### Importance of the Graded Chronic Pain Scale as a Biopsychosocial Screening Instrument in TMD Pain Patient Subtyping

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### Aims: To compare the suitability of Graded Chronic Pain Scale (GCPS) pain intensity and interference assessments (GCPS version 1.0 vs 2.0) for the biopsychosocial screening and subtyping of Finnish tertiary care referral patients with TMD pain. Methods: Altogether, 197 TMD pain patients participated in this study. All patients received Axis II specialist-level psychosocial questionnaires from the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD-FIN) and Research Diagnostic Criteria for Temporomandibular Disorders (RDC/ TMD-FIN), as well as questionnaires for the assessment of additional painrelated, biopsychosocial, and treatment-related variables. Clinical examinations were performed according to the DC/TMD Axis I protocol. The patients were categorized into TMD subtypes 1, 2, and 3 (GCPS I and II-low; II-high; and III and IV, respectively) based on their biopsychosocial profiles according to GCPS versions 1.0 and 2.0. Results: The distribution of TMD pain patients into TMD subtypes was similar according to the GCPS 1.0 compared to the GCPS 2.0. Over 50% of the patients were moderately (TMD subtype 2) or severely (TMD subtype 3) compromised. Patients in subtype 3 experienced biopsychosocial symptoms and reported previous health care visits significantly more often than patients in subtypes 1 and 2. Patients in subtype 2 reported intermediate biopsychosocial burden compared to subtypes 1 and 3. Conclusion: TMD pain patients differ in their biopsychosocial profiles, and, similarly to the GCPS 1.0, the GCPS 2.0 is a suitable instrument for categorizing TMD tertiary care pain patients into three biopsychosocially relevant TMD subtypes. The GCPS 2.0 can be regarded as a suitable initial screening tool for adjunct personalized or comprehensive multidisciplinary assessment. J Oral Facial Pain Headache 2021;35:303-316. doi: 10.11607/ofph.2983

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emporomandibular disorders (TMDs) are pain and functional disorders concerning the temporomandibular joints (TMJs), the masticatory muscles, and associated structures.<sup>1</sup> The etiology of TMDs is complex and multifactorial, as biopsychosocial, genetic, and environmental factors may influence their onset and persistence.<sup>2,3</sup> Based on the OPPERA study (Orofacial Pain: Prospective Evaluation and Risk Assessment), a large prospective cohort study designed to discover causal determinants of TMD pain, there are several variables-such as sociodemographic<sup>4</sup> and clinical orofacial characteristics,<sup>5</sup> psychologic and psychosocial factors,6 general health status,7 and health care behaviors<sup>8</sup>-that can predict the development of TMD. Psychologic variables such as depression, mood, somatic symptoms, perceived stress, previous life events, and negative affect predict first-onset TMD.<sup>6,9</sup> Various biopsychosocial risk factors such as distress, depression, anxiety, and nonspecific physical symptoms are often linked to pain-related TMD.<sup>10,11</sup> The association between psychologic distress and increased TMD pain, as well as increased pain-related disability, has also been corroborated in previous studies,<sup>10,12</sup> whereas somatic awareness and depression are common among patients with persistent TMD pain.<sup>13</sup> In addition, self-perceived poor general health and sleep dysfunction, as well as comorbid pains, are associated with the complexity of TMD

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© 2021 BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER. pain.<sup>14-16</sup> Poor coping<sup>17</sup> and increased pain-related worry<sup>14,18</sup> may also be associated with increased risk for constant and chronic pain.

Identifying individuals with a higher psychosocial burden aids in targeting tailored treatment for TMD patients. Previous studies have indicated that TMD pain patients vary in their biopsychosocial profiles. Bair et al<sup>3</sup> identified individuals in adaptive, pain-sensitive, and global symptoms clusters based on biopsychosocial measures. Turk and Rudy<sup>19</sup> presented three subgroups of chronic pain patients based on Multidimensional Pain Inventory (MPI) data and identified three pain profiles: *(1)* adaptive coping; *(2)* interpersonally distressed; and *(3)* dysfunctional chronic pain. Dworkin et al<sup>10,20</sup> and Suvinen et al<sup>14</sup> introduced three biopsychosocial TMD pain subtypes based on the Graded Chronic Pain Scale (GCPS).

The Research Diagnostic Criteria for TMD (RDC/ TMD) were developed in 1992 in order to understand the multifactorial nature of TMD. The RDC/TMD is a dual-axis system in which Axis I assigns physical diagnoses and Axis II indicates psychosocial variables, such as depression and nonspecific physical symptoms.<sup>21</sup> An integral part of the RDC/TMD Axis II is the GCPS version 1.0, which consists of two main subscales: Characteristic Pain Intensity (CPI) and pain-related interference (including disability days due to pain and pain interference on daily, work, and social activities). Many studies have demonstrated that the RDC/TMD are valid criteria for assessing pain grade and pain-related psychosocial dysfunction.<sup>12,14,22-27</sup>

Based on the GCPS assessment, patients are categorized into five levels of pain-related impairment, from grades 0 to IV. Grade II has been further divided into two grades (grade II-high and grade II-low). Previous studies have reported that patients in GCPS grades 0, I, and II-low are considered psychosocially functional, whereas patients with intense pain and moderate to severe disability (GCPS grades II-high, III, and IV) are considered psychosocially dysfunctional.<sup>10,20,21</sup> Psychosocially dysfunctional TMD patients have reported higher levels of psychosocial loading factors, such as depression, nonspecific physical or somatic symptoms, sleep dysfunction, pain-related worry, poor coping ability, poor self-perceived general health, catastrophizing thoughts, and chronic pain.<sup>10,14,20,27</sup> The GCPS 1.0 has been suggested as a useful instrument for classifying TMD patients into clinically relevant psychosocial subtypes in primary care<sup>28</sup> and into biopsychosocial subtypes in tertiary care.<sup>14</sup>

The Diagnostic Criteria for TMD (DC/TMD), a revised, evidence-based, and diagnostically more reliable version of the RDC/TMD, was introduced in 2014.<sup>29</sup> While the RDC/TMD criteria are mainly intended for research settings, the DC/TMD criteria are suited for implementation into clinical settings as well.

Furthermore, the DC/TMD criteria include new instruments for assessing pain behavior, psychologic status, and psychosocial functioning.<sup>29</sup> The DC/TMD Axis Il includes psychologic instruments for screening of psychologic distress (Patient Health Questionnaire-4 [PHQ-4]) and for comprehensive specialist-level assessments of depression symptoms (PHQ-9), anxiety symptoms (Generalized Anxiety Disorder-7 [GAD-7]), and nonspecific physical symptoms (PHQ-15).29 Moreover, the DC/TMD criteria include an updated GCPS guestionnaire (GCPS version 2.0), which evaluates pain-related intensity and interference during a 30-day time frame compared to the 6-month time frame of the previous GCPS 1.0. However, the discriminative properties of the GCPS 2.0 for biopsychosocial profiling and in relation to the GCPS 1.0 have not been previously investigated.

The primary aim of this cross-sectional study was to compare the Finnish versions of the DC/TMD and RDC/TMD Axis II specialist-level psychosocial assessments in Finnish tertiary care TMD pain patients. The second aim was to compare the suitability of the GCPS 2.0 to the GCPS 1.0 pain intensity/interference assessments for biopsychosocial subtyping of these patients as an initial screening tool for adjunct personalized or comprehensive multidisciplinary treatment. The primary working hypothesis was that the GCPS 2.0 is similar to the GCPS 1.0 as an initial screening and tailoring method in biopsychosocial subtyping of TMD pain patients. The second working hypothesis was that the GCPS 2.0 can be used as a biopsychosocial screening tool in the early identification of TMD patients with moderately or severely compromised biopsychosocial adaptation.

### **Materials and Methods**

Altogether, 197 TMD pain patients (158 women, 39 men, mean age 43.3 years, range 17 to 83 years) who had been referred for assessment and TMD treatment planning to tertiary care centers of the Oral and Maxillofacial Diseases Departments of Helsinki University Hospital, Kuopio University Hospital, Oulu University Hospital, and Turku University Hospital between July 2015 and March 2019 participated in this study. All patients 17 years or older who had clinically diagnosed TMD were included in the study. The sample size was set according to the guidelines of the INfORM (International Network for Orofacial Pain and Related Disorders Methodology) consortium.<sup>30</sup>

Participation in the study was voluntary, and the subjects provided informed consent. The Ethics Committee of the Hospital District of Southwest Finland approved the study (74/1082/2015).

Prior to this study, the Finnish translations of the RDC/TMD and DC/TMD instruments (RDC/TMD-FIN and DC/TMD-FIN, respectively) had undergone a comprehensive translation process by the International INfORM Consortium according to the Guidelines for Establishing Cultural Equivalency of Instruments.<sup>30</sup>

#### **Axis I Somatic Diagnostics**

The clinical TMD examinations and all questionnaire evaluations were performed by four examiners (P.K., R.N., K.S., and T.T.O.) according to the DC/TMD-FIN.<sup>29,31</sup> The examiners had been trained prior to this study by the Malmö International DC/TMD Training and Calibration Center and calibrated against a reference standard examiner in the Finnish language<sup>32</sup> according to the INfORM Consortium guidelines.<sup>30</sup>

Clinical Axis I diagnostics were based on the Symptom Questionnaire (DC/TMD-FIN-SQ), the DC/ TMD standardized clinical examination protocol, and Axis I decision trees.<sup>31</sup> The diagnoses included TMD pain-related diagnoses (myalgia, myofascial pain, arthralgia, TMD-related headache) and joint-related diagnoses. Multiple diagnoses were allowed. The SQ was also used for additional TMD pain assessments not included in the Axis I somatic diagnostics, as follows:

- Pain duration: How many years or months ago did your pain in the jaw, temple, in the ear, or in front of the ear first begin?
- Pain frequency: In the last 30 days, which of the following best describes any pain in your jaw, temple, in the ear, or in front of the ear on either side: No pain, Pain comes and goes (recurrent pain), Pain is always present (constant pain)

### Axis II Questionnaires and Additional Biopsychosocial Assessments

All patients received the Finnish versions of both the RDC/TMD and DC/TMD Axis II specialist-level psychosocial questionnaires and an additional questionnaire including supplementary pain-related, biopsychosocial, and treatment-related questions (not included in the RDC/TMD or DC/TMD) to be completed at home. The questionnaires were assessed for accuracy by the treating clinicians at the time of clinical examination.

### **RDC/TMD-FIN Axis II Questionnaires**

The RDC/TMD-FIN Axis II questionnaires include assessment of TMD pain intensity and interference using the GCPS 1.0 and assessment of the level of depression symptoms and nonspecific physical symptoms with and without pain items using the SCL-90-R (RDC/TMD-FIN).<sup>33</sup> The GCPS 1.0 assessed patient-based reports of TMD pain intensity and pain-related interference in three domains during the past 6 months, as follows:

- CPI (current, worst, average): range 0–10, where 0 = no pain, 10 = worst pain; scaled as mean value\*10, maximum 100
- Disability days: range 0–180 days/0–3 points; categorized as 0–6 days = 0 disability day points; 7–14 days = 1 disability day point; 15–30 days = 2 disability day points; 31+ days = 3 disability day points
- Disability/interference score: range 0-100/0-3 points; for pain interference with daily, social, and work-related activities: range 0-10, where 0 = no interference, 10 = unable to carry on any activities, scaled as mean value\*10, maximum 100; score of 0-29 = 0 disability points; score of 30-49 = 1 point; score of 50-69 = 2 points; score of 70+ = 3 points

The total count of pain interference/disability points (range 0–6) toward the GCPS 1.0 global score (including the CPI) is based on the sum of the points for disability days + the points for disability score (see GCPS Grade and TMD Pain Patient Subtyping).

With the RDC/TMD-FIN Axis II Symptom Checklist 90 Revised (SCL-90-R) questionnaire, patients reported how much they suffered during the last month from symptoms of depression (20 questions) and nonspecific physical symptoms, including pain items (12 questions) or without pain items (7 questions).<sup>21</sup> The range for each item on the questionnaire is 0-4, where 0 = not at all and 4 = very much.

### **DC/TMD-FIN Axis II Questionnaires**

The DC/TMD-FIN questionnaires included sociodemographic background data. For the analysis, marital status was dichotomized as married/cohabiting vs single (divorced, separated, widowed, or never married). Level of education was dichotomized as lower (basic education, high school, vocational school) vs higher (university of applied sciences, university, Master of Arts). Working status was dichotomized as employed (working outside home, at home) vs unemployed (unemployed, student, retired, on disability, retired due to sickness, sick leave, or in rehabilitation).

The DC/TMD-FIN Axis II questionnaires included the TMD pain intensity and interference assessment using the GCPS 2.0, as well as assessment of symptoms of depression (PHQ-9), anxiety (GAD-7), and physical symptoms (PHQ-15).<sup>31</sup>

The DC/TMD-FIN GCPS 2.0 was the same as the RDC/TMD-FIN GCPS 1.0, with differences in the following questions for pain interference:

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- Pain days during the past 6 months (range 0–180 days)
- Disability days (range 0-30 days/0-3 disability points), scored as: 1 day = score 1; 2-7 days = scores 2-7, respectively; 8-20 days = score 8; 21-25 days = score 9; 26-30 days = score 10. Disability day points were categorized as follows: 0-1 days (score 1) = 0 disability day points; 2 days (score 2) = 1 disability day point; 3-5 days (score 3-5) = 2 disability day points; 6+ days (score 6+) = 3 disability day points.

The total count of pain interference/disability points (range 0–6) toward the global GCPS 2.0 score (including the CPI) is based on the sum of points for disability days + points for pain-related activity interference (see GCPS Grade and TMD Pain Patient Subtyping).

With the DC/TMD-FIN Axis II questionnaires, the patients reported how much they suffered from various symptoms of:

- Depression (PHQ-9-FIN, 9 questions with a range of 0-3, where 0 = not at all and 3 = nearly every day during the past 2 weeks).
- Anxiety (GAD-7-FIN, 7 questions with a range of 0-3, where 0 = not at all and 3 = nearly every day during the last 2 weeks).
- Physical symptoms (PHQ-15-FIN, 15 questions with range from 0-2, where 0 = not bothered and 2 = bothered a lot during the past 4 weeks).

There may be potential bias linked to missing data. For the sum scores of depression, anxiety, and physical symptoms, missing values for items on the questionnaires were replaced with the mean values of other items. If there were missing values for more items than the following limits, the response was considered as missing for the instrument (The n value represents the number of missing responses for each instrument)<sup>21,34</sup>:

- GCPS 1.0 and GCPS 2.0: CPI: 0 items (n = 4 for GCPS 1.0 and n = 5 for GCPS 2.0)
- Pain-related activity interference: 1 item (n = 5 for both GCPS 1.0 and GCPS 2.0)
- RDC/TMD depression: 8 items (n = 9)
- Somatization with pain: 4 items (n = 8)
- Somatization without pain: 2 items (n = 8)
- PHQ-9: 3 items (n = 4)
- PHQ-15: 5 items (n = 4)
- GAD-7: 2 items (n = 6)

# Additional Pain-Related, Biopsychosocial, and Treatment-Related Variables

Additional pain-related, biopsychosocial, and treatment-related variables (not included in the RDC/ TMD or DC/TMD) were assessed as follows:

- Comorbid pains: Patients reported whether they suffered from any of the following comorbid pain problems: headache, neck ache, back pain, stomach pain, fibromyalgia pain, joint pain, other pain (chest pain, pain in the arms/legs, or any other pain; 1 = yes, 0 = no)<sup>35</sup>
- Patient-perceived general health status: In general, how would you rate your overall health? (with response options excellent, very good, good, fair, or poor; 1 = excellent, 5 = poor)
- Anxiety: How anxious have you felt during the last week? (range 0–10, where 0 = absolutely calm and 10 = as anxious as I've ever felt)<sup>36</sup>
- Stress: How nervous or stressed have you felt during the last week? (range 0–10, where 0 = no stress and 10 = I felt myself very stressed)<sup>36</sup>
- Patients' level of worry about their pain condition: How worried are you about the pain and symptoms? (range 0–10, where 0 = not worried at all and 10 = extremely worried)<sup>18</sup>
- Sleep dysfunction was assessed by the average score of 3 questions on the SCL-90-R measuring sleep disturbance (difficulty falling asleep, restless sleep, and early morning awakening; range 0–4, where 0 = no difficulty and 4 = a lot of difficulty)<sup>37</sup>
- Coping questions were derived from the Coping Strategies Questionnaire, measuring (1) ability to control pain (range 0–6, where 0 = no control and 6 = under control) and (2) ability to decrease pain (range 0–6, where 0 = no ability to decrease and 6 = ability to decrease)<sup>38</sup>
- Previous health care visits and current subjective treatment expectations: Patients were also asked to indicate the number of previous visits to dentists/doctors or other health care professionals and their current self-perceived goals and treatment expectations regarding the need to receive information and improvement of pain control, jaw function, stress management skills, and/or their performance in daily and/or work ability (0 = no, 1 = yes)

# GCPS Grades and TMD Pain Patient Subtyping

According to the GCPS 1.0 and 2.0, the grades were determined as follows according to Dworkin and LeResche<sup>21</sup> and Ohrbach and Knibbe<sup>34</sup>:

- GCPS grade I: low-intensity pain (CPI < 50) without disability or with low disability (0-2 disability points).
- GCPS grade II: high-intensity pain (CPI ≥ 50) without disability or with low disability (0-2 disability points). Patients in GCPS grade II were further subdivided into two grades according to Dworkin et al<sup>10,20</sup>: GCPS grade IIlow = no disability (disability points = 0); GCPS grade II-high = low disability (disability points = 1-2).
- GCPS grade III: 3–4 disability points regardless of CPI value (determined as moderately limiting).
- GCPS grade IV: 5–6 disability points regardless of CPI value (determined as severely limiting).

The biopsychosocial TMD pain subtyping assessments were grouped into three TMD subtypes (1, 2, and 3) for analysis based on the GCPS 1.0 and GCPS 2.0 grades according to Dworkin et al<sup>10,20</sup> and Suvinen et al,<sup>14</sup> as follows:

- TMD subtype 1 = GCPS grades I and II-low
- TMD subtype 2 = GCPS grade II-high
- TMD subtype 3 = GCPS grades III and IV

### **Statistical Analysis**

The differences in sociodemographic background, Axis I diagnoses, pain frequency, and comorbid pain sites between the GCPS 1.0 and 2.0 TMD subtypes were analyzed using chi-square test, and the differences in self-perceived goals and treatment expectations were analyzed using likelihood ratio test.

In the Axis II questionnaire assessments (SCL-90-R, PHQ-9, PHQ-15, GAD-7), the raw mean and median sum scores were calculated, and box plots were generated to include the interquartile ranges (IQR; 25th and 75th percentiles), as well as the minimum and maximum scores. The differences in continuous variables (sum scores of depression, anxiety, and nonspecific physical symptoms/somatization; number of Axis I diagnoses; pain duration; number of comorbid pain sites; number of visits to dentist/doctor; and additional psychosocial variables) between the TMD subtypes of the GCPS 1.0 and the GCPS 2.0 were analyzed using Jonckheere-Terpstra test. Statistical significance was set at P < .05.

In the pairwise comparisons of these variables (differences between TMD subtype 3 vs 1 and 2; and TMD subtype 2 vs 1 and 3), Mann-Whitney U test was used. After Bonferroni correction, the statistical

# Table 1 Distribution of GCPS 1.0 and 2.0 Scoring Items,<br/>GCPS Grades, and TMD Subtypes<sup>10,20</sup> in the<br/>Study Sample<br/>(N = 197)

	GCPS 1.0 (n = 180)		GCPS 2.0 (n = 184)	
	n	%	n	%
GCPS scoring items				
CPI				
1–50	55	28.6	74	38.8
≥ 50	137	71.4	115	60.2
Disability points (0-6)				
0	74	40.9	81	43.6
-2	38	21.0	29	15.6
3–4	28	15.5	31	16.6
5-6	41	22.6	45	24.2
GCPS grade				
	48	26.7	61	33.1
ll low	28	15.6	25	13.6
ll high	35	19.4	22	12.0
	28	15.6	31	16.8
IV	41	22.7	45	24.5
TMD subtype				
1 (I + II-low)	76	42.3	86	46.7
2 (II-high)	35	19.4	22	12.0
3 (III + IV)	69	38.3	76	41.3

significance was set at P < .017. Data were analyzed using SPSS version 25 software (IBM).

### **Results**

There were no significant differences in sociodemographic background (gender, mean age, marital status, education level), nor differences in age or gender distribution between the TMD subtypes according to the GCPS 1.0 or the GCPS 2.0. Of the patients, 61.9% were married, 41.1% had received higher education, and 49.7% were employed.

# GCPS 1.0 and 2.0 Assessment Data in TMD Subtypes

The distribution of GCPS item scores and GCPS grades, as well as classification into GCPS grades/ TMD subtypes, was similar among TMD pain patients as assessed with both the GCPS 1.0 and 2.0 (Table 1). A majority of the patients belonged to either TMD subtype 1 (42.3%) or TMD subtype 3 (38.3%) using the GCPS 1.0; similarly, the majority of the patients belonged to TMD subtype 1 (46.7%) or TMD subtype 3 (41.3%) based on the GCPS 2.0. More patients were classified into TMD subtype 2 based on the GCPS 1.0 in comparison to the GCPS 2.0. Over 50% of the patients were considered as moderately (TMD subtype 2) or severely (TMD subtype 3) compromised (GCPS 1.0; 57.7%; GCPS 2.0; 53.3%).

## Table 2a Mean (SD) Number of DC/TMD Axis I Diagnoses in Patients of Each TMD Subtype<sup>10,14,20</sup> According to the GCPS 1.0 and GCPS 2.0

		GCPS 1.0	(n = 180)		GCPS 2.0 (n = 184)					
TMD subtypes	1 (n = 76)	2 (n = 35)	3 (n = 69)	Pª	1 (n = 86)	2 (n = 22)	3 (n = 76)	Pa		
All diagnoses	2.53 (1.53)	3.39 (1.27)	3.63 (1.54)	< .001	2.64 (1.55)	3.05 (1.12)	3.75 (1.94)	< .001		
Pain-related diagnoses	1.72 (1.20)	2.56 (1.24)	2.81 (1.30)	< .001	1.81 (1.36)	2.45 (0.96)	2.87 (1.34)	< .001		
Joint-related diagnoses	0.57 (0.62)	0.68 (0.64)	0.54 (0.72)	.593	0.62 (0.64)	0.50 (0.51)	0.55 (0.72)	.690		

<sup>a</sup>Jonckheere-Terpstra test.

# Table 2b Distribution of DC/TMD Axis I Diagnoses in Patients of Each TMD Subtype<sup>10,14,20</sup> According to the GCPS 1.0 and 2.0

	Total	GCPS 1.0 (n = 180)				GCPS 2.0 (n = 184)			
TMD subtype	no. of patients	1 (n = 76)	2 (n = 35)	3 (n = 69)	$P^{a}$	1 (n = 86)	2 (n = 22)	3 (n = 76)	$P^{a}$
Pain-related diagnoses									
Myalgia	142	53.9	82.9	83.8	< .001	58.1	90.9	82.7	< .001
Myofascial pain with referral	93	30.3	48.6	63.2	< .001	31.4	45.5	66.7	< .001
Arthralgia	140	60.5	85.7	76.5	.012	64.0	77.3	80.0	.065
Headache attributed to TMD	79	27.6	34.3	55.9	.002	25.6	31.8	58.7	< .001
Joint-related diagnoses									
Disc dislocation with reduction	34	18.4	11.4	18.8	.598	19.8	9.1	18.4	.502
Disc dislocation with intermittent locking	1	1.3	2.9	0.0	.412	2.3	0.0	1.3	.715
Disc dislocation without reduction with limited opening	24	38.2	34.3	18.8	.241	40.9	9.1	50.0	.667
Disc dislocation without reduction without limited opening	57	38.2	34.3	18.8	.033	33.7	36.4	21.1	.146
Degenerative joint disease	39	15.8	14.3	25.0	.272	18.6	4.5	26.7	.066

Data are reported as % unless otherwise indicated.

<sup>a</sup>Chi-square test.

### Axis I Diagnoses in TMD Subtypes

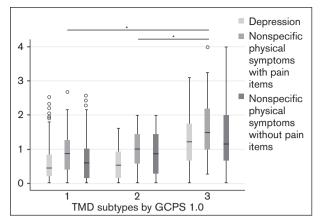
Most patients had multiple Axis I pain-related diagnoses. In the total sample, myalgia and arthralgia diagnoses were the most prevalent Axis I diagnoses. No TMJ subluxations were diagnosed. The total number of diagnoses and the number of pain-related diagnoses differed significantly among TMD subtypes, whereas no significant differences were found in the number of joint-related diagnoses (Tables 2a and 2b). Pain-related diagnoses were more prevalent in TMD subtypes 2 and 3 than in TMD subtype 1.

In pairwise comparisons, the total number of Axis I diagnoses differed significantly between TMD subtypes 1 and 2 (P = .006) and subtypes 1 and 3 (P < .001) of the GCPS 1.0. For the GCPS 2.0,

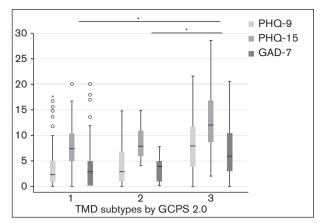
the difference between TMD subtypes 1 and 3 (P < .001) was statistically significant. The number of pain-related diagnoses differed significantly between TMD subtypes 1 and 2 (P = .003) and between sub-types 1 and 3 (P < .001) of the GCPS 1.0, as well as between TMD subtypes 1 and 3 (P < .001) of the GCPS 2.0.

### Axis II Psychosocial Variables in TMD Subtypes

The sum scores for depression and nonspecific physical symptoms (with pain items and without pain items) assessed using the SCL-90-R were the highest among those in TMD subtype 3 of the GCPS 1.0 (Fig 1). The differences among TMD subtypes



**Fig 1** Box plot showing sum scores of depression and nonspecific physical symptoms by TMD subtype based on the GCPS 1.0 (SCL-90-R) in TMD pain patients referred to tertiary specialist care for TMD treatment (N = 197). \*Statistical significance between TMD subtypes (P < .001). Differences in variables among TMD subtypes were analyzed using Jonckheere-Terpstra test. Mann-Whitney U test was used with Bonferroni correction for pairwise comparisons (differences between TMD subtype 3 vs 1 and 2, and TMD subtype 2 vs 1 and 3).



**Fig 2** Box plot showing sum scores of depression (PHQ-9), nonspecific physical/somatic (PHQ-15), and anxiety (GAD-7) symptoms by TMD subtype based on the GCPS 2.0 in TMD pain patients referred to tertiary specialist care for TMD treatment (N = 197). \*Statistical significance between TMD subtypes (P < .001). The differences in variables among TMD subtypes were analyzed using Jonckheere-Terpstra test. Mann-Whitney U test was used with Bonferroni correction for pairwise comparisons (differences between TMD subtype 3 vs 1 and 2; and TMD subtype 2 vs 1 and 3).

were statistically significant (P < .001, Jonckheere-Terpstra test). In pairwise comparisons, TMD subtype 3 differed significantly from TMD subtypes 1 and 2 in all measured items.

For the GCPS 2.0, the sum scores for depression (PHQ-9), physical symptoms (PHQ-15), and anxiety (GAD-7) were the highest in TMD subtype 3 (Fig 2). The differences among TMD subtypes were statistically significant (P < .001, Jonckheere-Terpstra test). In pairwise comparisons, TMD subtype 3 differed significantly from TMD subtypes 1 and 2 in all measured items (P < .001, Mann-Whitney U test).

#### Additional Pain Data in TMD Subtypes

The mean pain duration differed significantly among TMD subtypes. In pairwise comparisons, a statistical difference was found in pain duration between TMD subtypes 1 and 3 (P = .014) of the GCPS 2.0. The responses for pain frequency were similarly distributed among the TMD subtypes of both the GCPS 1.0 and GCPS 2.0, with constant pain being reported most frequently in TMD subtype 3 (Table 3).

The most prevalent self-reported comorbid pains were headache and neck pain. The number of different comorbid pains tended to be the highest in TMD subtype 3. The mean number of pain sites differed significantly among TMD subtypes (P < .001; Table 3).

# Additional Biopsychosocial Variables in TMD Subtypes

Additional biopsychosocial variable scores are presented in Table 4. Significant differences among TMD subtypes of the GCPS 1.0 and 2.0 were noted in all measured additional biopsychosocial variables (items). In pairwise comparisons, the difference between TMD subtypes 1 and 2 of the GCPS 2.0 was statistically significant for the item "worry" (P = .003). Between TMD subtypes 2 and 3 of the GCPS 1.0, there was a statistically significant difference for the items "worry" (P = .004), "control" (P = .004), "anxiety" (P = .001), and "sleep dysfunction" (P < .001). For TMD subtypes 2 and 3 of the GCPS 2.0, the only significant difference was in sleep dysfunction (P <.001); however, the differences between TMD subtypes 1 and 3 were statistically significant concerning all items (P < .001).

#### Additional Treatment-Related Variables in TMD Subtypes

The number of previous health care visits and patients' self-perceived treatment expectations are presented in Table 5. Patients in TMD subtype 3 of both the GCPS 1.0 and 2.0 reported the highest number of previous visits to the dentist/doctor or other health care professionals. In pairwise comparisons,

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Table 3 Pain Data for Patients in Each TMD Subtype According to the GCPS 1.0 and 2.0								
GCPS 1.0 (n =					GCPS 2.0 (n = 184)			
TMD subtype	1 (n = 76)	2 (n = 35)	3 (n = 69)	Р	1 (n = 86)	2 (n = 22)	3 (n = 76)	Р
Mean (SD) pain duration (DC/TMD-FIN-SQ), y	6.6 (9.7)	7.2 (9.0)	7.3 (8.6)	.044ª < .001 <sup>b</sup>	6.7 (9.8)	6.4 (7.3)	7.3 (8.8)	.012ª < .001b
Pain frequency (DC/TMD-FIN-SQ), %	of patients							
No pain	3	0	1		1	0	1	
Recurrent pain	74	57	36		75	50	39	
Constant pain	23	43	63		24	50	60	
Comorbid pains, % of patients								
Headache	75	91	96	.002 <sup>b</sup>	74	86	96	.001 <sup>b</sup>
Neck	81	83	96	.031	82	86	93	.120
Low back	70	71	75	.752	68	55	79	.063
Stomach	42	37	71	.001	42	47	67	.006
Chest	18	3	33	.003	15	6	33	.006
Hands	43	50	59	.170	48	46	55	.625
Feet	49	45	66	.067	52	45	63	.214
Fibromyalgia	6	11	35	< .001	7	11	35	< .001
Joints	53	63	68	.205	54	70	67	.161
Mean (SD) no. of comorbid pain sites (0–9)	4.2 (2.0)	4.3 (1.8)	5.7 (2.3)	< .001ª	4.2 (2.0)	4.2 (1.7)	5.6 (2.3)	< .001ª

DC/TMD-FIN-SQ = Symptom Questionnaire.

<sup>a</sup>Jonckheere-Terpstra test.

<sup>b</sup>Chi-square test.

### Table 4 Mean (SD) Additional Biopsychosocial Variable Scores for Each TMD Subtype According to the GCPS 1.0 and 2.0

	GCPS 1.0 (n = 180)				GCPS 2.0 (n = 184)				
TMD subtype	1 (n = 76)	2 (n = 35)	3 (n = 69)	Р	1 (n = 86)	2 (n = 22)	3 (n = 76)	Р	
Self-perceived general health (1-5)	2.81 (0.91)	3.11 (0.90)	3.55 (0.85)	< .001	2.87 (1.00)	3.09 (0.87)	3.55 (0.82)	< .001	
Worry about pain (0–10)	5.22 (2.66)	6.24 (2.39)	7.65 (2.29)	< .001	5.33 (2.50)	7.14 (2.25)	7.28 (2.46)	< .001	
Ability to control pain (0–6)	4.30 (1.33)	3.85 (1.35)	3.11 (1.21)	< .001	4.26 (1.34)	3.86 (1.42)	3.18 (1.20)	< .001	
Ability to decrease pain $(0-6)$	3.50 (1.33)	3.33 (1.41)	2.77 (1.25)	.001	3.49 (1.42)	3.32 (1.25)	2.82 (1.25)	< .001	
Anxiety (0–10)	1.95 (2.51)	1.70 (2.14)	4.00 (2.93)	< .001	1.94 (2.69)	2.72 (2.11)	3.74 (2.87)	< .001	
Stress (0–10)	3.05 (2.52)	3.61 (2.66)	5.09 (2.78)	< .001	3.11 (2.64)	4.56 (2.28)	4.96 (2.80)	< .001	
Sleep dysfunction (0–4)	1.00 (1.00)	1.02 (0.94)	2.16 (1.23)	< .001	1.02 (0.90)	0.92 (1.06)	2.19 (1.21)	< .001	

Jonckheere-Terpstra test was used for comparison.

significant differences were noted in the number of previous health care visits when comparing TMD subtypes 1 and 3 for both the GCPS 1.0 and GCPS 2.0 (P < .001). TMD subtypes 2 and 3 also differed significantly in the number of previous health care visits (P < .001) for the GCPS 1.0, but only in visits to other health care professionals for the GCPS 2.0 (P = .008).

Almost all TMD pain patients in this study reported the need to receive information as well as an improvement of pain control and jaw function as their treatment expectations. About half of the patients reported the need to improve their stress control. More patients in TMD subtypes 2 and 3 in comparison to those in TMD subtype 1 also reported a need to improve their performance in daily and/or work activities.

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 Table 5 Number of Previous Consultations and Self-Perceived Goals and Treatment Expectations in

 Patients of Each TMD Subtype According to the GCPS 1.0 and 2.0

		GCPS 1.0 (n = 180)				GCPS 2.0 (n = 184)				
	1	2	3		1	2	3			
TMD subtype	(n = 76)	(n = 35)	(n = 69)	Р	(n = 86)	(n = 22)	(n = 76)	Р		
Mean (SD) no. of previous visits to										
health care professionals Dentist/doctor	6.6 (12.6)	7.2 (5.5)	23.9 (35.6)	< .001ª	6.5 (11.9)	8.1 (5.9)	22.6 (34.8)	< .001ª		
Other health care	4.7 (9.9)	5.8 (11.8)	28.2 (71.5)	< .001	6.5 (11.9)	7.1 (14.4)	26.7 (69.1)	< .001		
Self-perceived treatment expectations, % of patients										
Receive information	93	91	90	.449 <sup>b</sup>	90	95	91	.755 <sup>b</sup>		
Improve pain control	94	100	99	.136	95	100	99	.197		
Improve jaw function	88	100	88	.028	89	95	92	.646		
Increase the ability to perform daily activities	48	76	91	< .001	50	90	90	< .001		
Improve work ability	36	48	85	< .001	31	67	85	< .001		
Improve stress control	44	33	54	.208	61	50	45	.208		

<sup>a</sup>Jonckheere-Terpstra test.

<sup>b</sup>Likelihood ratio test.

### Discussion

The results of the present study showed that the GCPS 1.0 and GCPS 2.0 distinguished the three TMD subtypes similarly. Therefore, the 30-day version of the GCPS 2.0 can also be considered applicable for categorizing TMD pain patients into biopsychosocially relevant subtypes, similar to the 180-day version of the GCPS 1.0 presented in the previous studies of Dworkin et al<sup>10,20</sup> and Suvinen et al.<sup>14</sup> These results thus support the working hypotheses.

As the present study is among the first to investigate the comparison of the GCPS 1.0 and GCPS 2.0 in the same study population, there are currently few previous data on the subject. For both the GCPS 1.0 and 2.0, the differences between TMD pain patients in TMD subtypes 1 and 3 were statistically significant for the levels of Axis II depression, anxiety, and nonspecific physical symptoms; Axis I clinical diagnoses; and additional pain-related, biopsychosocial, and treatment-related variables. Differences between TMD subtypes 2 and 3 were more clearly seen for the GCPS 1.0 than the GCPS 2.0. The different results between the GCPS 1.0 and 2.0 might be due to the different time frames used (6 months vs 30 days, respectively); it is noteworthy that a shorter 1-month time frame may be more useful in screening more current or ongoing pain impact, similar to other DC/TMD instruments, while a 6-month time frame may be more useful for the assessment of pain impact over a longer time period, especially in the

compromised TMD subtypes or chronic TMD. This has also been supported in the DC/TMD instrument scoring manual that includes both versions of GCPS instruments.<sup>34</sup>

Overall, with both the GCPS 1.0 and 2.0, over 50% of the TMD pain patients in this study presented with either severely (TMD subtype 3) or moderately (TMD subtype 2) compromised biopsychosocial profiles, thus supporting the second hypothesis; ie, that the GCPS 2.0 can be used as an initial screening tool for the early identification of TMD patients with moderately or severely compromised biopsychosocial adaptation. A minor difference was found in the prevalence of patients in subtype 2 for the GCPS 1.0 vs GCPS 2.0, with more patients in this subtype based on GCPS 1.0 categorizing. A previous study of Suvinen et al<sup>14</sup> on tertiary care patients in Finland showed a higher prevalence of patients in TMD subtype 2 (33.3%), but a lower prevalence in TMD subtype 3 (22.9%), compared to the present study (19.4% and 38.3%, respectively, based on GCPS 1.0). Other previous GCPS 1.0 studies have reported varying prevalences in different study populations. In a previous study by Dworkin et al,<sup>10</sup> a total of 117 usual treatment (n = 58) and comprehensive care (n = 59) TMD pain patients with disability were distributed into GCPS grades as follows: II-high (30.8%), III (27.3%), and IV (41.9%). Others have reported lower prevalences; eg, a study by De La Torre Canales et al<sup>39</sup> on 691 Italian tertiary care TMD patients reported that only a small proportion (4.3%) of the patients showed severely limiting, high-disability, pain-related impairment (GCPS grade IV), while the majority presented no or low disability (GCPS grades I and II). Similarly, in a multicenter study by Manfredini et al,<sup>12</sup> a total of 16.9% of tertiary care TMD patients showed severely limiting disability (GCPS grades III and IV) and distinct national differences between centers. Compared to these previous studies, the higher percentages reported in the present study for TMD subtypes 2 and 3 might be due to the differences between the study populations, cultures, or nationalities, or to variations in the paths of referral in different countries.

In other subtyping or categorization studies of TMD pain patients based on biopsychosocial profiles, Bair et al<sup>3</sup> found that almost all (91.5%) of the subjects with TMD belonged to the pain-sensitive and global symptoms clusters, whereas the adaptive cluster included 8.5% of the TMD subjects and 41.2% of the non-TMD subjects. Compared to the adaptive cluster, the pain-sensitive cluster participants showed heightened sensitivity to experimental pain, and those in the global symptoms cluster showed both greater pain sensitivity and greater psychologic distress. In addition, the TMD subjects in the pain-sensitive and global symptoms clusters also showed higher pain intensity, jaw functional limitation, and more comorbid pains compared to non-TMD subjects.<sup>3</sup> More psychologic distress and more comorbid pains were also found most often in the compromised TMD subtypes 2 and 3 of the present study, which are similar to the pain-sensitive and global symptoms clusters.<sup>3</sup> In addition, the TMD subtypes in the present study are also comparable to the adaptive coping, interpersonally distressed, and dysfunctional chronic pain profiles of patients grouped based on MPI data by Turk and Rudy.<sup>19</sup> Patients with dysfunctional chronic pain profiles report more severe pain and more remarkable interference of pain in their lives than patients with other profiles, which is similar to the patients in TMD subtype 3 reporting more disability days and more pain interference with daily, social, and work-related activities than patients in TMD subtypes 1 and 2 in the present study. Patients with the adaptive coping profile and in TMD subtype 1 of the present study seemed to be similar as well, reflecting a lower impact of their pain problems and appearing to cope better with their conditions than patients in TMD subtype 3, while subtype 2 formed an intermediate subtype.

Multiple pain-related clinical diagnoses were discovered in all patients regardless of TMD subtype. For myalgia and arthralgia diagnoses, the distributions were quite similar in TMD subtypes 2 and 3, whereas for the other pain-related diagnoses, TMD subtype 2 formed an intermediate subtype between subtypes 1 and 3. Patients in GCPS 2.0 TMD subtype 3 and in GCPS 1.0 TMD subtypes 2 and 3 had significantly more TMD subdiagnoses, as well as pain-related diagnoses, in comparison to their respective TMD subtype 1 groups. Therefore, the study findings confirm the importance of pain-related diagnostics, as implemented in the new DC/TMD criteria. The joint-related diagnoses did not differ between TMD subtypes. It has been stated that muscle-related diagnoses are more often associated with psychosocial factors than joint-related diagnoses,<sup>40</sup> which are usually more anatomically originated and linked to structural disturbances of the TMJ, such as loose ligaments or disc problems, rather than to pain chronicity.

The sum scores of depression and nonspecific physical symptoms, as assessed by both the RDC/ TMD and DC/TMD Axis II instruments, as well as anxiety symptoms based on the GAD-7, were higher in TMD subtypes 2 and 3 compared to TMD subtype 1. These results, based on both the RDC/TMD and DC/TMD, are in line with previous studies investigating the association between depression/somatization symptoms and pain-related disability using the RDC/ TMD Axis II instruments.<sup>10,12,14,26,27,41</sup> It has been reported in a recent study using the GCPS 2.0 that among psychologic and sociodemographic factors, somatization was the best predictor of pain intensity, while depression was the best predictor for pain-related disability.<sup>42</sup>

Various biopsychosocial assessment variables have been presented as risk factors related to TMD pain onset or chronicity in the biopsychosocial models of pain and in studies concerning TMD pain patients, as well as in OPPERA cohort studies.3,11,14,17,19 Of the variables that are not included in the RDC/ TMD or DC/TMD, self-perceived general health status, stress, pain-related worry, sleep dysfunction, and ability to control pain (coping) have shown an association with chronic TMD pain or with pain continuity.<sup>14–17</sup> In the present study, besides the DC/TMD and RDC/TMD Axis II variables, these additional pain-related, biopsychosocial, and treatment-related variables were selected for the profiling of TMD patients based on previous TMD risk factor studies.14,18,36,38 Significant differences among TMD subtypes were noted for all additional biopsychosocial variables for both the GCPS 1.0 and GCPS 2.0. The differences were most remarkable between TMD subtypes 1 and 3. In addition, the GCPS 1.0, with a longer assessment period of 180 days, was also more sensitive for distinguishing between TMD subtypes 2 and 3 (in the items worry, control, anxiety, and sleep dysfunction), while with the 30-day version of the GCPS 2.0, only sleep dysfunction differed significantly between these TMD subtypes. These results indicate that the burden linked to these additional biopsychosocial

Patients in the present study in all TMD subtypes reported multiple comorbid pain problems, as they reported on average at least four body pain sites. Earlier studies have also shown an association of TMD with comorbid pains and fibromyalgia.<sup>35,43,44</sup> Comorbid pains have also been shown to predict clinical TMD<sup>44</sup> and increase the risk for poor prognosis of TMD pain treatment.<sup>45</sup> Headache, stomachache, and fibromyalgia pain, as well as the number of comorbid pain sites, differed significantly between the TMD subtypes in the present study, which is in line with Suvinen et al.<sup>35</sup> Furthermore, TMD subtype 3 showed a similar profile compared to the global symptoms cluster in the study by Bair et al.<sup>3</sup> which had the most severe symptoms related to clinical pain and more comorbid pains.

It is of clinical relevance and noteworthy in this study that the most severely compromised patients (TMD subtype 3) reported the most severe biopsychosocial burden. In addition, patients in TMD subtype 2 (with intense pain and low disability) formed an intermediate subgroup between the uncompromised TMD subtype 1 patients and the most vulnerable TMD subtype 3 patients. TMD subtype 2 was characterized by clinical findings comparable to TMD subtype 3, but reported intermediate biopsychosocial burden compared to TMD subtypes 1 and 3, similar to Suvinen et al.14 This is also in line with Bair et al,<sup>3</sup> which reported modest but greater psychologic distress in the pain-sensitive cluster compared to the adaptive cluster. Special attention should be paid not only to the patients in TMD subtype 3 but also to those in this intermediate TMD subtype 2, since they may be at potential risk of their symptoms becoming chronic.10,14,20,46,47

The dual-axis approach of the DC/TMD addressed the need for identifying not only clinical diagnostics, but also measures related to other biopsychosocial risk factors and the overall psychosocial impact of TMD pain. Multiaxial classifications, such as the triaxial or subtyping approaches presented here or by Turk and Rudy<sup>19</sup> and Bair et al,<sup>3</sup> can help to identify patients with compromised TMD pain profiles and to plan personalized and/or multiaxial treatment approaches suitable for the identified patient subtypes. GCPS grading has previously been used for planning tailored treatment.<sup>10,20</sup> The randomized controlled studies by Dworkin et al<sup>10,20</sup> evaluated the effect of usual conservative treatment of TMD for TMD patients with no disability (TMD subtype 1) and conservative TMD treatment with six-session cognitive behavioral therapy for TMD patients with low (TMD subtype 2) or moderately or severely limiting (TMD subtype 3) disability.<sup>10,20</sup> The patients in TMD subtype 1 benefited from a self-care program,<sup>20</sup> whereas more comprehensive treatment was more effective for patients with higher pain-related disability.<sup>10</sup>

All patients in the present study, irrespective of TMD subtype, reported a long history of pain duration (on average 6 to 7 years) before referral to tertiary care. In addition, the use of health care services (dentist/doctor or other) increased along with the increasing pain intensity/interference, as the number of visits to either the dentist or doctor was 2 to 3 times higher, and the number of visits to other health care services roughly 4 to 6 times higher, among patients in TMD subtype 3 than in subtypes 1 and 2. Early recognition and tailored treatment, especially for patients in TMD subtypes 2 and 3 at risk for chronic TMD, might decrease the number of visits to dentists, doctors, or other health care professionals, also taking into account the cost-effectiveness of the TMD treatment.48 In addition, those with higher pain-related disability/interference indicated the highest need for improved daily performance, especially work ability, which is in accordance with a study performed in patients in primary care.49 Regardless of TMD subtype, almost all patients expected to receive more information and improved pain control and jaw function from the treatment. This might be due to the fact that the patients had not previously received enough information about their pain problems or that the treatment received earlier had not worked for them. Therefore, it is important that appropriate information and counseling are given and emphasized during the very early stages of TMD treatment for all TMD patients.10,20,50

The size of the study population can be considered one of the strengths of the present research, together with the use of comparative RDC/TMD and DC/TMD assessments in the same patient population. Furthermore, the clinical examinations and questionnaires were based on internationally valid instruments, and all examiners were trained in the use of the DC/TMD, as well as calibrated and reliability trained for the DC/TMD Axis I clinical examination. It should be noted that the Axis II instruments used in the present study are mainly intended for screening and assessing the level and impact of psychosocial factors as a part of comprehensive specialist-level assessment, not for diagnosis. To avoid potential intercultural variation, raw mean and median scores were calculated for the Axis II questionnaire assessments (SCL-90-R, PHQ-9, PHQ-15, GAD-7) for comparison, and no subclassifications were per-

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formed. The primary limitation of the present study may be that the patient population was composed of TMD pain patients referred for specialist care, and the results may thus not be comparable to primary care. Potential bias may also be linked to missing data; however, their proportions were considered to be relatively low (highest for RDC/TMD depression, 4.5%). In addition, the patient population did not allow for comparison between women and men, and the cross-sectional nature of the study does not allow for longitudinal data concerning the patients at this point, thus creating a need for follow-up studies. The number of 17- to 19-year-old patients was 6, which is 3.0% of the total sample. Therefore, the influence of adolescent age can be regarded as minor. Research is needed to evaluate the effect of tailored treatment based on the categorization of TMD pain patients into TMD subtypes. Further investigation is also needed regarding patients in TMD subtypes 2 and 3 to study their profiles more intensively in tailored treatment programs and longitudinally.

The impact of biopsychosocial variables is similar in TMD compared to other pain conditions, as TMD has similar risk factors compared to other musculoskeletal and chronic pain disorders.<sup>11,51</sup> In addition to its use for TMD, the GCPS has been widely used in epidemiologic and clinical research and has also been recently used (as revised) in screening other chronic pain patients for differentiating mild, bothersome, and high-impact chronic pain.<sup>18,52</sup> The findings of the present study are in line with studies and recommendations that emphasize the importance of the biopsychosocial model in the clinical assessment of prolonged or chronic pain patients, including TMD patients, and also the implementation of biopsychosocial screening and assessment methods in dental and medical education.53,54

### Conclusions

Biopsychosocial screening is important in TMD pain assessment because the patients differ in their biopsychosocial profiles. Similar to the GCPS 1.0, the GCPS 2.0 is a suitable initial instrument for distributing TMD tertiary care pain patients into three biopsychosocially relevant TMD subtypes. Biopsychosocial symptoms, such as depression and anxiety symptoms, nonspecific physical or somatic symptoms, comorbid pains, and other biopsychosocial burdens (impaired general health, worry, lack of pain control/ coping, stress, sleep dysfunction), are more prevalent among patients in TMD subtype 3 than in TMD subtypes 1 and 2. TMD subtype 2 forms an intermediate group with regard to biopsychosocial symptoms.

### **Key Findings**

- The GCPS 2.0, similar to the GCPS 1.0, is a useful initial screening instrument for the biopsychosocial subtyping of TMD pain patients for personalized treatment planning.
- The prevalence of several biopsychosocial symptoms is highest among patients in TMD subtype 3, whereas TMD subtype 2 forms an intermediate group between TMD subtypes 1 and 3.

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