</td>
<td>0.23</td>
</tr>
<tr>
<td>El geniohyoid muscle (z-score)</td>
<td>−0.99</td>
<td>−1.84</td>
<td>−0.14</td>
<td>0.024*</td>
<td>0.22</td>
</tr>
</tbody>
</table>

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The mandibular ROM is influenced by many factors, that is age, gender, body height, ethnicity, status of the masticatory system, cervical column function, and head and neck posture (32, 36, 37). In patients with DMD, sonography indicated fatty infiltration related to the dystrophic changes of the masseter muscle and the suprahyoid muscles (4, 11). Muscle dystrophy may lead to muscle stiffness and consequently may hamper mouth opening and horizontal jaw movements. In our study, 5 of 6 patients with a limited MMO (≤40 mm) had a normal sliding of the condyle, indicating that structural changes in the muscles may primarily be responsible for the reduced mandibular ROM in general and the aMMO specifically.

The differences between patients and controls regarding the mandibular ROM, and not only maximum mouth opening, indicates a more general muscle involvement than the muscles responsible for mouth opening and closing. The lateral pterygoid muscles play an important role in mouth opening but also in the control of horizontal mandibular movements such as protrusion and laterotrusion (38). In patients with spinal muscular atrophy, involvement of the lateral pterygoid muscle was found to play an important role in the impairment of the mandibular movement in this type of neuromuscular disorder (39). To our knowledge, the effect of DMD on the lateral pterygoid muscle is not investigated by MR imaging.

In healthy individuals, the strength of the vertical component of the mouth opening muscle force (suprahyoid and indirectly the infra-hyoid muscles) is important in mouth opening (40). The structural changes found in the anterior belly of the digastric muscles and geniohyoid muscles in DMD may lead to a decreased strength and contribute to a limited maximum mouth opening. Our linear regression analysis confirms this hypothesis: the echo intensity of the digastrics and geniohyoid muscle correlated with the maximum mouth opening (Table 3). Moreover, the quantitative muscle ultrasound imaging in the patient group showed that the muscle echo intensity of the suprahyoid muscles increased gradually (z-score > 2) with ambulatory loss (11). The influence of DMD on the suprahyoid (and probably the lateral pterygoid) muscles in our patients seems to follow a tendency like other physical characteristics that start to develop according to the stage of the disease.

Table 4. Multiple linear regression analysis of predictors of the impaired active maximal mouth opening (aMMO)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Effect</th>
<th>95% confidence interval for effect</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>−14.360</td>
<td>−45.550 to 16.831</td>
<td>0.348</td>
</tr>
<tr>
<td>Body height (cm)</td>
<td>0.247</td>
<td>0.078 to 0.415</td>
<td>0.006*</td>
</tr>
<tr>
<td>MFM total raw score</td>
<td>0.932</td>
<td>0.639 to 1.225</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

$R^2 = 0.71$.

The study of L van de Engel-Hoek et al., 2012 showed the feasibility of quantitative muscle ultrasound of digastric muscles, the geniohyoid muscles in healthy subjects and patients with DMD (11). Quantitative muscle ultrasound imaging showed significant differences in echo intensity between healthy subjects and DMD patients, especially in the geniohyoid muscle. The anatomic location and structure of, for example, the mylohyoid muscle proved to be too thin to be measured and analysed. However, we do not expect that other oral muscles such as the mylohyoid muscles are spared from DMD.

In this cohort of 23 boys and adults with DMD, the linear regression analysis revealed the severity of DMD, assessed by the MFM, and the height of the patient to be the strongest independent predictive factors for a restricted aMMO (Table 4). Although age and height are generally related, in patients with DMD, due to the growth disturbances, height turned out to be a stronger independent factor for a restricted aMMO than age (Table 4).

A restricted mouth opening may hamper feeding, oral hygiene and dental care. Recognising this impairment and their predictive factors by medical staff, patients, parents and caretakers is a first step. Furthermore, in terms of management, it is important to take measures to slow down the development of the mouth opening reduction, possibly by developing a training programme. The programme has to be easy to implement in daily life and with low intensity aerobic exercises as suggested in other training programmes for patients with DMD (41, 42).

Conclusion

Mandibular movements in DMD are significantly reduced compared to the healthy controls and become

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more hampered with loss of motor function, including the sitting position, arm function, and the neck and head control. We suggest that evaluation of the aMMO as an expression of the reduced mandibular range of motion becomes a part of routine care of patients with DMD.

**Ethical approval**

The study was approved by the Committee on Research Involving Human Subjects of Arnhem and Nijmegen, the Netherlands (Registration Number 2009/331).

**Author contributions**

All authors contributed substantially to the design of the study, drafting the article and revising it and gave final approval of the version to be published.

**Declaration of conflicting interests**

The authors declared no potential conflicts of interest with respect to the authorship and/or publication of this article.

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**References**


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