

1 **Patterns of Cervical and Masticatory Impairment in Subgroups of People**  
2 **with Temporomandibular Disorders—an Explorative Approach Based on**  
3 **Factor Analysis**  
4

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8 **Abstract**

9 **Objectives**

10 To identify clinical patterns of impairment affecting the cervical spine and masticatory  
11 systems in different subcategories of TMD by an explorative data driven approach.

12 **Methods**

13 For this observational study 144 subjects were subdivided according to Research  
14 Diagnostic Criteria for Temporomandibular Disorders into: healthy controls,  
15 temporomandibular joint (TMJ) signs without symptoms, TMJ affected,  
16 temporomandibular muscles affected, or TMJ and muscles affected. Factor analysis was  
17 applied to cervical spine and masticatory data while linear regression was applied to  
18 characterize clinical patterns in subgroups.

19 **Results**

20 Factor analysis identified five clinical dimensions which explained 59% of all variance:  
21 mechanosensitivity, cervical movement, cervical and masticatory dysfunction, jaw  
22 movement, and upper cervical movement. Regression analysis identified different  
23 clinical dimensions in each TMD subgroup.

24 **Conclusion**

25 Distinct clinical patterns of cervical spine and masticatory function were found among  
26 subgroups of TMD, which has clinical implications for therapeutic management.

27 Factor analysis, subgroup, TMD, cervical, explorative

## 28 **Introduction**

29 Temporomandibular disorder (TMD) is an umbrella term for structural and functional  
30 disorders related to the masticatory muscles and/or the temporomandibular joint  
31 (TMJ) with or without clinical signs and symptoms (1). It is the second most common  
32 cause of orofacial pain following dental pain (2). The prevalence of signs and  
33 symptoms related to TMD ranges widely, reported as low as 1% and as high as 75%,  
34 affecting more women and younger people which is uncommon for chronic pain  
35 conditions (2–6). The inconsistent epidemiological data is assumed to be a result of  
36 different unstandardized and heterogeneous diagnostic criteria used in the studies to  
37 define TMD and its symptoms (2, 7). The major clinical signs and symptoms associated  
38 with TMD are pain both local and referred into the temporal region of the head, lower  
39 face and neck, as well as clicking sound's, reduced and painful mouth opening, and  
40 bruxism (8–10). However, not all individuals diagnosed with TMD have symptoms (11)  
41 and thus it is estimated that only 3% of people with signs of TMD seek medical aid  
42 (10).

43 Biological as well as psychological aspects are assumed to be factors in the  
44 development of TMD (12). As a consequence, according to Research Diagnostic  
45 Criteria/TMD (RDC/TMD), classification of TMD will include physical or psychological  
46 diagnoses. Under physical diagnosis, patients are classified into muscle disorders  
47 and/or disc displacements and/or arthralgia, osteoarthritis or osteoarthrosis (1, 6, 13).  
48 The importance of diagnosis is to identify the appropriate management strategy from  
49 the broad spectrum of therapies described for this condition.

50 Within the contributing factors to TMD the cervical spine is considered to play a crucial  
51 role (14). Studies show anatomical and pathophysiological interactions between the

52 cervical spine and TMJ region (15–21). For example, people with TMD show higher  
53 prevalence and one-year-incidence for neck pain than those without TMD (20, 22).

54 Furthermore, it has been demonstrated that the neck disability index is highly  
55 correlated with the jaw function scale (23). Studies have also demonstrated the  
56 influence of various head and neck postures on the masticatory muscles and their  
57 mechanosensitivity (18, 24). Additionally, there is some evidence that cervical  
58 dysfunction is the consequence of TMD. As such, various authors describe a positive  
59 effect of orofacial therapy (21, 25) on the function of the cervical spine. Yet, a clear  
60 causal relationship remains unclear.

61 Despite this, there is little high quality research evidence that has investigated the  
62 relationship between cervical dysfunction and TMD. Furthermore, according to the  
63 author's knowledge, there are no studies investigating whether subgroups of TMD  
64 show distinct patterns of cervical and masticatory impairment. Finally, studies are  
65 lacking that give a comprehensive picture of the interaction between the cervical spine  
66 and the TMJ.

67 Consequently, the aim of this study is to describe and perform an extensive analysis in  
68 a study sample consisting of individuals classified into five subgroups according to  
69 physical diagnostic criteria of RDC/TMD. Subgroups of TMD are characterized with  
70 respect to patterns of impairment based on clinical and functional measurements  
71 associated with the masticatory and cervical systems. Therefore, instead of testing  
72 predefined, clinically driven hypotheses (which is the common way), this study uses an  
73 explorative data driven approach based on factor analysis. More detailed knowledge of  
74 clinical patterns of cervical and masticatory impairment among subgroups of TMD may  
75 ultimately direct management and thereby improve therapeutic outcomes.

76 **Methods**

77 ***Participants***

78 For this observational study, subjects were recruited from physiotherapy practices in  
79 Northern Germany by information flyers. Subjects were evaluated for inclusion by a  
80 clinical expert with 15 years of experience managing orofacial pain according to the  
81 following criteria: (1) age at least 18 years, (2) score of less than 3 on the modified  
82 *Chronic Grade Pain Scale* (26–29) indicating chronic condition status , (3) conversant in  
83 the German language, (4) score of more than 3 measured on the CONTI questionnaire  
84 suggesting evidence of TMD (30).

85 Subjects acting as controls were selected from the same environment if they met the  
86 following criteria: (1) age at least 18 years, (2) conversant in the German language, (3)  
87 score of  $\leq 3$  measured by the CONTI questionnaire. Subjects were excluded if they had  
88 (1) a history of surgery or fractures in the neck and jaw or (2) neurologic deficits or (3)  
89 pain at night or other red flags or (4) were currently undergoing orthodontic  
90 treatment. Prior to participation, subjects gave written informed consent. The study  
91 was conducted in accordance with the Declaration of Helsinki and was approved by  
92 the local ethics committee of the University of Applied Science Of Osnabrück.

93 For further stratification subjects were subdivided according to RDC/TMD. Therefore  
94 the presence of painful and restricted mouth opening, painful masticatory muscles on  
95 palpation, and TMJ sounds were assessed. These criteria are designed to define the  
96 subgroup of TMD. (31). As a consequence, patients with TMD (CONTI > 3) were  
97 subdivided into group “Arthogen” when joint disorders were present, group “Myogen”  
98 when myofascial disorders were present, or into group “Mixed” when both joint  
99 disorders and myofascial disorders were present. Subjects acting as controls (CONTI  $\leq$

100 3) were subdivided into group “Controls” having no TMD signs or pain or group “Just  
101 signs” having TMD signs that are not clinically relevant based on the Conti scale (30).  
102 Consequently, five subgroups were investigated with different diagnoses of TMD. We  
103 proposed that the “Mixed” group would be the most severe as they had both joint  
104 disorders and myofascial involvement.

#### 105 ***Functional measurements***

106 The TMJ and the cervical spine were examined and measured separately by two  
107 clinically experienced physiotherapists who had 8 hours intensive training in the  
108 management of orofacial disorders. The investigator who executed the neck  
109 measurements was blind to subjects TMD subgroup classification.

#### 110 *TMJ Region*

##### 111 *Range of motion*

112 Measurements of TMJ range of motion (ROM) included mouth opening, active lateral  
113 shift of the jaw to both sides as well as active backward and forward movement of the  
114 jaw. Inter- and Intra-rater reliability has been shown to be moderate to excellent for  
115 these measurements.

##### 116 *Mechanosensitivity*

117 Mechanosensitivity of the Masseter and Temporalis muscles was determined by  
118 measuring pressure pain threshold (PPT) using an algometer (*Wagner instruments,*  
119 *Force dial FDK 10*). Pressure was applied at a constant rate of approximately 1  
120 kg/cm<sup>2</sup>/s until subjects reported the point when the sensation changed from pressure  
121 to pain. Two readings were taken over each site and each muscle and averaged for  
122 analysis. PPT has been shown to be a valid and reliable method for measuring  
123 mechanosensitivity (32–34).

124 *CONTI*

125 The Conti questionnaire (30) was used for assessing TMD symptoms. This scale  
126 comprises ten questions concerning typical TMD features and has a score from 0,  
127 indicating no clinically relevant TMD, to 23. Prior to the examination subjects were  
128 asked whether they suffered from pain in the masticatory and cervical region.

129 *PAIN*

130 Pain was graded according to the Colored Analogue Scale (CAS) from 0 to 10. The CAS  
131 has high reproducibility (35).

132 *Cervical spine*

133 *ROM*

134 Active cervical ROM in all planes (flexion, extension, lateral flexion, and rotation) was  
135 measured by the Cervical ROM (CROM) device (36, 37). Maximum angles within  
136 comfortable limits were recorded. The CROM device is described as valid and reliable  
137 (36, 38, 39).

138 *Mechanosensitivity*

139 Mechanosensitivity of Upper Trapezius and Obliquus Capitis Inferior muscles were  
140 determined by measuring PPT using the method described above.

141 *Neck disability index*

142 The Neck disability index (NDI) was used to assess neck related disability and  
143 comprises 10 self-report questions covering activities of daily living, concentration and  
144 pain. The scale ranges from 0 (no pain and disability) to 50 (severe pain and disability)  
145 and has been shown to have good to excellent psychometric properties (40, 41).

146 *Flexion-Rotation Test*

147 Upper cervical rotation in end-range flexion (FRT) (42, 43) was recorded using a digital  
148 goniometer (Halo Medical Device), while pain during the FRT was recorded by the CAS.

#### 149 *Cranio-cervical Flexion-Test*

150 The Cranio-cervical Flexion-Test (CCFT) was used to measure endurance of the cervical  
151 deep flexor muscles (44, 45) evaluated using a pressure biofeedback device  
152 (*Chattanooga, USA*) according to a reliable procedure described by Hudswell (46–48).

#### 153 *Number of cervical signs*

154 Palpation of the three upper cervical spine motion segments was conducted to assess  
155 segmental mobility and pain. The number of symptomatic findings were aggregated  
156 and termed “cervical signs”. This procedure has good reliability (49).

157 All measurements are summarized in Table S1 available online.

#### 158 ***Analysis***

159 All statistical analysis was performed with R (50) including the psych package (51).

160 Analysis of variance and  $\chi^2$  was used to test for differences in baseline characteristics  
161 between subgroups of participants. P-values < 0.05 were considered significant. The  
162 basis of our analysis strategy was as follows: Rather than confirming whether clinically  
163 driven predefined clinical patterns are present among subjects with TMD, we  
164 performed a data driven explorative analysis strategy in order to identify clinically  
165 relevant patterns among subgroups of individuals with TMD. Therefore we conducted  
166 five steps including factor analysis and linear regression analysis.

167 Step 1: Factor analysis was used as a dimension reduction method. Measured variables  
168 were condensed to a reduced number of factors that would still contain the majority  
169 of the information from the original data. The dimensionality of the data was assessed,  
170 where each factor represents a clinical dimension which was characterized with

171 respect to a clinical meaning. The appropriate number of relevant clinical dimensions  
172 was established by applying the Very Structure Criterion (52) and the Parallel Analysis  
173 Criterion (53) as implemented in the psychological package. Where inconsistency of  
174 the statistical solutions was detected the more interpretable solution with respect to  
175 clinical meaning was selected. The amount of information (variance) that is captured  
176 by each of extracted factors was calculated by determining their eigenvalues.

177 Step 2: graphical descriptive means were used to assess the ability of the data to  
178 discriminate people with TMD from controls in general. A scatterplot representing  
179 each individual's score for each pair of factors was constructed demonstrating the  
180 general clinical relevance of the identified dimensions.

181 Step 3: the extracted factors (clinical dimensions), were interpreted with respect to a  
182 clinical and functional meaning. Therefore, all measured variables were correlated  
183 with the extracted factors. Their correlation coefficients represent their loadings on  
184 the factors. By inspecting the correlation coefficients of each measured variable with  
185 each factor the contribution of each variable to the respective factor was evaluated. As  
186 a consequence, the clinical meaning of the factors was interpreted. In order to  
187 facilitate interpretation, the factor solution was rotated before calculating the  
188 correlation structure, in our case by Varimax rotation. Conceptually, the factors have  
189 the function of summary variables of the underlying clinical dimension. The score of  
190 each individual on each factor was calculated. As a consequence, it was possible to  
191 quantify each person's score on the respective clinical dimension, i.e. a low/high  
192 person's score represents a low/high summary score of the respective clinical  
193 dimension.

194 Step 4: subgroup characterization was performed with respect to the clinical  
195 dimensions. Therefore, we aimed to determine to what extent each of the TMD  
196 subgroups was affected with respect to the respective clinical dimension. To do so we  
197 conducted the analysis with both the extracted factors, representing the clinical  
198 dimensions as summary variables, and with the original variables contributing to the  
199 respective clinical dimensions. For this purpose we used linear regression with  
200 subgroup membership as independent variables and all variables standardized  
201 (Mean=0, SD=1). Results are given as standardized mean differences and interpreted  
202 as effect sizes according to Cohen (<0.2 no effect, 0.2-0.5 small effect, 0.5-0.8  
203 moderate, 0.8>large effect) (56). This approach is analogous to meta- analysis in order  
204 to be able to compare results across outcomes with different units.

205 Step 5: Finally, a summary was generated of how the TMD subgroups were  
206 characterized with respect to the identified clinical dimensions. Also, here the strength  
207 of clinical impairment in each dimension was given as interpretable values according to  
208 Cohen. Hence, the clinical pattern of each subgroup was presented indicating which  
209 clinical dimension was affected to which extent.

210 The quality of the factor analysis models was assessed using Bartlett's test for  
211 sphericity (54) and the Kaiser-Meyer-Olkin test (55). For regression analysis, variables  
212 that assessed bilateral measurements were combined to one variable by calculating  
213 the mean of left and right sides as no significant side differences were present.

214 Additionally, we added age and gender as covariates into regression models as  
215 potential confounders. If p-values of confounders according to t-statistics were >0.1, or  
216 changed the estimate less than 10%, those variables were withdrawn from the model.

217 **Results**

218 Of 175 people assessed for inclusion 144 participants met the study criteria. These  
219 people were divided into five subgroups and characterized with respect to clinical  
220 patterns of impairment based on clinical and functional measurements from the TMJ  
221 and cervical spine as depicted in the work flow diagram in Figure 1.

222 Figure 1:

223 Baseline characteristics are summarized in Table 1.

224 Bartlett's Test of Sphericity was highly significant (Chi square = 1513.003,  $P < 0.001$ )  
225 and the KMO test was 0.82, supporting the suitability of the data for factor analysis.

226 Step 1 clinical dimensionality of data: We extracted 5 independent factors by factor  
227 analysis representing five clinical dimensions. In total, the five dimensions explained  
228 59% of the total variance (dimension 1 - 23%, dimension 2 - 13%, dimension 3 - 8%,  
229 dimension 4 - 8%, and dimension 5 - 5%).

230 Step 2 general overview of distinction between subjects with TMD and controls: Figure  
231 2 shows the scores of all individuals on each of the five factors, i.e. on each clinical  
232 dimension. Each scatter plot shows each individual's score of a pair of dimensions. E.g.  
233 the very left top plot depicts scores of dimension 1 on the x-axis and scores of  
234 dimension 2 on the y-axis. Black Cs represent the control group including the control  
235 group with symptoms of TMD. Grey Ts represent the TMD group including sub-groups  
236 "Arthrogn", "Myogen" and "Mixed". Plots of dimension 1 to dimension 4 show, albeit  
237 some overlap of the dots, that the scores of subjects with TMD are separate to the  
238 scores of controls indicating that subjects with TMD generally possess distinct  
239 underlying clinical patterns compared to controls. This especially holds true for the  
240 third dimension. Factor 5 suggests no distinct pattern between the groups.

241 Figure 2:

242 Step 3 Characterization of clinical dimensions. In Table 2 the factor loadings of each  
243 measured variable are listed. The key variables of each independent factor, i.e. clinical  
244 dimension, are marked in grey. The values are the correlation coefficients of each  
245 measured variable with each factor. This allows the clinical and functional  
246 interpretation of the clinical dimensions. As a consequence, factor 1 represents the  
247 clinical dimension “mechanosensitivity” as it includes all variables measuring  
248 mechanosensitivity of muscle sites in the masticatory and cervical region as well as the  
249 variable “cervical signs” (coefficient range: 0.64-0.89). Factor 2 is characterized by the  
250 clinical dimension cervical ROM which includes movement in all directions (coefficient  
251 range: 0.54-0.81). Factor 3 comprises both cervical and masticatory dysfunction  
252 measured by the NDI and CONTI questionnaires, as well as the presence of pain when  
253 performing the FRT (coefficient range: 0.47-0.72). As a consequence we called this  
254 clinical dimension “Cervical/masticatory dysfunction and pain”. Factor 4 represents the  
255 clinical dimension “jaw movements” which includes TMJ movement in all directions  
256 (coefficient range: 0.43-0.7). The last factor consists of the clinical dimension FRT ROM  
257 and the CCFT (coefficient range: 0.45-0.78).

258 Table 2:

259 Step 4 Characterization of TMD subgroups: Figure 3 shows the pairwise differences  
260 between each of the subgroups compared to the Control group with respect to all  
261 clinical dimensions including all contributing variables. Linear regression was used for  
262 this analysis. The first variable of each column and each pairwise comparison  
263 (summary variable) represents the extracted factors by factor analysis and is  
264 considered as the summary variable of each corresponding clinical dimension for the  
265 respective group comparison. Below each summary variable the contributing variables

266 to each clinical dimension, according to Table 2, are listed. The effects of the  
267 subgroups “Mixed”, “Myogen”, “Arthrogen” and “Just signs” in comparison to the  
268 reference group (control group without TMD signs) are presented as standardized  
269 mean differences (SMD) and  $\pm 95\%$  Confidence Intervals. It allows interpretation of the  
270 coefficients in effect size. In the dimension “mechanosensitivity” the overall effect size  
271 represented by its summary variable for the comparison “Mixed” group vs control  
272 group is -0.83 [-1.32;-0.38] suggesting a large effect. In others words this means that in  
273 general, mechanosensitivity of the “Mixed” group is greatly elevated when compared  
274 to “Controls”. This effect is consistent across all single variables of the clinical  
275 dimension “mechanosensitivity”. The variables range from -0.77 for Temporalis muscle  
276 to 0.92 for “cervical signs”. The second largest effect size with respect to the clinical  
277 dimension “mechanosensitivity” is observed between the “Myogen” group and the  
278 control group with an effect size of -0.39 [-0.96;0.21]. In the remaining two groups the  
279 effect size is below -0.25. For the dimension “cervical mobility” a similar pattern is  
280 observed. Also here the “Mixed” group has the most reduced cervical ROM with an  
281 effect size of -0.58 [-1.06;-0.10] followed by the “Myogen” group having an effect size  
282 of -0.38 [-0.99;0.23]. The most affected direction in both the “Mixed” and “Myogen”  
283 group is extension with effect sizes of -0.69 [-1.16;-0.23] and -0.63 [-1.19;-0.06]  
284 respectively. The least affected variable in both groups is flexion (effect size in the  
285 “Mixed” group: -0.27[-0.78;0.24], effect size in the “Myogen” group: -0.36 [-  
286 0.98;0.26]).

287 Dimension “Cervical/masticatory dysfunction and pain”, is similarly impaired in all  
288 subgroups apart from “Just signs” group. The large effect sizes of the summary  
289 variables range from -0.94[-0.50;-1.38] in the “Mixed” group to -1.28 [-0.72;-1.83] in

290 the “Myogen” group. The effect sizes for the single variables CONTI, NDI and pain  
291 during FRT range in the three affected subgroups between -0.78 [-0.33;1.20] and -1.69  
292 [-1.35;-2.04]. Acute pain is only present in the “Myogen” group with an moderate  
293 effect size of -0.71 [-0.27;-1.15]. Dimension 4 “jaw movement” is restricted across all  
294 subgroups with moderate effects sizes of the summary variables from -0.54 [-  
295 1.15;0.08] in the “Myogen” group to -0.77[-1.27;-0.26] in the “Mixed” group. Finally,  
296 the last dimension has no clinical meaning for any of the subgroups indicated by effect  
297 sizes lower than 0.20.

298 Figure 3:

299 Step 5 summary of clinical patterns in TMD subgroups:

300 In Table 3 the clinical patterns with respect to the cervical and masticatory systems of  
301 the subgroups are depicted. Arrows indicate to which extent a subgroup is restricted in  
302 each clinical dimension and represent effect sizes stemming from the summary  
303 variables of each clinical dimension shown in figure 3. One arrow is a small effect, two  
304 arrows a medium effect and three arrows a large effect. As a consequence, the  
305 “Mixed” group is the most affected group, with moderate to large limitations in the  
306 dimensions “mechanosensitivity”, “cervical ROM”, “cervical and masticatory  
307 dysfunction and pain” and “jaw movement”. The “Myogen” group is also affected in  
308 the same dimensions, however, less with respect to “mechanosensitivity” and “cervical  
309 ROM”. Groups “Arthrogen” and “Just signs” have only medium to large limitations in  
310 dimensions “cervical and masticatory dysfunction and pain” and jaw movement.

311 Table 3:

312 **Discussion**

313 In this explorative data driven analysis five independent clinical dimensions were  
314 identified based on 28 functional measurements from the cervical spine and  
315 masticatory systems using factor analysis with varimax rotation and linear regression  
316 analysis. These dimensions are interpreted as mechanosensitivity, cervical ROM,  
317 cervical and masticatory dysfunction, jaw movement and upper cervical  
318 ROM/endurance. The five factors explain 59% of all variance. Furthermore, the 144  
319 subjects divided into five subgroups according to RDC/TMD were characterized with  
320 respect to the five clinical dimensions. The “Mixed“ group is the most affected group  
321 with moderate to large limitations in all dimensions followed by the “Myogen“ group  
322 with limitations in the same dimensions, however, less with respect to  
323 mechanosensitivity and cervical ROM. Groups “Arthrogen“ and “Just signs“ show  
324 medium to large limitations only concerning cervical and masticatory dysfunction and  
325 jaw movement. A clear dose response relationship was observed indicating that  
326 subjects with a diagnosis of TMD in two aspects (myogenic and arthrogenic) are most  
327 affected.

328 The main advantage of this explorative data driven approach is that it revealed clinical  
329 patterns that were quite unexpected and probably would have not been identified by  
330 a clinically driven approach. This is illustrated by two findings as examples: Firstly, the  
331 clinical dimension “mechanosensitivity“ consisted of variables measuring  
332 mechanosensitivity at all muscle sites, not just over cervical or masticatory muscles.  
333 From the clinical point of view one might have expected two distinct dimensions,  
334 namely “cervical mechanosensitivity“ and “masticatory mechanosensitivity“. However,  
335 due to the high correlation structure the analysis revealed that the two regions are  
336 highly interrelated with respect to mechanosensitivity and may not be seen as

337 clinically different problems. On the one hand this finding confirms the fact that  
338 subjects with TMD suffer from referred pain into the neck region. On the other hand,  
339 this finding perhaps suggests that patients with TMD are dominated by mechanism(s)  
340 of central sensitization with associated areas of secondary hyperalgesia.

341 A similar surprising result was seen for the variables NDI and CONTI which were found  
342 to occur together in one dimension. Even though it is known (25, 57–59) that these  
343 two variables are correlated, it was surprising that both variables were related so  
344 much to each other that they loaded equally highly on the same factor. From the  
345 clinical point of view one might have expected that the variable NDI would cluster  
346 together with variables measuring neck muscle mechanosensitivity or cervical ROM.  
347 Additionally, the CONTI might be expected to cluster together with jaw movements or  
348 variables measuring masticatory muscle mechanosensitivity .

349 In this study, ROM of the upper cervical spine together with endurance of the neck  
350 flexors were not found to have any clinical relevance for any subgroup. (60) This is in  
351 contrast to previous studies showing evidence of altered upper cervical spine ROM and  
352 muscle performance in TMD overall and in specific sub-groups of people with TMD (16,  
353 59–61). The difference could be explained by the small sample size in some studies  
354 (60, 61), but that was not the case in the study by Armijo-Olivo and Magee (59).

355 Further studies are required to elucidate this.

356 Less surprising is that fact that the “Mixed” group was the most affected group. One  
357 might expect this finding from the clinical point of view as well.

358 A further advantage of the present study is the use of the extracted factors as  
359 summary variables of each identified clinical dimension. In that way a summary score  
360 of each clinical dimension could be calculated for each individual. As a consequence

361 high/low individual scores mean large/low limitations in the respective dimension. The  
362 clinical relevance of this information requires careful consideration. These results  
363 confirm that patient's with TMD are not homogenous, different subgroups exist with  
364 different clinical presentations. Each subgroup may therefore require a different form  
365 of intervention to address the underlying mechanisms.

#### 366 Clinical Implications

367 The findings of this study have clinical implications for practice. In general there is a  
368 need to subgroup patients with TMD as they have distinct functional profiles with  
369 respect to the cervical and masticatory systems. Typically, this kind of procedure is  
370 conducted in daily clinical practice by therapists where individuals are categorized  
371 based on a comprehensive clinical evaluation in order to initialize individually tailored  
372 therapy and patient management programs (63). Similar broad-based evaluative  
373 approaches are undertaken in patients with low back pain (64). Furthermore it has  
374 been shown that sub-classification based therapy is more effective than standard  
375 protocols (65–68).

376 The fact that NDI and CONTI are highly interrelated to form one clinical dimension  
377 suggests that when patients present with high levels of impairment of TMD, high levels  
378 of disability of the cervical region should also be expected. This holds true across all  
379 subgroups of TMD. As a consequence, management should address impaired domains  
380 detected by the NDI and CONTI.

381 It would appear reasonable to suggest that for patients with arthrogenic and myogenic  
382 features of TMD, management should address mechanosensitivity of masticatory and  
383 neck muscles. However, the underlying pain mechanism in this dimension are  
384 indicative of central sensitization which requires a different management approach.

385 Impaired mechanosensitivity seems to be less likely among patients with myogenic  
386 TMD and almost nonexistent in patients with arthrogenic TMD.

387 Cervical ROM is another clinical dimension that seems to be problematic and needs  
388 attention in clinical practice in patients with „Mixed“ TMD, but less so in myogenic  
389 and arthrogenic TMD. In contrast, restricted ROM of the TMJ is similarly present  
390 across all TMD subgroups.

391 In general, it can be noted that in none of the clinical dimensions does a single variable  
392 stand out that requires specific attention. For example, in the clinical dimension  
393 mechanosensitivity, there is not a single muscle alone that is affected. All muscles are  
394 equally affected. The same holds true for cervical ROM, where it is not a single  
395 movement but all planes that are equally affected.

396 Strengths

397 The strength of this paper is the application of factor analysis as an explorative data  
398 driven approach to characterize predefined subgroups with respect to until now  
399 unknown clinical patterns. This approach is unusual and not commonly applied.  
400 However, it has yielded unexpected but clinically meaningful and relevant implications.  
401 This was only possible due to a large sample size and detailed and extensive  
402 measurements which is uncommon in studies of TMD.

403 However, there are other statistical approaches that perform subgroup classification  
404 based on data modelling. Common statistical techniques include among others cluster  
405 or latent class analysis. Instead of predefining subgroups based on clinical diagnosis  
406 these techniques create subgroups based on the observed data. Consequently, built  
407 classes are interpreted and analyzed with respect to clinical relevance (69).

408 Limitations

409 A potential weakness of this study is the exclusion of patients with chronic disease. As  
410 a result, it is not possible to draw any conclusions regarding those patients.  
411 Furthermore, this study did not include psychosocial aspects in the factor analysis. In  
412 addition, in an attempt to control for potential confounders it was not possible to use  
413 a matched case controlled design. Matched case controlled designs allow more  
414 efficient statistical analysis approaches resulting in more power. Finally, in order to  
415 disentangle the temporal relationship between onset of cervical spine and masticatory  
416 complaints, a longitudinal study designs is necessary.  
417 For the purpose of validation it is essential to replicate the study findings in further  
418 research. The presence of the identified clinical dimensions and patterns among  
419 subgroups of TMD need to be confirmed by confirmatory factor analysis in other  
420 samples.

#### 421 Conclusion

422 An explorative data driven analysis was used for identifying clinical patterns among  
423 subgroups of TMD. These results have implications for clinical decision making and  
424 therapeutic management in patients with TMD. As a consequence, it is proposed that  
425 subgrouping patients with TMD is essential as these show distinctly different clinical  
426 patterns with respect to the masticatory and cervical spine systems in order to improve  
427 outcomes.

428

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644

645 Table S1 online: Functional measurements of TMJ region and cervical spine

646 Variables were used for identifying clinical patterns among TMD patients by explorative data analysis

<b>Measurements</b>	<b>Description</b>
<i>Conti Questionnaire</i>	Contains 10 questions that are related to problems originating from the temporomandibular region. Each question has three ranking options (0=none: 1=present: and 3=strong or bilateral). The likelihood of a CMD is divided into 4 subgroups: 4- 9, none: 9-14, minimal: 15-21, moderate: 21-23, strong
<i>Colored Analogue Scale (CAS)</i>	Pain intensity scale similar to the visual analogue scale transformed in an increasing colored line in mm that represents the pain intensity
<i>Range of motion of TMJ</i>	Using a ruler of 15 cm, starting at 0, the active ROM of TMJ is measured including mouth opening, lateral shift, backward and forward movement of the jaw
<i>Mechanosensitivity of cervical and masticatory muscles</i>	The mechanical pressure pain threshold is assessed of the masticatory system and the neck muscles by a digital in kilogram force (Kgf). Muscles measured: Masseter, Temporalis, Upper Trapezius and Obliquus Capitis Inferior
<i>Neck Disability Index (NDI)</i>	A dimension-specific index that reflects "functional limitation" in neck disorders (includes 10 items (activities) with six different response options, ranging from "no disability" (0) to "complete disability."(5) The total score is 50. A higher score indicates more pain and disability
<i>Cervical Range of Motion (CROM)</i>	Measurement of cervical spine flexion, extension, rotation and lateral flexion using an inclinometer

<i>Cranial cervical Flexion Test (CCFT)</i>	Measures the cervical flexor muscle synergy during upper cervical flexion. A pressure sensor positioned under the neck enables targeted increases in upper cervical flexion ROM by raising pressure in the sensor at 2 mm Hg increments from a baseline of 20, rising to 30mm Hg.
<i>Flexion Rotation Test (FRT)</i>	Passive rotation of the cervical spine in maximal flexion measured in supine. Subjective pain response and range of rotation is recorded.
<i>N° of cervical signs</i>	Palpation of the three upper cervical spine motion segments was to assess segmental mobility and pain. Score is sum of number of symptomatic findings.

647

648 Table 1: baseline characteristic of the study participants according to subgroups

	<b>Healthy (n=21)</b>	<b>Just signs (n=23)</b>	<b>Arthrogen (n=18)</b>	<b>Myogen (n=19)</b>	<b>Mixed (n=63)</b>	<b>p-Value</b>
<b>Female sex: n (%)</b>	11 (52%)	18(78%)	15 (84%)	15 (89%)	54 (83%)	0.045
<b>Age in years: mean (SD)</b>	33.15 (9.86)	32.61 (7.91)	35.11 (9.58)	31.11(8.55)	36 (13.61)	0.44
<b>CONTI: mean (SD)</b>	1.619 (1.15)	1.91 (0.99)	6.50 (2.55)	7.23 (3.33)	8.57 (3.59)	<0.0001
<b>Mouth opening in mm: mean (SD)</b>	46.95 (5.47)	42.34 (4.45)	42.61 (6.91)	46.52 (5.11)	42.30 (6.65)	0.005

649

650

651 Table 2: Factor loadings of measured variables

652 The table shows contribution of each measured variable to each identified dimension by means of  
 653 correlation coefficients. Grey shaded cells indicate high contribution. Based on correlation coefficients  
 654 clinical characterization of dimensions is carried out.

variables	Factor 1 "mechano- sensitivity"	Factor 2 "cervical ROM"	Factor 3 "Cervical/mastic at. dysfunction and pain"	Factor 4 "jaw movement"	Factor 5 "ROM and endurance upp. cervical spine"
MS trap right	<b>0.88</b>	-0.13	-0.15	0.12	-0.02
MS trap left	<b>0.83</b>	-0.13	-0.28	0.03	-0.10
MS obliq right	<b>0.86</b>	-0.08	-0.16	0.04	0.09
MS obliq left	<b>0.89</b>	-0.04	-0.17	0.11	0.06
MS temp right	<b>0.85</b>	0.02	-0.01	-0.03	-0.10
MS temp left	<b>0.85</b>	0.06	-0.01	-0.03	0.02
MS mass right	<b>0.82</b>	0.16	0.00	0.00	0.09
MS mass left	<b>0.80</b>	0.12	0.06	0.07	0.10
Nr° of cervical signs	<b>-0.64</b>	-0.25	0.33	-0.14	-0.37
Flexion	-0.14	<b>0.54</b>	-0.05	0.18	0.04
Extension	0.10	<b>0.72</b>	-0.13	0.11	0.05
Lateralflex right	0.12	<b>0.77</b>	-0.08	0.00	0.11
Lateralflex left	0.08	<b>0.80</b>	-0.05	-0.10	0.08
Rotation right	-0.06	<b>0.67</b>	-0.13	0.13	0.05
Rotation left	-0.04	<b>0.81</b>	-0.08	0.13	0.10
pain acute	0.07	-0.13	<b>0.47</b>	0.11	0.11

NDI	-0.21	-0.28	<b>0.62</b>	-0.10	0.16
CONTI	-0.28	-0.16	<b>0.57</b>	-0.24	0.21
pain FRT right	-0.18	0.02	<b>0.72</b>	-0.01	-0.42
pain FRT left	-0.25	-0.08	<b>0.67</b>	-0.10	-0.29
mouth opening	0.20	0.22	0.17	<b>0.43</b>	-0.06
lateral shift left	-0.04	-0.03	0.03	<b>0.70</b>	-0.01
lateral shift right	-0.09	0.10	-0.25	<b>0.69</b>	0.04
Forward movement	0.08	0.16	-0.02	<b>0.67</b>	-0.02
Backward movement	0.11	0.03	-0.06	<b>0.45</b>	0.11
FRT ROM left	0.09	0.29	0.04	0.03	<b>0.67</b>
FRT ROM right	0.01	0.02	-0.11	-0.05	<b>0.78</b>
CCFT endurance	-0.01	0.11	0.24	0.30	<b>0.45</b>

655

656

657 Table 3: clinical pattern of subgroups is shown with respect to the cervical and masticatory systems.

658 Legend table 3: Arrows indicate effects according to effect sizes. One arrow is a small effect, two arrows

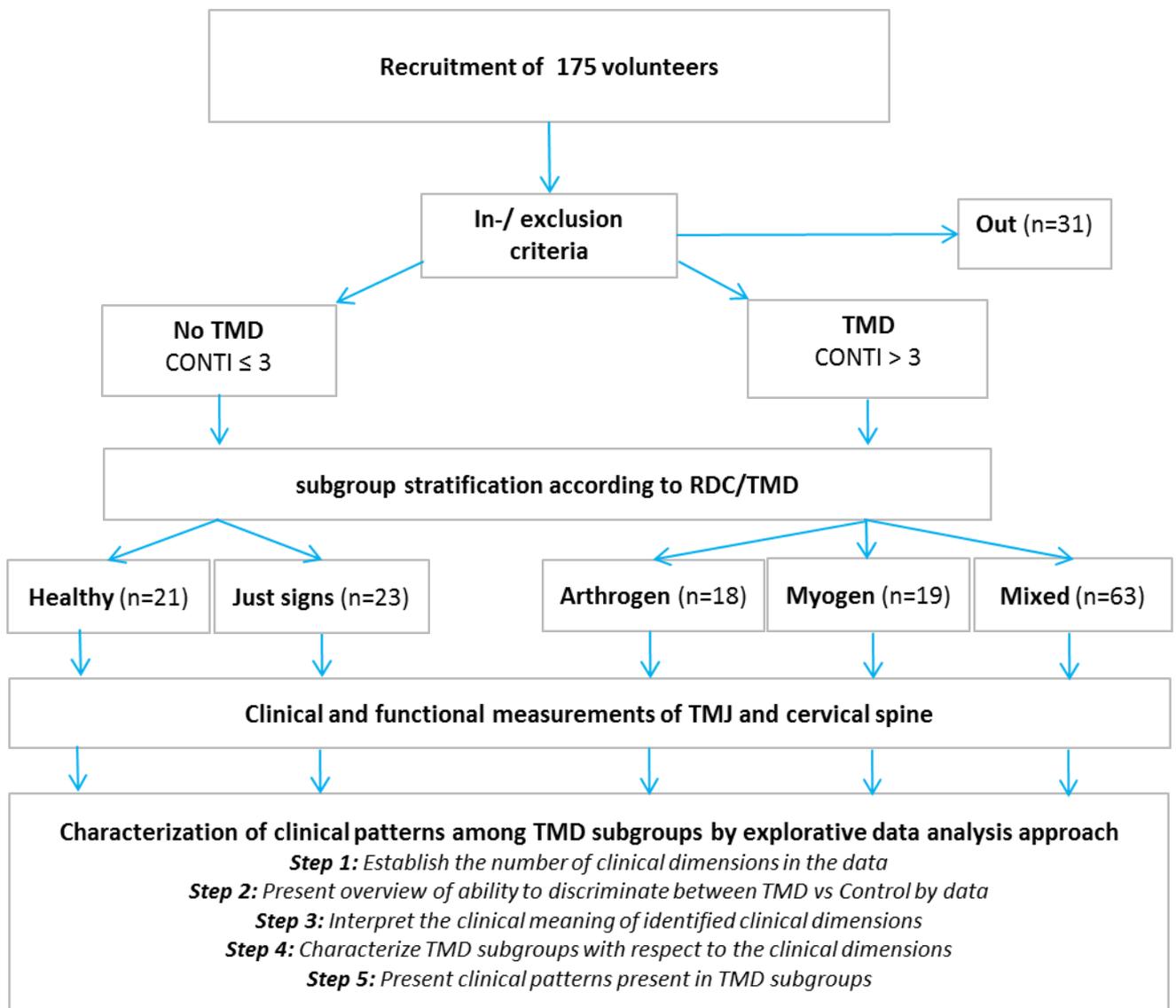
659 a medium effect and three arrows a large effect.

	mechanosensitivity	Cervical ROM	Cervical and masticatory dysfunction	Jaw movement	Upper cervical ROM/endurance
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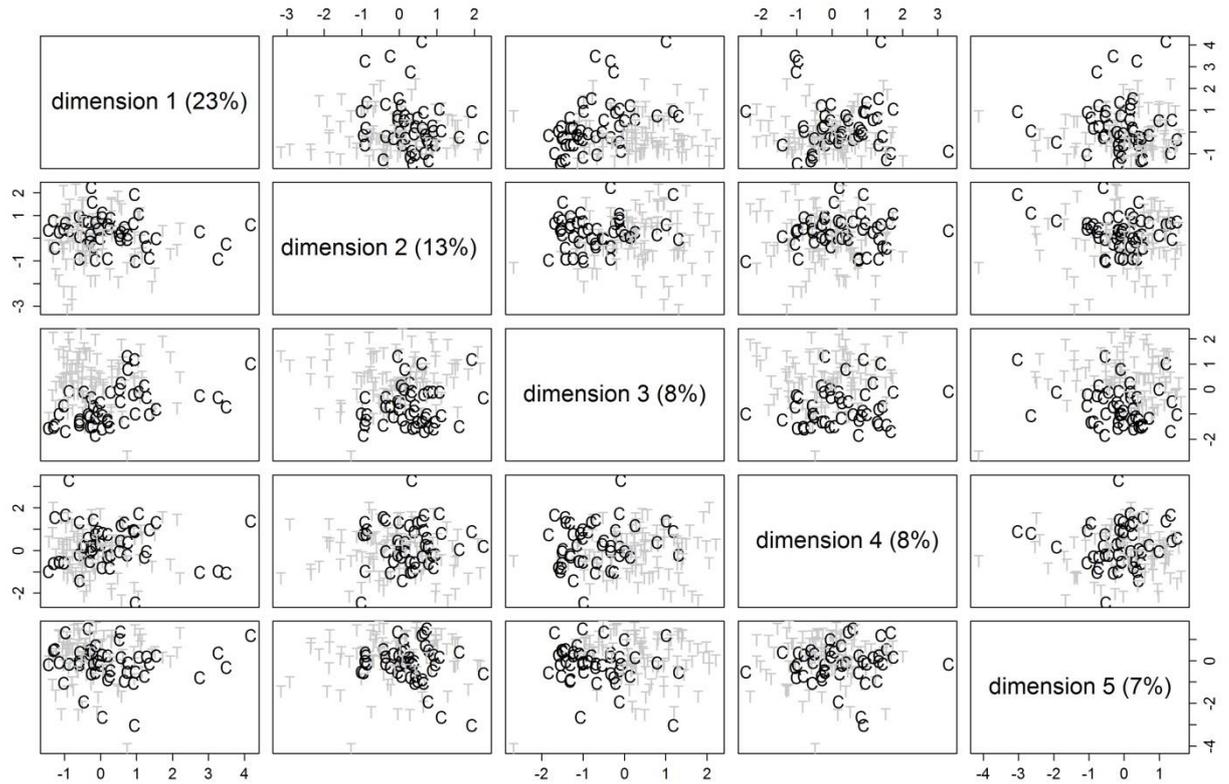
Mixed	↓↓↓	↓↓	↓↓↓	↓↓	-
Myogen	↓	↓	↓↓↓	↓↓	-
Arthogen	-	-	↓↓↓	↓↓	-
Just signs	-	-	-	↓↓	-

660

661



663 Title figure 2: Scores of all individuals on each of the five extracted factors representing clinical  
 664 dimensions  
 665 Legend figure 2: Black Cs represent the control group including the control group with symptoms of  
 666 TMD (“Just signs”). Grey Ts represent the TMD group including the “Arthrophen”, “Myogen” and “Mixed”  
 667 subgroup. Each plot shows scores of two dimension. E.g. the very left top plot depicts scores of  
 668 dimension 1 on x-axis and scores of dimension 2 on y-axis Separation of dots with respect to group  
 669 membership indicate distinct patterns.



670

671 Title figure 3: Standardized mean differences of clinical dimensions between subgroups of TMD

672 Legend figure 3: Differences ( $\pm 95\%$  Confidence Intervals) are shown between each of the subgroups to

673 control group with respect to all clinical dimensions calculated by linear regression analysis. Factors

674 representing a summary variable of each clinical dimension and single variables contributing to

675 respective dimension are depicted. Results are to be interpreted as effect sizes (beta). Model is adjusted

676 for age and gender where necessary.

