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Reliability and Validity of the Japanese Version of the Ocular Surface Disease Index for Dry Eye Disease

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-033940
Article Type:	Original research
Date Submitted by the Author:	29-Aug-2019
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Keywords:	dry eye disease, ocular surface disease index, OSDI, reliability, validity

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5 1 Original article—Clinical Science
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7 3 **Reliability and Validity of the Japanese Version of the**
8 **Ocular Surface Disease Index for Dry Eye Disease**
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52
53 32 **Word count: 3365**

54
55 33 **Declaration of competing/conflicting interests:** There are no conflicts of interest to declare.

56
57 34 **Funding sources:** This research received no external funding or any specific grant from
58 35 funding agencies in the public, commercial, or not-for-profit sectors.

59
60 36 **Data Availability Statement:** The data that support the findings of this study are available from
37 the corresponding author upon reasonable request.

38

39 **ABSTRACT**

40 **Objectives:** The ocular surface disease index (OSDI) questionnaire is widely used to evaluate
41 subjective symptoms of dry eye disease (DED) as a primary diagnostic criterion. This study
42 aimed to develop a Japanese version of the OSDI (J-OSDI) and assess its reliability and
43 validity.

44 **Design and Setting:** Hospital-based cross-sectional observational study.

45 **Participants:** A total of 209 patients recruited from the Department of Ophthalmology at
46 Juntendo University Hospital.

47 **Methods:** We translated and culturally adapted the OSDI into Japanese. The J-OSDI was then
48 assessed for internal consistency, reliability, and validity. We also evaluated the optimal cut-off
49 value to suspect DED using an area under the receiver operating characteristic curve (AUC)
50 analysis.

51 **Primary Outcome Measures:** Internal consistency, test-retest reliability, and discriminant
52 validity of the J-OSDI as well as the optimal cut-off value to suspect DED.

53 **Results:** Of the participants, 152 had DED and 57 did not. The J-OSDI total score showed good
54 internal consistency (Cronbach alpha = 0.884), test-retest reliability (interclass correlation
55 coefficient = 0.910), and discriminant validity by known-group comparisons (non-DED, 19.4 ±
56 16.0; DED, 37.7 ± 22.2; $p < 0.001$). Factor validity was used to confirm 3 subscales within the
57 J-OSDI according to the original version of the questionnaire. Concurrent validity was assessed
58 by Pearson correlation analysis, and the J-OSDI total score was positively associated with the
59 Dry Eye-Related Quality-of-Life Score ($\gamma = 0.829$). The optimal cut-off value of the J-OSDI
60 total score was 36.3 (AUC = 0.744).

61 **Conclusions:** The J-OSDI was validated in terms of reliability and validity as an effective tool
62 for DED assessment and monitoring in the Japanese population.

63

64 **Keywords:** dry eye disease, J-OSDI, ocular surface disease index, OSDI, reliability, validity

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6 66 **Strengths and limitations of this study:**
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9 67 • This study provides the first validation data on the Japanese version of the ocular surface
10 68 disease index (J-OSDI) questionnaire as the primary evaluation for dry eye disease (DED)
11 69 diagnosis.

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14 70 • The validated J-OSDI allows across-country epidemiological comparisons of
15 71 patient-reported subjective symptoms of DED.

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17 72 • The main limitation is that this study was conducted at a single university hospital, which
18 73 may limit the generalizability of the findings.
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75 INTRODUCTION

76 The prevalence of dry eye disease (DED) continues to grow due to several
77 psychosocioeconomic factors, including an increase in digital screen usage time, an aging
78 population, and stressful social environments.[1, 2] DED can cause ocular surface damage, eye
79 discomfort and impaired vision, and can also lead to substantial economic problems due to
80 decreased quality of life and work productivity.[3, 4]

81 Diagnosis of DED can be made using various methods, including tear film breakup time
82 (TFBUT), ocular surface staining, and osmolarity as a homeostasis marker. Additionally, the
83 use of a questionnaire to determine if symptoms of DED are present is recommended as a
84 primary examination method in the DED diagnosis protocol by the TFOS DEWS II Diagnostic
85 Methodology report and in the 2016 Asia Dry Eye Society (ADES) consensus report.[5, 6]
86 Although previous research has established a divergence between the subjective symptoms of
87 DED and clinical severity of the disease,[7-9] questionnaires that can quantitatively measure the
88 subjective symptoms of DED are indispensable for DED diagnosis and management.

89 The 2016 dry eye diagnostic criteria published by the ADES[6] recommend that DED be
90 diagnosed according to both subjective symptoms and TFBUT, indicating that subjective
91 symptoms are now widely recognized as playing an important role in DED. We previously
92 showed that this change in diagnostic criteria could lead to a 28.0% increase in DED patients in
93 Japan[2]; thus, the need for effective DED treatments may increase in the future. Both the OSDI
94 and the Dry Eye-Related Quality-of-Life Score (DEQS)[10] are widely used to assess subjective
95 symptoms of DED in Japan, but the reliability and validity of the OSDI have not been
96 confirmed in Japan.[11] Determining the reliability and validity of the Japanese version of the
97 OSDI (J-OSDI) is essential for making epidemiological and symptomatic comparisons with
98 other countries.[11-14]

99 In this study, we developed and evaluated the reliability and validity of J-OSDI and
100 determined the cut-off value of the J-OSDI total score using the 2016 diagnostic criteria put
101 forth by the ADES.[6]

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6 103 **MATERIALS AND METHODS**7
8 104 **Translation of the Japanese version of the Ocular Surface Disease Index**

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10 105 The OSDI questionnaire contains 12 questions divided into three subscales: ocular
11 106 symptoms, vision related function, and environmental triggers.[11] The questionnaire asks
12 107 patients to rate each symptom on a 5-point scale according to their frequency, from “all of the
13 108 time” (score 4) to “none of the time” (score 0). The OSDI total score and each subscale score
14 109 are separately translated to scores of 0–100. According to the OSDI total score, patients are
15 110 classified as normal (0–12 points), mild (13–22 points), moderate (23–32 points), or severe
16 111 DED (33–100 points). To obtain a scientifically accurate translation and to perform a
17 112 transcultural validation of the original version of the questionnaire, a forward-backward
18 113 procedure was applied to translate the OSDI from English to Japanese. The translation and
19 114 transcultural adaptation process included translation of the original English version (Allegan
20 115 Inc., Irvine, CA) of the OSDI into Japanese by five bilingual ophthalmologists, two bilingual
21 116 epidemiologists, and one native-English researcher, each working individually. A cultural
22 117 adaptation was conducted to ensure that the translated questionnaire is easily understandable for
23 118 Japanese patients. The J-OSDI was then translated into English by five native-English
24 119 researchers and was assessed for comprehensibility.

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4546 121 **Study design and participants**

47 122 This cross-sectional observational study included 209 patients recruited between
48 123 September 2017 to May 2018 from the Department of Ophthalmology at Juntendo University
49 124 Hospital in Tokyo, Japan. Written informed consent was obtained from all participants. The
50 125 study was approved by the Independent Ethics Committee at Juntendo University Hospital
51 126 (Approval number, 17-088 and 18-082) and adhered to the tenets of the Declaration of Helsinki
52 127 as revised in Brazil in 2013.

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129 **Exclusion criteria**

130 We excluded patients with BCVA values < 20/20 and those with a history of eyelid
131 disorder, ptosis, Parkinson disease, ocular surface surgery, eyelid surgery, hereditary corneal
132 disease, or any other disease that could affect blinking.

134 **Environmental conditions**

135 The temperature and humidity of the examination room were controlled at 26°C in the
136 summer and 24°C in the winter with 50% relative humidity, according to the Guideline for
137 Design and Operation of Hospital HVAC Systems established by the Healthcare Engineering
138 Association of Japan.[15]

140 **Dry eye disease diagnosis and classification**

141 All patients underwent a complete ophthalmic evaluation for both eyes, including
142 measuring BCVA, IOP, and subjective symptoms. Additionally, TFBUT, CFS for
143 kerato-conjunctival vital staining, MBI, and Schirmer test I for reflex tear production were
144 assessed for both eyes. TFBUT, CFS, and Schirmer test I values from the worst eye were
145 examined. The mean value of MBI was used in accordance with a previous study.[16] For each
146 patient, we evaluated TFBUT, CFS, and MBI before performing the Schirmer test I. We
147 diagnosed DED and non-DED using the ADES 2016 diagnostic criteria,[6] which is based on
148 two positive items: the presence of subjective symptoms and decreased TFBUT (≤ 5 seconds).

150 **Subjective symptoms and DEQS**

151 Subjective symptoms were evaluated by interviewing subjects with DED. The DEQS
152 questionnaire was administered to subjects in order to assess the severity of dry eye-associated
153 symptoms and the multifaceted effects of DED on daily life.[10] The score derived from this
154 questionnaire is a subjective measurement of DED symptoms, where 0 indicates the best score
155 (no symptoms) and 100 indicates the worst score (maximum symptoms).

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6 157 **TFBUT**7
8 158 TFBUT was measured using a fluorescein dye according to the standard methodology.[6]9
10 159 Only a small quantity of dye was administered using the wetted fluorescein strip in order to11
12 160 minimize the effect of the dye on tear volume and TFBUT. Each subject was instructed to blink13
14 161 three times after the dye was applied to ensure adequate mixing of the dye and tears. The time15
16 162 interval between the last blink and the appearance of the first dark spot on the cornea was17
18 163 measured with a stopwatch. The mean value of three measurements was used. A cut-off value of19
20 164 TFBUT \leq 5 seconds was used to diagnose DED.[6]21
22 16523
24 166 **Kerato-conjunctival vital staining (CFS)**25
26 167 CFS was graded according to the van Bijsterveld grading system,[17] which divides the27
28 168 ocular surface into three zones: the nasal bulbar conjunctiva, the temporal bulbar conjunctiva,29
30 169 and the cornea. Each zone was evaluated on a scale of 0–3, with 0 indicating no staining and 331
32 170 indicating confluent staining. The maximum possible score was thus 9.33
34 17135
36 172 **MBI**37
38 173 MBI was considered as the length of time that subjects could keep their eyes open before39
40 174 blinking.[16] We calculated MBI twice by stopwatch under a light microscope without using41
42 175 the light. MBI was recorded as 30 seconds if the blink interval exceeded 30 seconds.43
44 17645
46 177 **Schirmer test I**47
48 178 The Schirmer test I was performed without topical anesthesia after all other examinations49
50 179 had been completed. Schirmer's test strips (Ayumi Pharmaceutical Co., Tokyo, Japan) were51
52 180 placed on the outer third of the temporal lower conjunctival fornix for 5 minutes. The strips53
54 181 were then removed, and the length of dampened filter paper (in mm) was recorded.55
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183 **Reliability**

184 The internal consistency of the J-OSDI was assessed using Cronbach's alpha coefficient,
185 with an alpha > 0.70 considered to be acceptable.[18] Test-retest reliability was evaluated by
186 calculating the ICC values from the first and second entries. An ICC value of ≥ 0.70 was
187 considered acceptable for test-retest reliability.[19]

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189 **Validity**

190 Discriminant validity was evaluated by comparing the non-DED and DED groups. For
191 factor validity, confirmatory factor analysis was conducted by an equamax rotation to determine
192 whether the subscales in the J-OSDI cluster together in the same way as in the original OSDI.
193 Factors with an eigenvalue > 0.90 were retained. Concurrent validity was assessed by
194 calculating the correlations (Pearson coefficients) between J-OSDI total score or subscale scores
195 and DEQS or other clinical results, including TFBUT, CFS, MBI, and Schirmer test I values.

196

197 **Statistical analyses**

198 To compare general characteristics between DED and non-DED participants, 2-tailed *t* tests
199 were used for continuous variables and χ^2 tests were used for categorical variables. Pearson rank
200 correlation coefficients were calculated to determine the correlations between J-OSDI, DEQS,
201 TFBUT, MBI, and Schirmer test I results. ROC analysis was used to determine the optimal
202 cut-off value of the J-OSDI total score for suspecting DED. AUC was computed using the
203 trapezoidal rule. Data are presented as mean \pm standard deviation (SD) or proportion (%).
204 Statistical analyses were performed using STATA version 15 (Stata Corp, TX) and SPSS
205 Statistics v.1.0.0 (IBM Corp, Chicago, IL). $p < 0.05$ was considered significant.

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207 **Patient and public involvement**

208 No patients were involved in the research design and conception of this research study.

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211 **RESULTS**212 **Participant characteristics**

213 Table 1 shows the general characteristics of the study participants. All subjects responded
 214 to the questionnaires, completed the examination, and were eligible for the study. Overall, 209
 215 participants were included. The average age was 58.9 ± 15.3 years, and 83.7% of the
 216 participants were women. Using the diagnostic criteria put forth by the ADES,[6] 152 and 57
 217 patients were classified as DED (72.7%) and non-DED (27.3%), respectively. The mean best
 218 corrected visual acuity (BCVA) value for both eyes was -0.07 ± 0.02 logMAR. The mean
 219 intraocular pressure (IOP) for both eyes was 14.1 ± 2.9 mmHg. Both the J-OSDI total score and
 220 DEQS were significantly higher in the DED group than in the non-DED group, indicating that
 221 DED patients showed a greater rate of subjective symptoms. Furthermore, both TFBUT and
 222 maximum blink interval (MBI) were significantly lower in the DED group than the non-DED
 223 group. Neither BCVA, IOP, corneal fluorescence staining (CFS), nor Schirmer test I results
 224 differed significantly between DED and non-DED participants.

226 **Table 1.** Characteristics of study participants.

	non-DED	DED	p value	Total
	n = 57	n = 152		n = 209
Age, year \pm SD	61.4 \pm 15.5	57.9 \pm 15.2	0.149	58.9 \pm 15.3
Gender, female (%)	48 (84.2)	127 (83.6)	1.000	175 (83.7)
BCVA, logMAR \pm SD	-0.1 \pm 0.0	-0.1 \pm 0.0	0.513	-0.1 \pm 0.0
IOP, mmHg \pm SD	14.6 \pm 2.9	13.8 \pm 2.7	0.062	14.0 \pm 2.8
Subjective symptoms, yes (%)	5 (8.8)	152 (100)	***< 0.001	157 (75.1)
J-OSDI, 0–100 \pm SD	19.4 \pm 16.0	37.7 \pm 22.2	***< 0.001	32.7 \pm 29.7

DEQS, 0–100 ± SD	16.0 ± 14.7	32.7 ± 21.6	***< 0.001	28.1 ± 21.3
TFBUT, seconds ± SD	2.5 ± 2.4	1.5 ± 0.8	***< 0.001	1.7 ± 1.5
CFS, 0–9 ± SD	2.8 ± 2.5	3.3 ± 2.6	0.192	3.2 ± 2.6
Schirmer I, mm ± SD	7.2 ± 8.2	5.7 ± 6.2	0.162	6.1 ± 6.8
MBI, seconds ± SD	15.1 ± 8.1	10.5 ± 6.3	***< 0.001	11.7 ± 7.1

DED, dry eye disease; BCVA, best-corrected visual acuity; IOP, intraocular pressure; J-OSDI, Japanese version of ocular surface disease index; DEQS, Dry Eye-Related Quality-of-Life Score; TFBUT, tear film breakup time; CFS, corneal fluorescein staining; MBI, maximum blink interval. p values were determined using the Student's t-test (two-tailed) for continuous variables and the chi-square test for categorical variables. ***p < 0.001.

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234 Reliability

235 We tested the J-OSDI total score and subscale scores for internal consistency and test-retest
 236 reliability, and the results are shown in Table 2. For internal consistency, the Cronbach's alpha
 237 coefficient was 0.884 for the J-OSDI total score and 0.788, 0.669, and 0.902 for the ocular
 238 symptoms, vision-related function, and environmental triggers subscales, respectively.
 239 Test-retest reliability was evaluated in 173 participants, with a median (IQR) period of 119
 240 (81–182) days between the test and retest. The intraclass correlation coefficient (ICC) values
 241 were 0.910, 0.649, 0.817, and 0.859 for the J-OSDI total score, ocular symptoms subscale,
 242 vision-related function subscale, and environmental triggers subscale, respectively.

243 **Table 2.** Reliability for each subscale

		Cronbach α	ICC
	Number of items	(n = 209)	(n = 173)
J-OSDI total score	12	0.884	0.910
Ocular symptoms	5	0.788	0.649
Vision-related function	4	0.669	0.817

Environmental triggers 3 0.902 0.859

244 J-OSDI, Japanese version of the ocular surface disease index; ICC; intra-class correlation
245 coefficient.

246

247 **Discriminant validity**

248 Table 3 shows the mean values for the J-OSDI total score, each of the subscale scores, and
249 each of the component scores. The mean J-OSDI total score was significantly higher in the
250 DED group than in the non-DED group (DED, 37.7 ± 22.2 ; non-DED, 19.4 ± 16.0 ; $p < 0.001$).
251 Additionally, all three subscales were significantly higher in the DED group than in the
252 non-DED group (ocular symptoms: DED, 34.6 ± 21.6 ; non-DED, 20.9 ± 17.4 ; $p < 0.001$;
253 vision-related function: DED, 36.5 ± 27.7 ; non-DED, 20.8 ± 22.0 ; $p < 0.001$; environmental
254 triggers: DED, 45.2 ± 29.7 ; non-DED, 15.5 ± 19.8 ; $p < 0.001$). Eleven of the 12 (92%)
255 component scores were significantly higher in the DED group than in the non-DED group, with
256 only question 2 showing a non-significant difference.

257 **Table 3.** J-OSDI score for each question.

Classification, score \pm SD, score	non-DED n = 57	DED n = 152	p value	Total n = 209
J-OSDI total score, 0–100	19.4 ± 16.0	37.7 ± 22.2	*** < 0.001	32.7 ± 22.2
Ocular symptoms, 0–100	20.9 ± 17.4	34.6 ± 21.6	*** < 0.001	30.9 ± 21.4
1. Eyes that are sensitive to light?	0.8 ± 0.9	1.5 ± 1.3	*** < 0.001	1.3 ± 1.3
2. Eyes that feel gritty?	0.8 ± 1.2	1.0 ± 1.0	0.338	1.0 ± 1.1
3. Painful or sore eyes?	0.4 ± 0.7	1.0 ± 1.0	*** < 0.001	0.8 ± 1.0
4. Blurred vision?	1.1 ± 1.0	1.6 ± 1.2	**0.002	1.5 ± 1.2
5. Poor vision?	1.1 ± 1.1	1.8 ± 1.3	*** < 0.001	1.6 ± 1.3
Vision-related function	20.8 ± 22.0	36.5 ± 27.7	*** < 0.001	32.2 ± 27.2

6. Reading?	0.8 ± 1.1	1.6 ± 1.3	***< 0.001	1.4 ± 1.3
7. Driving at night?	0.4 ± 0.6	1.1 ± 1.4	*0.022	0.9 ± 1.3
8. Working with a computer or bank machine (ATM)?	1.1 ± 1.3	1.6 ± 1.4	*0.030	1.5 ± 1.4
9. Watching TV?	0.7 ± 1.0	1.3 ± 1.2	**0.002	1.1 ± 1.1
Environmental triggers	15.5 ± 19.8	45.2 ± 29.7	***< 0.001	37.1 ± 30.4
10. Windy conditions?	0.7 ± 0.9	1.9 ± 1.4	***< 0.001	1.5 ± 1.3
11. Places or areas with low humidity (very dry)?	0.5 ± 0.8	1.6 ± 1.3	***< 0.001	1.3 ± 1.3
12. Areas that are air conditioned?	0.6 ± 0.9	2.0 ± 1.3	***< 0.001	1.6 ± 1.3

258 DED, Dry eye disease; J-OSDI, Japanese version of ocular surface disease index. p values

259 were determined using the Student's t-test. *p < 0.05, **p < 0.01, and ***p < 0.001.

260

261 Factor validity

262 Factor validity was assessed by confirmatory factor analysis to determine the subscales. As
 263 shown in Figure 1, correspondent with the three homogeneous content domains that were
 264 identified and constructed; three factors were rotated to an equamax solution. These three
 265 factors accounted for 71.9% of the total variance, and each factor was comprised of sets of items
 266 that were interpretable and relevant in content. Factor 1, accounting for 53.0% of the total
 267 variance and 23.6% of the common variance, was comprised of items assessing the frequency of
 268 ocular symptoms (5 items). Factor 2, accounting for 11.1% of the total variance and 22.8% of
 269 the common variance, was comprised of items assessing the frequency of vision-related
 270 function (4 items). Factor 3, accounting for 7.7% of the total variance and 17.7% of the
 271 common variance, was comprised of items assessing the frequency of environmental triggers (3
 272 items). All factors were in accordance with the subscales in the original version. The factor

273 matrix of each J-OSDI component can be viewed in Supplemental Table 1. All subscales and
 274 the total instrument underwent formal reliability and validity testing.

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276 **Concurrent validity**

277 Table 4 shows the correlations between J-OSDI total score, subscale scores, and other
 278 clinical items related to DED diagnosis, including DEQS, TFBUT, CFS, Schirmer test I results,
 279 and MBI. J-OSDI total score was significantly and positively correlated with DEQS ($\gamma = 0.829$).
 280 Among the clinical items related to DED diagnosis, there was a modest but significant negative
 281 correlation between J-OSDI total score and MBI ($\gamma = -0.258$). The subscales were each
 282 significantly and positively correlated with DEQS score ($\gamma = 0.786, 0.702$ and 0.650 ,
 283 respectively), while ocular symptoms and environmental triggers were significantly and
 284 negatively correlated with MBI ($\gamma = -0.195$ and -0.370 , respectively).

285

286 **Table 4.** Correlation between J-OSDI total score and other clinical assessments.

Clinical Items	OSDI total score		Ocular symptoms		Vision-related function		Environmental triggers	
	γ	p value	γ	p value	γ	p value	γ	p value
DEQS	0.829	***< 0.001	0.786	***< 0.001	0.702	***< 0.001	-0.650	***< 0.001
TFBUT	-0.066	0.349	-0.044	0.532	-0.057	0.416	-0.131	0.063
CFS	0.018	0.791	-0.013	0.852	-0.137	*0.049	0.161	*0.022
Schirmer I	-0.090	0.195	-0.013	0.844	-0.071	0.311	-0.129	0.067
MBI	-0.283	***< 0.001	-0.215	**0.002	-0.135	0.053	-0.407	***< 0.001

287 J-OSDI, Japanese version of the ocular surface disease index; DEQS, Dry Eye-Related

288 Quality-of-Life Score; TFBUT, tear film breakup time; CFS, corneal fluorescein staining;

289 MBI, maximum blink interval. Pearson rank correlation coefficient was used to determine

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4 290 the correlations between the J-OSDI total score and subscale scores and various clinical
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6 291 assessments. * $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$.
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10 293 **J-OSDI severity results and cut-off value for detecting DED**

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13 294 Figure 2A shows the proportion of DED participants in each severity category as
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15 295 determined by J-OSDI total score. The clinically diagnosed DED patients were divided
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17 296 according to their J-OSDI scores as follows: 22.0% were categorized as normal, 17.2% were
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19 297 categorized as mild DED, 12.9% were categorized as moderate DED, and 47.8% were
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21 298 categorized as severe DED. Figure 2B shows the proportion of patients who were clinically
22
23 299 diagnosed with DED in each severity category determined by J-OSDI total scores. Overall,
24
25 300 47.8% of the patients who were classified as normal by their J-OSDI total score were clinically
26
27 301 diagnosed with DED, while 66.7%, 74.0%, and 86.0% of patients classified as mild, moderate,
28
29 302 and severe, respectively, were clinically diagnosed with DED. Figure 2C shows the receiver
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31 303 operating characteristic (ROC) curve of the J-OSDI total score from the non-DED and DED
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33 304 groups, which was used to determine the diagnostic efficacy of the J-OSDI total score. The
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35 305 optimum cut-off value for detecting DED was 36.3 points, with an area under the curve (AUC),
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37 306 sensitivity, and specificity of 0.744, 51.3%, and 87.7%, respectively. Supplemental Table 1
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39 307 shows the details of the J-OSDI total score sensitivity and specificity analysis.
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44 309 **DISCUSSION**

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47 310 DED is a major ocular disease that affects at least 344 million people worldwide and
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49 311 causes a variety of symptoms.[1, 5, 6]. Particularly in Japan, many people have DED due to
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51 312 genetic risk factors and increasing usage of digital devices.[2, 20] Therefore, quantifying the
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53 313 symptoms and severity of DED is important for the diagnosis, monitoring, and treatment of this
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55 314 condition. Indeed, evaluation of subjective symptoms for DED diagnosis is regarded as the
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57 315 primary examination tool in both the DEWS II report[5] and the 2016 ADES diagnostic
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4 316 criteria.[6] In particular, the diagnostic criteria from the ADES use the presence of subjective
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6 317 symptoms and a decreased TFBUT, indicating the importance of accurately quantifying
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8 318 subjective symptoms in DED. The OSDI is a questionnaire widely used to quantify subjective
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10 319 symptoms in DED but the reliability and validity of this test has not been examined in Japan. In
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12 320 this study, we assessed the reliability and validity of the J-OSDI, which is the Japanese version
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14 321 of OSDI, and determined a cut-off value using the ADES diagnostic criteria of 2016. Our results
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16 322 validate the use of the J-OSDI in Japan and make it possible to compare epidemiological results
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18 323 between Japan and other countries.

21 324 We used factor analysis to confirm three subscales within the J-OSDI: ocular symptoms,
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23 325 vision-related function, and environmental triggers. All of these were in accordance with the
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25 326 subscales in the original English version (Figure 1). The J-OSDI total score showed both high
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27 327 internal consistency and test-retest reliability (Table 2). For the subscales, factor analysis
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29 328 confirmed three subscales which were in accordance with the subscales in the original English
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31 329 version (Figure 1). Two of the subscales, ocular symptoms and environmental triggers, showed
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33 330 good internal consistency, while the third subscale, vision-related function, only showed modest
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35 331 internal consistency. Because the questions in the vision-related function subscale are concerned
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37 332 with daily activities, including reading, driving at night, working with a computer or bank
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39 333 machine (ATM), and watching TV, the individual variation for these behaviors naturally affects
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41 334 the internal consistency of this subscale. The test-retest reliability of the subscales demonstrates
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43 335 that vision-related function and environmental triggers have good reliability. However, the
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45 336 reliability of the ocular symptoms subscale was only modest, indicating that the answers to this
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47 337 subscale may have varied because of the known fluctuations in the subjective symptoms of
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49 338 DED.[21, 22]

52 339 The J-OSDI total score and subscale scores were significantly higher in the DED group
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54 340 compared to the non-DED group, verifying the discriminant validity of the J-OSDI (Table 3).
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56 341 Further, the percentage of participants who were clinically diagnosed with DED increased
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58 342 proportionally in each severity category, indicating that the J-OSDI total score can discriminate
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4 343 DED (Figure 2B). Our study also determined that the optimal J-OSDI total score cut-off value
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6 344 for detecting DED according to ADES criteria was 36.3. One previous study reported an OSDI
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8 345 total score cut-off value of 15.[11] However, the difference between this cut-off value and that
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10 346 of the current study is probably the result of differences in the methods used to clinically
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12 347 diagnose severity of DED, as the previous study used lissamine green staining, Schirmer test I,
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14 348 and patient perception of ocular symptoms. In contrast, the current study used TFBUT as an
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16 349 essential part of our diagnostic criteria.[5, 6] Supplemental Table 2 shows the sensitivity and
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18 350 specificity of our reported cut-off value and the cut-off values for the different severity
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20 351 categories: normal (0–12), mild (13–22), moderate (23–32) and severe (33–100).[11] Our
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22 352 results suggest that it is necessary to re-evaluate the OSDI total score cut-off values for
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24 353 diagnosis and severity categories to reflect the changes made to the diagnostic criteria for
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26 354 DED.[5, 6, 23-28]

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28
29 355 Table 4 shows the correlations between J-OSDI total score and other clinical tests,
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31 356 including DEQS, TFBUT, CFS, MBI, and Schirmer test I. J-OSDI total score showed a strong
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33 357 positive correlation with DEQS score. Because the DEQS has been validated in Japan,[10] this
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35 358 result supports the use of the J-OSDI as a valid method of quantifying subjective symptoms. In
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37 359 contrast, the respective correlations between J-OSDI total score and TFBUT, CFS, and
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39 360 Schirmer I were relatively low. This is consistent with previous studies that reported low
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41 361 correlations and high divergence between subjective symptoms assessed by questionnaires and
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43 362 clinical tools,[2, 19, 25] underscoring the importance of combining knowledge about subjective
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45 363 symptoms and clinical tools in order to effectively evaluate and monitor DED. Our group[16]
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47 364 has proposed MBI as a simple self-check screening test for DED because it is highly correlated
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49 365 with subjective symptoms compared with other dry eye items (Table 4). Because of the
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51 366 divergence between the subjective and clinical symptoms of DED,[2] it is necessary to perform
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53 367 multilateral evaluations using not only OSDI total scores but also the subscales and each
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55 368 component. In the present study, we assessed the respective relationship between each subscale
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57 369 and various clinical tools for DED examination and found that the ocular symptoms and
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4 370 environmental trigger subscales were negatively correlated with MBI. We recently reported that
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6 371 MBI is also significantly associated with TFBUT and CFS.[16] Our previous results and those
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8 372 of this study suggest that MBI reflects both TFBUT and CFS results, possibly explaining its
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10 373 negative correlation with the ocular symptoms and environmental triggers subscale scores of
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12 374 J-OSDI.

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14 375 This study has several limitations. First, it was conducted at a single university hospital in
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16 376 Japan, possibly introducing selection bias into our sample. Second, under the simplified ADES
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18 377 diagnostic criteria, those with low TFBUTs can still be classified as non-DED due to a lack of
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20 378 subjective symptoms; thus, our non-DED group showed a low TFBUT. Third, the test-retest
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22 379 method that we used to confirm reliability introduced recall bias from the necessary length of
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24 380 the test-retest period. Next, we did not account for differences in variables such as
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26 381 socioeconomic status or education level, possibly affecting the responses. Finally, this study
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28 382 was designed to investigate the J-OSDI as a primary evaluation and monitoring method for
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30 383 DED. Thus, rose bengal stain scores, tear osmolality, meibomian gland dysfunction
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32 384 assessments, and corneal sensations were not applied in this study. Despite these limitations, we
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34 385 verified the reliability and validity of the J-OSDI for DED assessment and monitoring in Japan.

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36 386 In summary, we validated the J-OSDI by assessing its reliability and validity. We report
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38 387 that a J-OSDI score of 36.3 is the optimal cut-off value for suspecting DED under the 2016
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40 388 ADES criteria. We believe that J-OSDI will be useful for primary assessment and monitoring of
41
42 389 DED in routine clinical practice and in remote diagnosis.

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49 391 **Acknowledgments:** The authors thank the nurses and orthoptists of the Department of
50
51 392 Ophthalmology at the Juntendo University Hospital for collecting the data for DED diagnosis.

52
53 393 **Author Contributions:**

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4 394 A.MI.: Performance of the research, data collection, data analysis, and writing of the paper; T.I.:
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6 395 Performance of the research, research design, data analysis, and writing of the paper; S.N.:
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8 396 Research design, data analysis; M.N.: Data analysis; M.I.: Research design, data analysis; K.F.:
9
10 397 Data collection, data analysis; Y.O.: Data collection, data analysis; N.I.: Data collection, data
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12 398 analysis; A. E.: Data collection, data analysis; H.H.: Data collection, data analysis; H.K.:
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14 399 Performance of the research; A.M.: Research design, writing of the paper; H.K.: Research
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16 400 design, writing of the paper.

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20 401 **References**

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48 **Figure 1. Three subscales of J-OSDI as determined by factor analysis.** The existence of
49
50 461 3 clusters that were used as subscales are shown. These were in accordance with the
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52 462 subscales that are used in the original version of OSDI: vision-related function
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54 463 (components 1–5), ocular symptoms (components 6–9), and environmental triggers
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56 464 (components 10–12).

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7 466 **Figure 2. Clinical utility of J-OSDI for evaluating dry eye disease (DED).** (a) The
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9 467 proportion of patients in each DED severity category as determined by the J-OSDI total
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11 468 score. (b) The proportion of patients who were clinically diagnosed with DED by category
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13 469 of severity according to the J-OSDI total score. (c) The Receiver Operator Characteristic
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15 470 (ROC) curve for the diagnosis of DED determined by the Asia Dry Eye Society 2016
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17 471 criteria using J-OSDI. The area under the ROC curve (AUC) is 0.744.
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23 473 **Supplementary Information**

24
25 474 **Supplemental Table 1: Factor matrix of each J-OSDI question.** Results of factor analysis of each J-OSDI
26 475 question. All of three subscales were in accordance with the subscales in the original version.

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28 476 **Supplemental Table 2: J-OSDI total score sensitivity and specificity analysis results.** Full results of the
29 477 sensitivity and specificity analysis. Our reported cut-off value for suspecting dry eye disease was 36.3.
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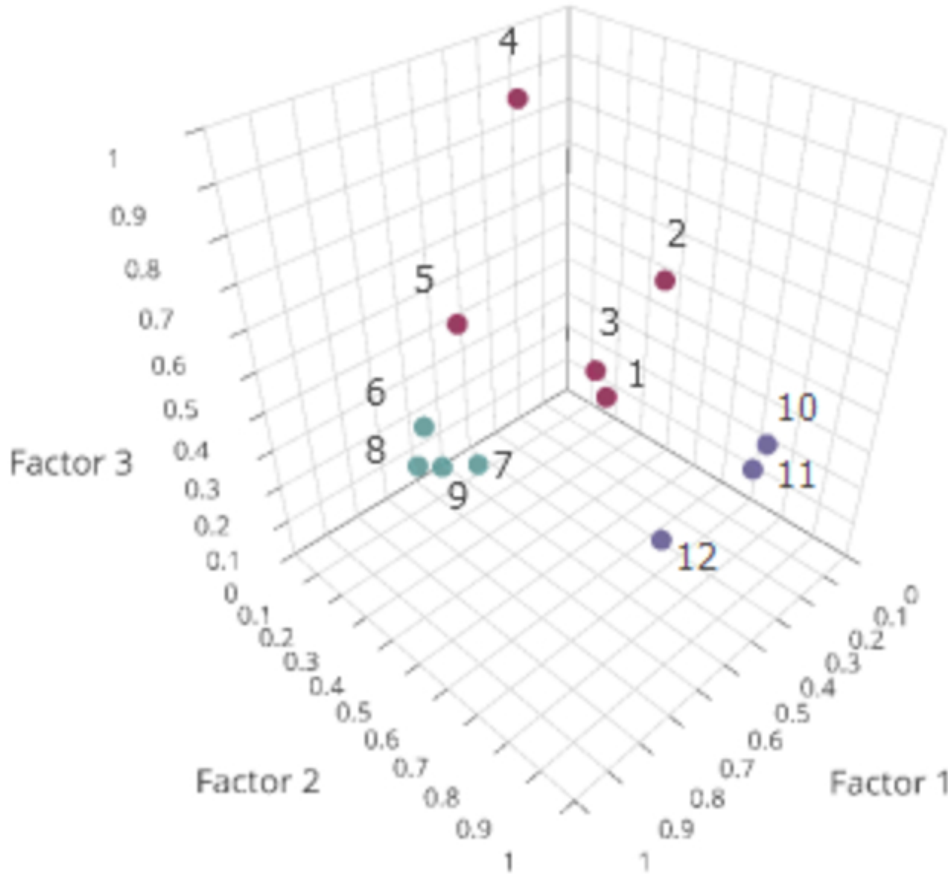


Figure 1

185x173mm (90 x 90 DPI)

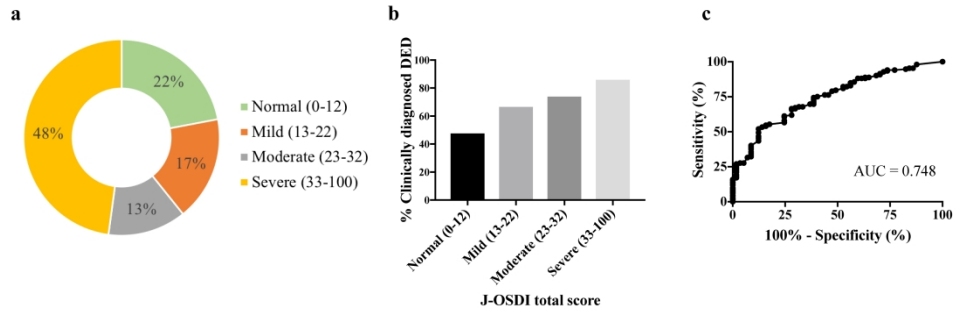


Figure 2

Supplementary Information

From: Reliability and Validity of the Japanese Version of the Ocular Surface Disease Index for Dry Eye Disease

Akie Midorikawa-Inomata RN, MPH, Takenori Inomata MD, PhD, MBA, Soko Nojiri, MPH, Masahiro Nakamura MD, PhD, Masao Iwagami MD, MPH, MSc, PhD, Keiichi Fujimoto MD, Yuichi Okumura MD, Nanami Iwata, Atsuko Eguchi, Hitomi Hasegawa MD, Hikaru Kinouchi, Akira Murakami MD, PhD, and Hiroyuki Kobayashi MD, PhD.

Supplemental Table 1: Factor matrix of each J-OSDI question

Components	Factor		
	1	2	3
1	0.352	0.474	0.361
2	0.055	0.393	0.504
3	0.256	0.349	0.331
4	0.335	0.167	0.927
5	0.632	0.269	0.573
6	0.706	0.208	0.323
7	0.576	0.246	0.171
8	0.710	0.172	0.198
9	0.719	0.283	0.260
10	0.156	0.815	0.307
11	0.239	0.837	0.295
12	0.441	0.742	0.159

J-OSDI, Japanese version of the Ocular Surface Disease Index.

Extraction Method: Maximum likelihood method; Rotation Method: Equamax with Kaiser normalization

Supplemental Table 2: J-OSDI total score sensitivity and specificity analysis results

J-OSDI total score	Sensitivity (%)	Specificity (%)
> 1.05	98.03	12.28
> 2.2	95.39	14.04
> 2.4	95.39	15.79
> 3.35	94.74	17.54
> 4.9	94.08	22.81
> 5.95	94.08	26.32
> 6.55	92.76	28.07
> 6.95	91.45	29.82
> 7.3	90.79	29.82
> 7.9	90.13	31.58
> 9.15	88.82	35.09
> 10.2	88.82	36.84
> 10.9	88.16	38.6
> 11.95	88.16	40.35
> 13.05	84.87	42.11
> 14.1	84.21	43.86
> 14.8	82.24	43.86
> 15.3	81.58	45.61
> 15.75	81.58	47.37
> 16.3	80.26	47.37
> 17.45	78.95	50.88
> 18.5	78.29	52.63
> 19.1	75.66	54.39
> 19.7	75.66	56.14

> 20.25	74.34	59.65
> 20.65	73.68	61.4
> 21.35	72.37	61.4
> 22.05	71.05	61.4
> 22.35	70.39	61.4
> 22.6	69.08	61.4
> 23.85	69.08	63.16
> 26.15	67.11	66.67
> 27.4	67.11	68.42
> 27.8	66.45	70.18
> 28.65	65.79	70.18
> 29.35	65.13	71.93
> 29.75	61.18	71.93
> 30.3	60.53	75.44
> 30.95	59.87	75.44
> 31.55	57.24	75.44
> 32.55	55.92	75.44
> 33.7	54.61	82.46
> 34.55	53.95	84.21
> 35.2	53.29	84.21
> 35.75	52.63	85.96
> 36.25	51.32	87.72
> 36.95	48.68	87.72
> 38.55	46.05	87.72
> 39.8	44.74	87.72
> 40.85	42.76	87.72
> 42.1	39.47	91.23

> 42.85	38.82	91.23
> 43.5	38.16	91.23
> 44.4	36.84	91.23
> 45.4	34.87	91.23
> 46.5	33.55	91.23
> 47.35	32.89	91.23
> 47.6	32.24	91.23
> 47.8	31.58	91.23
> 48.95	30.92	92.98
> 51.05	27.63	94.74
> 52.2	26.97	98.25
> 52.4	25.66	98.25
> 53.35	25	98.25
> 54.35	23.03	98.25
> 55.4	21.71	98.25
> 56.55	21.05	98.25
> 57.15	20.39	98.25
> 57.9	18.42	98.25
> 58.7	17.11	98.25
> 59.75	16.45	98.25
> 61.45	15.79	100
> 63.05	15.13	100
> 63.75	13.82	100
> 64.25	13.16	100
> 66.05	11.84	100
> 67.7	9.868	100
> 68.35	9.211	100

> 69.65	8.553	100
> 70.65	7.895	100
> 71.85	7.237	100
> 75	6.579	100
> 77.2	5.921	100
> 78.25	4.605	100
> 82.1	3.947	100
> 85.7	2.632	100
> 87.5	1.974	100
> 89.3	1.316	100

J-OSDI, Japanese version of the Ocular Surface Disease Index

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1,2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	17
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	8
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9, 10
		(b) Indicate number of participants with missing data for each variable of interest	9
Outcome data	15*	Report numbers of outcome events or summary measures	9-11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A

		(b) Report category boundaries when continuous variables were categorized	5
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	16
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Reliability and Validity of the Japanese Version of the Ocular Surface Disease Index for Dry Eye Disease

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-033940.R1
Article Type:	Original research
Date Submitted by the Author:	10-Oct-2019
Complete List of Authors:	Midorikawa-Inomata, Akie; Juntendo University Graduate School of Medicine, Department of Hospital Administration Inomata, Takenori; Juntendo University Faculty of Medicine, Ophthalmology Nojiri, Shuko ; Juntendo University, Clinical Research Support Center Nakamura, Masahiro; Graduate School of Bioengineering, The University of Tokyo, Precision Health, Department of Bioengineering Iwagami, Masao; University of Tsukuba, Department of Health Services Research Keiichi, Fujimoto; Juntendo University Graduate School of Medicine, Department of Ophthalmology Okumura, Yuichi; Juntendo University Graduate School of Medicine, Department of Ophthalmology Iwata, Nanami; Juntendo University Graduate School of Medicine, Department of Ophthalmology Eguchi, Atsuko; Juntendo University Graduate School of Medicine, Department of Hospital Administration Hasegawa, Hitomi; Juntendo University Faculty of Medicine, Ophthalmology Kinouchi, Hikaru; Aoyama Gakuin University, School of Cultural and Creative Studies Murakami, Akira; Juntendo University Faculty of Medicine, Ophthalmology Kobayashi, Hiroyuki; Juntendo University Graduate School of Medicine, Department of Hospital Administration
Primary Subject Heading:	Ophthalmology
Secondary Subject Heading:	Epidemiology
Keywords:	dry eye disease, ocular surface disease index, OSDI, reliability, validity

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5 1 Original article—Clinical Science
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7 3 **Reliability and Validity of the Japanese Version of the**
8 **Ocular Surface Disease Index for Dry Eye Disease**
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52 32 **Word count: 4163**

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54 33 **Declaration of competing/conflicting interests:** There are no conflicts of interest to declare.

55
56 34 **Funding sources:** This research received no external funding or any specific grant from
57 35 funding agencies in the public, commercial, or not-for-profit sectors.

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4 36 **Data Availability Statement:** The data that support the findings of this study are available from
5 37 the corresponding author upon reasonable request. The J-OSDI is provided for others to use as
6 38 Supplemental Figure 1.
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10 40 **ABSTRACT**

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12 41 **Objectives:** The ocular surface disease index (OSDI) questionnaire is widely used to evaluate
13 42 subjective symptoms of dry eye disease (DED) as a primary diagnostic criterion. This study
14 43 aimed to develop a Japanese version of the OSDI (J-OSDI) and assess its reliability and
15 44 validity.
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20 45 **Design and Setting:** Hospital-based cross-sectional observational study.
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22 46 **Participants:** A total of 209 patients recruited from the Department of Ophthalmology at
23 47 Juntendo University Hospital.
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26 48 **Methods:** We translated and culturally adapted the OSDI into Japanese. The J-OSDI was then
27 49 assessed for internal consistency, reliability, and validity. We also evaluated the optimal cut-off
28 50 value to suspect DED using an area under the receiver operating characteristic curve (AUC)
29 51 analysis.
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34 52 **Primary Outcome Measures:** Internal consistency, test-retest reliability, and discriminant
35 53 validity of the J-OSDI as well as the optimal cut-off value to suspect DED.
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38 54 **Results:** Of the participants, 152 had DED and 57 did not. The J-OSDI total score showed good
39 55 internal consistency (Cronbach alpha = 0.884), test-retest reliability (interclass correlation
40 56 coefficient = 0.910), and discriminant validity by known-group comparisons (non-DED, 19.4 ±
41 57 16.0; DED, 37.7 ± 22.2; $p < 0.001$). Factor validity was used to confirm 3 subscales within the
42 58 J-OSDI according to the original version of the questionnaire. Concurrent validity was assessed
43 59 by Pearson correlation analysis, and the J-OSDI total score showed a strong positive correlation
44 60 with the Dry Eye-Related Quality-of-Life Score ($\gamma = 0.829$). The optimal cut-off value of the
45 61 J-OSDI total score was 36.3 (AUC = 0.744).
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55 62 **Conclusions:** The J-OSDI was developed and validated in terms of reliability and validity as an
56 63 effective tool for DED assessment and monitoring in the Japanese population.
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6 65 **Keywords:** dry eye disease, J-OSDI, ocular surface disease index, OSDI, reliability, validity
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11 67 **Strengths and limitations of this study:**
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14 68 • This study provides the first validation data on the Japanese version of the ocular surface
15 69 disease index (J-OSDI) questionnaire as the primary evaluation for dry eye disease (DED)
16 70 diagnosis.

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18 71 • We conducted a cross-cultural adaptability thoroughly compared by a committee of experts
19 72 for conceptual equivalence.

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21 73 • This study confirmed the reliability and validity of the J-OSDI in the 209 patients.
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23 74 • The main limitation is that this study was conducted at a single university hospital, which
24 75 may limit the generalizability of the findings.

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26 76 • The validated J-OSDI allows cross-country epidemiological comparisons of
27 77 patient-reported subjective symptoms of DED.
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80 INTRODUCTION

81 The prevalence of dry eye disease (DED) continues to grow due to several
82 psychosocioeconomic factors, including an increase in digital screen usage time, an aging
83 population, and stressful social environments.[1, 2] DED can cause ocular surface damage, eye
84 discomfort, and impaired vision and can also lead to substantial economic problems due to
85 decreased quality of life and work productivity.[3, 4] Therefore, quantifying the symptoms and
86 severity of DED is important for the diagnosis, monitoring, and treatment of the condition.[5, 6]

87 Diagnosis of DED can be made using various methods, including tear film breakup time
88 (TFBUT), ocular surface staining, and osmolarity as a homeostasis marker. Additionally, the
89 use of a questionnaire to determine if symptoms of DED are present is recommended as a
90 primary examination method in the DED diagnosis protocol by the TFOS DEWS II Diagnostic
91 Methodology report and in the 2016 Asia Dry Eye Society (ADES) consensus report.[7, 8]
92 Although previous research has established a divergence between the subjective symptoms of
93 DED and clinical severity of the disease,[9-11] questionnaires that can quantitatively measure
94 the subjective symptoms of DED are indispensable for DED diagnosis and management.

95 The 2016 dry eye diagnostic criteria published by the ADES[8] recommend that DED be
96 diagnosed according to both subjective symptoms and TFBUT, indicating that subjective
97 symptoms are now widely recognized as playing an important role in DED. We previously
98 showed that this change in diagnostic criteria could lead to a 28.0% increase in DED patients in
99 Japan[2]; thus, the need for effective DED treatments may increase in the future. Both the
100 Ocular Surface Disease Index (OSDI) and the Dry Eye-Related Quality-of-Life Score
101 (DEQS)[12] are widely used to assess subjective symptoms of DED in Japan, but the reliability
102 and validity of the OSDI have not been confirmed in Japan.[13] Determining the reliability and
103 validity of the Japanese version of the OSDI (J-OSDI) is essential for making epidemiological
104 and symptomatic comparisons with other countries.[13-16]

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4 105 In this study, we developed and evaluated the reliability and validity of the J-OSDI and
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6 106 determined the cut-off value of the J-OSDI total score using the 2016 diagnostic criteria put
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8 107 forth by the ADES.[8]
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109 **MATERIALS AND METHODS**

110 **OSDI questionnaire**

111 The OSDI questionnaire contains 12 questions divided into three subscales: ocular symptoms,
112 vision related function, and environmental triggers.[13] The questionnaire asks patients to rate
113 each symptom on a 5-point scale according to their frequency, from “all of the time” (score 4) to
114 “none of the time” (score 0). The OSDI total score and each subscale score are separately
115 translated to scores of 0–100. According to the OSDI total score, patients are classified as
116 normal (0–12 points), or as having mild (13–22 points), moderate (23–32 points), or severe
117 DED (33–100 points).

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119 **Translation of the Japanese version of the Ocular Surface Disease Index**

120 To obtain a scientifically accurate translation and to perform a transcultural validation of
121 the original version of the questionnaire, a forward-backward procedure was applied to translate
122 the OSDI (Allegan Inc., Irvine, CA) from English to Japanese following previously established
123 guidelines.[17-19] First, a forward translation was carried out independently by five bilingual
124 ophthalmologists to produce a consensus version. A cultural adaptation was conducted to ensure
125 that the translated questionnaire is easily understandable by Japanese patients. Second, the
126 consensus version was back-translated into English by two native-English researchers and was
127 assessed for comprehensibility. Finally, the original translated and back-translated versions
128 were thoroughly compared by a committee of experts for conceptual equivalence. The J-OSDI
129 is provided for others to use in Supplemental Figure 1.

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131 **Study design and participants**

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4 132 This was a cross-sectional observational study. Adult patients (aged 20 years) who visited
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6 133 the Department of Ophthalmology at Juntendo University Hospital in Tokyo, Japan, between
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8 134 September 2017 to May 2018 were included. Of them, we excluded patients with best-corrected
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10 135 visual acuity (BCVA) values < 20/20 and those with a history of eyelid disorder, ptosis,
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12 136 Parkinson disease, ocular surface surgery, eyelid surgery, hereditary corneal disease, or any
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14 137 other disease that could affect blinking. Written informed consent was obtained from all
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16 138 participants. The study was approved by the Independent Ethics Committee at Juntendo
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18 139 University Hospital (Approval number, 17-088 and 18-141) and adhered to the tenets of the
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20 140 Declaration of Helsinki as revised in Brazil in 2013.
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23 141 All patients underwent a complete ophthalmic evaluation for both eyes, including
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25 142 measuring BCVA, intraocular pressure (IOP), and subjective symptoms. Additionally, TFBUT,
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27 143 corneal fluorescein staining (CFS) for kerato-conjunctival vital staining, maximum blink
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29 144 interval (MBI), and Schirmer test I for reflex tear production were assessed for both eyes.
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31 145 TFBUT, CFS, and Schirmer test I values from the worst eye were examined. The mean value of
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33 146 the MBI was used in accordance with a previous study.[20] For each patient, we evaluated the
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35 147 TFBUT, CFS, and MBI before performing Schirmer test I. We diagnosed DED and non-DED
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37 148 using the ADES 2016 diagnostic criteria,[8] which are based on two positive items: the presence
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39 149 of subjective symptoms and decreased TFBUT (≤ 5 seconds).
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43 151 **Environmental conditions**

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46 152 The temperature and humidity of the examination room were controlled at 26°C in the
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48 153 summer and 24°C in the winter with 50% relative humidity, according to the Guideline for
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50 154 Design and Operation of Hospital HVAC Systems established by the Healthcare Engineering
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52 155 Association of Japan.[21]
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55 157 **Other instruments for DED diagnosis and management**

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4 158 Subjective symptoms were evaluated by interviewing subjects with DED. The DEQS
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6 159 questionnaire was administered to subjects in order to assess the severity of dry eye-associated
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8 160 symptoms and the multifaceted effects of DED on daily life.[12] The score derived from this
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10 161 questionnaire is a subjective measurement of DED symptoms, where 0 indicates the best score
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12 162 (no symptoms) and 100 indicates the worst score (maximum symptoms).

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14 163 TFBUT was measured using a fluorescein dye according to the standard methodology.[8]
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16 164 Only a small quantity of dye was administered using the wetted fluorescein strip in order to
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18 165 minimize the effect of the dye on tear volume and TFBUT. Each subject was instructed to blink
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20 166 three times after the dye was applied to ensure adequate mixing of the dye and tears. The time
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22 167 interval between the last blink and the appearance of the first dark spot on the cornea was
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24 168 measured with a stopwatch. The mean value of three measurements was used. A cut-off value of
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26 169 TFBUT ≤ 5 seconds was used to diagnose DED.[8]

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28 170 CFS was graded according to the van Bijsterveld grading system,[22] which divides the
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30 171 ocular surface into three zones: the nasal bulbar conjunctiva, the temporal bulbar conjunctiva,
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32 172 and the cornea. Each zone was evaluated on a scale of 0–3, with 0 indicating no staining and 3
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34 173 indicating confluent staining. The maximum possible score was thus 9.

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36 174 The MBI was considered as the length of time that subjects could keep their eyes open
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38 175 before blinking.[20] We calculated the MBI twice by stopwatch under a light microscope
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40 176 without using the light. The MBI was recorded as 30 seconds if the blink interval exceeded 30
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42 177 seconds.

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44 178 Schirmer test I was performed without topical anesthesia after all other examinations had
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46 179 been completed. Schirmer's test strips (Ayumi Pharmaceutical Co., Tokyo, Japan) were placed
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48 180 on the outer third of the temporal lower conjunctival fornix for 5 minutes. The strips were then
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50 181 removed, and the length of dampened filter paper (in mm) was recorded.

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57 183 **Statistical analyses**

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4 184 To compare general characteristics between DED and non-DED participants, 2-tailed *t* tests
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6 185 were used for continuous variables and χ^2 tests were used for categorical variables. Pearson rank
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8 186 correlation coefficients were calculated to determine the correlations between J-OSDI, DEQS,
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10 187 TFBUT, MBI, and Schirmer test I results. Receiver operating characteristic (ROC) analysis was
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12 188 used to determine the optimal cut-off value of the J-OSDI total score for suspecting DED. The
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14 189 area under the curve (AUC) was computed using the trapezoidal rule. Data are presented as
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16 190 mean \pm standard deviation (SD) or proportion (%). Statistical analyses were performed using
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18 191 STATA version 15 (Stata Corp, College Station, TX) and SPSS Statistics v.1.0.0 (IBM Corp,
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20 192 Chicago, IL). $p < 0.05$ was considered significant.
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24 194 **Reliability**

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27 195 The internal consistency of the J-OSDI was assessed using Cronbach's alpha coefficient,
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29 196 with an alpha > 0.70 considered to be acceptable.[23] Test-retest reliability was evaluated by
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31 197 calculating the intraclass correlation coefficient (ICC) values from the first and second entries.
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33 198 An ICC value of ≥ 0.70 was considered acceptable for test-retest reliability.[24]
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37 200 **Validity**

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40 201 Discriminant validity was evaluated by comparing the non-DED and DED groups. For
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42 202 factor validity, confirmatory factor analysis was conducted by an equamax rotation to determine
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44 203 whether the subscales in the J-OSDI clustered together in the same manner as in the original
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46 204 OSDI. Factors with an eigenvalue > 0.90 were retained. Concurrent validity was assessed by
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48 205 calculating the correlations (Pearson coefficients) between the J-OSDI total score or subscale
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50 206 scores and the DEQS or other clinical results, including TFBUT, CFS, MBI, and Schirmer test I
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52 207 values.
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55 209 **Patient and public involvement**

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58 210 No patients were involved in the research design and conception of this research study.
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213 **RESULTS**214 **Participant characteristics**

215 Table 1 shows the general characteristics of the study participants. All subjects responded
 216 to the questionnaires, completed the examination, and were eligible for the study. Overall, 209
 217 participants were included. The average age was 58.9 ± 15.3 years, and 83.7% of the
 218 participants were women. Using the diagnostic criteria put forth by the ADES,[8] 152 and 57
 219 patients were classified as DED (72.7%) and non-DED (27.3%), respectively. The mean BCVA
 220 value for both eyes was -0.07 ± 0.02 logMAR. The mean IOP for both eyes was 14.1 ± 2.9
 221 mmHg. Both the J-OSDI total score and the DEQS were significantly higher in the DED group
 222 than in the non-DED group, indicating that DED patients showed a greater rate of subjective
 223 symptoms. Furthermore, both TFBUT and the MBI were significantly lower in the DED group
 224 than in the non-DED group. Neither BCVA, IOP, CFS, nor the Schirmer test I results differed
 225 significantly between DED and non-DED participants.

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227 **Table 1.** Characteristics of study participants.

	non-DED	DED	p value	Total
	n = 57	n = 152		n = 209
Age, year \pm SD	61.4 ± 15.5	57.9 ± 15.2	0.149	58.9 ± 15.3
Gender, female (%)	48 (84.2)	127 (83.6)	1.000	175 (83.7)
BCVA, logMAR \pm SD	-0.1 ± 0.0	-0.1 ± 0.0	0.513	-0.1 ± 0.0
IOP, mmHg \pm SD	14.6 ± 2.9	13.8 ± 2.7	0.062	14.0 ± 2.8
Subjective symptoms, yes (%)	5 (8.8)	152 (100)	***< 0.001	157 (75.1)
J-OSDI, 0–100 \pm SD	19.4 ± 16.0	37.7 ± 22.2	***< 0.001	32.7 ± 29.7

DEQS, 0–100 ± SD	16.0 ± 14.7	32.7 ± 21.6	***< 0.001	28.1 ± 21.3
TFBUT, seconds ± SD	2.5 ± 2.4	1.5 ± 0.8	***< 0.001	1.7 ± 1.5
CFS, 0–9 ± SD	2.8 ± 2.5	3.3 ± 2.6	0.192	3.2 ± 2.6
Schirmer I, mm ± SD	7.2 ± 8.2	5.7 ± 6.2	0.162	6.1 ± 6.8
MBI, seconds ± SD	15.1 ± 8.1	10.5 ± 6.3	***< 0.001	11.7 ± 7.1

DED, dry eye disease; BCVA, best-corrected visual acuity; IOP, intraocular pressure; J-OSDI, Japanese version of ocular surface disease index; DEQS, Dry Eye-Related Quality-of-Life Score; TFBUT, tear film breakup time; CFS, corneal fluorescein staining; MBI, maximum blink interval. p values were determined using the Student's t-test (two-tailed) for continuous variables and the chi-square test for categorical variables. ***p < 0.001.

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235 Reliability

236 We tested the J-OSDI total score and subscale scores for internal consistency and test-retest
 237 reliability, and the results are shown in Table 2. For internal consistency, the Cronbach's alpha
 238 coefficient was 0.884 for the J-OSDI total score and 0.788, 0.669, and 0.902 for the ocular
 239 symptoms, vision-related function, and environmental triggers subscales, respectively.
 240 Test-retest reliability was evaluated in 173 participants, with a median (interquartile range, IQR)
 241 period of 119 (81–182) days between the test and retest. The ICC values were 0.910, 0.649,
 242 0.817, and 0.859 for the J-OSDI total score, ocular symptoms subscale, vision-related function
 243 subscale, and environmental triggers subscale, respectively.

244 **Table 2.** Reliability for each subscale

		Cronbach α	ICC
	Number of items	(n = 209)	(n = 173)
J-OSDI total score	12	0.884	0.910
Ocular symptoms	5	0.788	0.649
Vision-related function	4	0.669	0.817

Environmental triggers 3 0.902 0.859

245 J-OSDI, Japanese version of the ocular surface disease index; ICC; intraclass correlation
246 coefficient.

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248 Discriminant validity

249 Table 3 shows the mean values for the J-OSDI total score, each of the subscale scores, and
250 each of the component scores. The mean J-OSDI total score was significantly higher in the
251 DED group than in the non-DED group (DED, 37.7 ± 22.2 ; non-DED, 19.4 ± 16.0 ; $p < 0.001$).
252 Additionally, all three subscales were significantly higher in the DED group than in the
253 non-DED group (ocular symptoms: DED, 34.6 ± 21.6 ; non-DED, 20.9 ± 17.4 ; $p < 0.001$;
254 vision-related function: DED, 36.5 ± 27.7 ; non-DED, 20.8 ± 22.0 ; $p < 0.001$; environmental
255 triggers: DED, 45.2 ± 29.7 ; non-DED, 15.5 ± 19.8 ; $p < 0.001$). Eleven of the 12 (92%)
256 component scores were significantly higher in the DED group than in the non-DED group, with
257 only question 2 showing a non-significant difference.

258 **Table 3.** J-OSDI score for each question.

Classification, score \pm SD, score	non-DED n = 57	DED n = 152	p value	Total n = 209
J-OSDI total score, 0–100	19.4 ± 16.0	37.7 ± 22.2	*** < 0.001	32.7 ± 22.2
Ocular symptoms, 0–100	20.9 ± 17.4	34.6 ± 21.6	*** < 0.001	30.9 ± 21.4
1. Eyes that are sensitive to light?	0.8 ± 0.9	1.5 ± 1.3	*** < 0.001	1.3 ± 1.3
2. Eyes that feel gritty?	0.8 ± 1.2	1.0 ± 1.0	0.338	1.0 ± 1.1
3. Painful or sore eyes?	0.4 ± 0.7	1.0 ± 1.0	*** < 0.001	0.8 ± 1.0
4. Blurred vision?	1.1 ± 1.0	1.6 ± 1.2	**0.002	1.5 ± 1.2
5. Poor vision?	1.1 ± 1.1	1.8 ± 1.3	*** < 0.001	1.6 ± 1.3
Vision-related function	20.8 ± 22.0	36.5 ± 27.7	*** < 0.001	32.2 ± 27.2

6. Reading?	0.8 ± 1.1	1.6 ± 1.3	***< 0.001	1.4 ± 1.3
7. Driving at night?	0.4 ± 0.6	1.1 ± 1.4	*0.022	0.9 ± 1.3
8. Working with a computer or bank machine (ATM)?	1.1 ± 1.3	1.6 ± 1.4	*0.030	1.5 ± 1.4
9. Watching TV?	0.7 ± 1.0	1.3 ± 1.2	**0.002	1.1 ± 1.1
Environmental triggers	15.5 ± 19.8	45.2 ± 29.7	***< 0.001	37.1 ± 30.4
10. Windy conditions?	0.7 ± 0.9	1.9 ± 1.4	***< 0.001	1.5 ± 1.3
11. Places or areas with low humidity (very dry)?	0.5 ± 0.8	1.6 ± 1.3	***< 0.001	1.3 ± 1.3
12. Areas that are air conditioned?	0.6 ± 0.9	2.0 ± 1.3	***< 0.001	1.6 ± 1.3

259 DED, Dry eye disease; J-OSDI, Japanese version of ocular surface disease index. p values

260 were determined using the Student's t-test. *p < 0.05, **p < 0.01, and ***p < 0.001.

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262 Factor validity

263 Factor validity was assessed by confirmatory factor analysis to determine the subscales. As
 264 shown in Figure 1, correspondent with the three homogeneous content domains that were
 265 identified and constructed, three factors were rotated to an equamax solution. These three
 266 factors accounted for 71.9% of the total variance, and each factor comprised sets of items that
 267 were interpretable and relevant in content. Factor 1, accounting for 53.0% of the total variance
 268 and 23.6% of the common variance, comprised items assessing the frequency of ocular
 269 symptoms (5 items). Factor 2, accounting for 11.1% of the total variance and 22.8% of the
 270 common variance, comprised items assessing the frequency of vision-related function (4 items).
 271 Factor 3, accounting for 7.7% of the total variance and 17.7% of the common variance,
 272 comprised items assessing the frequency of environmental triggers (3 items). All factors were in
 273 accordance with the subscales in the original version. The factor matrix of each J-OSDI

274 component can be viewed in Supplemental Table 1. All subscales and the total instrument
275 underwent formal reliability and validity testing.

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277 **Concurrent validity**

278 Table 4 shows the correlations between the J-OSDI total score, subscale scores, and other
279 clinical items related to DED diagnosis, including DEQS, TFBUT, CFS, Schirmer test I results,
280 and the MBI. The J-OSDI total score showed a significant strong positive correlation with the
281 DEQS ($\gamma = 0.829$). Among the clinical items related to DED diagnosis, there was a modest but
282 significant negative correlation between the J-OSDI total score and MBI ($\gamma = -0.258$). The
283 subscales were each significantly and positively correlated with the DEQS ($\gamma = 0.786, 0.702$ and
284 0.650 , respectively), while ocular symptoms and environmental triggers were significantly and
285 negatively correlated with the MBI ($\gamma = -0.195$ and -0.370 , respectively).

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287 **Table 4.** Correlation between the J-OSDI total score and other clinical assessments.

Clinical Items	OSDI total score		Ocular symptoms		Vision-related function		Environmental triggers	
	γ	p value	γ	p value	γ	p value	γ	p value
DEQS	0.829	***< 0.001	0.786	***< 0.001	0.702	***< 0.001	-0.650	***< 0.001
TFBUT	-0.066	0.349	-0.044	0.532	-0.057	0.416	-0.131	0.063
CFS	0.018	0.791	-0.013	0.852	-0.137	*0.049	0.161	*0.022
Schirmer I	-0.090	0.195	-0.013	0.844	-0.071	0.311	-0.129	0.067
MBI	-0.283	***< 0.001	-0.215	**0.002	-0.135	0.053	-0.407	***< 0.001

288 J-OSDI, Japanese version of the ocular surface disease index; DEQS, Dry Eye-Related

289 Quality-of-Life Score; TFBUT, tear film breakup time; CFS, corneal fluorescein staining;

290 MBI, maximum blink interval. Pearson rank correlation coefficient was used to determine

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4 291 the correlations between the J-OSDI total score and subscale scores and various clinical
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6 292 assessments. * $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$.
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10 294 **J-OSDI severity results and cut-off value for detecting DED**

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13 295 Figure 2A shows the proportion of DED participants in each severity category as
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15 296 determined by the J-OSDI total score. The clinically diagnosed DED patients were divided
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17 297 according to their J-OSDI scores as follows: 22.0% were categorized as normal, 17.2% were
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19 298 categorized as mild DED, 12.9% were categorized as moderate DED, and 47.8% were
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21 299 categorized as severe DED. Figure 2B shows the proportion of patients who were clinically
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23 300 diagnosed with DED in each severity category determined by the J-OSDI total scores. Overall,
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25 301 47.8% of the patients who were classified as normal by their J-OSDI total score were clinically
26
27 302 diagnosed with DED, while 66.7%, 74.0%, and 86.0% of patients classified as mild, moderate,
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29 303 and severe, respectively, were clinically diagnosed with DED. Figure 2C shows the ROC curve
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31 304 of the J-OSDI total score from the non-DED and DED groups, which was used to determine the
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33 305 diagnostic efficacy of the J-OSDI total score. The optimum cut-off value for detecting DED was
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35 306 36.3 points, with an AUC, sensitivity, and specificity of 0.744, 51.3%, and 87.7%, respectively.
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37 307 Supplemental Table 1 shows the details of the J-OSDI total score sensitivity and specificity
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39 308 analysis.
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45 310 **DISCUSSION**

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47 311 This study developed, and assessed the reliability and validity, of the J-OSDI, which is the
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49 312 Japanese version of OSDI, and determined a cut-off value for detecting DED using the ADES
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51 313 diagnostic criteria of 2016. Our results validate the use of the J-OSDI in Japan and make it
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53 314 possible to compare epidemiological results between Japan and other countries.

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55 315 In this study, the J-OSDI total score showed both high internal consistency and test-retest
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57 316 reliability (Table 2). The factor analysis confirmed three subscales within the J-OSDI, ocular
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4 317 symptoms, vision-related function, and environmental triggers, in accordance with the subscales
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6 318 in the original English version (Figure 1).[13] The environmental triggers subscale showed good
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8 319 internal consistency and reliability, whereas the other two subscales, ocular symptoms and
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10 320 vision-related function, showed lower internal consistency and reliability compared to
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12 321 environmental triggers. Vision-related function only showed modest internal consistency.
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14 322 Internal consistency denotes whether all items of an instrument measure the same
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16 323 characteristic.[25] In the sensitivity analysis, deleting question item 7 (i.e., night driving)
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18 324 provided the highest ICC value of 0.74 (Supplemental Table 2). This study was conducted in
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20 325 central Tokyo, where the traffic network was developed, and numerous elderly people were
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22 326 included. Therefore, question item 7 on night driving may have affected the internal consistency.
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24 327 This result indicates that the question items included in OSDI need to be adjusted to the
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26 328 changing demands. The ocular symptoms of DED patients have typically varied because of the
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28 329 known fluctuations in the subjective symptoms of DED,[26, 27] thus violating this assumption
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30 330 of reliability.

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34 331 The discriminant validity of the J-OSDI was verified from the finding that the J-OSDI total
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36 332 score and subscale scores were significantly higher in the DED group than in the non-DED
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38 333 group (Table 3). Further, the percentage of participants who were clinically diagnosed with
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40 334 DED increased proportionally in each severity category, indicating that the J-OSDI total score
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42 335 can discriminate DED (Figure 2B). Our study also determined that the optimal J-OSDI total
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44 336 score cut-off value for detecting DED according to the ADES criteria was 36.3. One previous
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46 337 study reported an OSDI total score cut-off value of 15.[13] However, the difference between
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48 338 this cut-off value and that of the current study is probably the result of differences in the
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50 339 methods used to clinically diagnose the severity of DED, as the previous study used lissamine
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52 340 green staining, Schirmer test I, and patient perception of ocular symptoms. In contrast, the
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54 341 current study used TFBUT as an essential part of the diagnostic criteria.[7, 8] Supplemental
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56 342 Table 3 shows the sensitivity and specificity of our reported optimal cut-off value and the
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58 343 sensitivity and specificity for the different severity categories: normal (0–12), mild (13–22),
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4 344 moderate (23–32), and severe (33–100).[13] Our results suggest that it is necessary to
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6 345 re-evaluate the OSDI total score cut-off values for diagnosis and the severity categories to
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8 346 reflect the changes made to the diagnostic criteria for DED.[7, 8, 28-33]
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10 347 Table 4 shows the correlations between the J-OSDI total score and other clinical tests,
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12 348 including DEQS, TFBUT, CFS, MBI, and Schirmer test I. The J-OSDI total score showed a
13
14 349 strong positive correlation with the DEQS. Because the DEQS has been validated in Japan,[12]
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16 350 this result supports the use of the J-OSDI as a valid method of quantifying subjective symptoms.
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18 351 In contrast, the respective correlations between the J-OSDI total score and TFBUT, CFS, and
19
20 352 Schirmer I were relatively low. This is consistent with previous studies that reported low
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22 353 correlations and high divergence between subjective symptoms assessed by questionnaires and
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24 354 clinical tools,[2, 24, 30] underscoring the importance of combining knowledge about subjective
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26 355 symptoms and clinical tools in order to effectively evaluate and monitor DED. Our group[20]
27
28 356 has proposed the MBI as a simple self-check screening test for DED because it is highly
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30 357 correlated with subjective symptoms compared with other dry eye items (Table 4). Because of
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32 358 the divergence between the subjective and clinical symptoms of DED,[2] it is necessary to
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34 359 perform multilateral evaluations using not only the OSDI total scores but also the subscales and
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36 360 each component. In the present study, we assessed the respective relationship between each
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38 361 subscale and various clinical tools for DED examination and found that the ocular symptoms
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40 362 and environmental trigger subscales were negatively correlated with MBI. We recently reported
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42 363 that the MBI is also significantly associated with TFBUT and CFS.[20] Our previous results and
43
44 364 those of this study suggest that the MBI reflects both TFBUT and CFS results, possibly
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46 365 explaining its negative correlation with the ocular symptoms and environmental triggers
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48 366 subscale scores of the J-OSDI.
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52 367 This study has several limitations. First, it was conducted at a single university hospital in
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54 368 Japan, possibly introducing selection bias into our sample. Second, under the simplified ADES
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56 369 diagnostic criteria, those with low TFBUTs can still be classified as non-DED due to lack of
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58 370 subjective symptoms; thus, our non-DED group showed a low TFBUT. Third, the test-retest
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4 371 method that we used to confirm reliability introduced recall bias due to the required length of
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6 372 the test-retest period between 2 days to 2 weeks.[34]. Next, we did not account for differences
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8 373 in variables such as socioeconomic status or education level, possibly affecting the responses.
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10 374 Finally, this study was designed to investigate the J-OSDI as a primary evaluation and
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12 375 monitoring method for DED. Thus, rose bengal stain scores, tear osmolality, meibomian gland
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14 376 dysfunction assessments, and corneal sensations were not applied in this study. Despite these
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16 377 limitations, we verified the reliability and validity of the J-OSDI for DED assessment and
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18 378 monitoring in Japan.

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21 379 In summary, we developed and validated the J-OSDI by assessing its reliability and
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23 380 validity. We report that a J-OSDI score of 36.3 is the optimal cut-off value for suspecting DED
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25 381 under the 2016 ADES criteria. We believe that the J-OSDI will be useful for primary
26
27 382 assessment and monitoring of DED in routine clinical practice and in remote diagnosis.

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33 384 **Acknowledgments:** The authors thank the nurses and orthoptists of the Department of
34
35 385 Ophthalmology at the Juntendo University Hospital for collecting the data for DED diagnosis.

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38 386 **Author Contributions:**

39
40 387 A.MI.: Performance of the research, data collection, data analysis, and writing of the paper; T.I.:
41
42 388 Performance of the research, research design, data analysis, and writing of the paper; S.N.:
43
44 389 Research design, data analysis; M.N.: Data analysis; M.I.: Research design, data analysis; K.F.:
45
46 390 Data collection, data analysis; Y.O.: Data collection, data analysis; N.I.: Data collection, data
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48 391 analysis; A. E.: Data collection, data analysis; H.H.: Data collection, data analysis; H.K.:
49
50 392 Performance of the research; A.M.: Research design, writing of the paper; H.K.: Research
51
52 393 design, writing of the paper.

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465 **Figure 1. Three subscales of the J-OSDI as determined by factor analysis.** The
466 existence of 3 clusters that were used as subscales are shown. These were in accordance
467 with the subscales that are used in the original version of the OSDI: vision-related function
468 (components 1-5), ocular symptoms (components 6-9), and environmental triggers
469 (components 10-12).

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4 471 **Figure 2. Clinical utility of the J-OSDI for evaluating dry eye disease (DED).** (a) The
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6 472 proportion of patients in each DED severity category as determined by the J-OSDI total
7
8 473 score. (b) The proportion of patients who were clinically diagnosed with DED by category
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10 474 of severity according to the J-OSDI total score. (c) The receiver operator characteristic
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12 475 (ROC) curve for the diagnosis of DED determined by the Asia Dry Eye Society 2016
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14 476 criteria using the J-OSDI. The area under the ROC curve (AUC) is 0.744.
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478 **Supplementary Information**

479 **Supplemental Figure 1: The Japanese version of Ocular Disease Index (J-OSDI).** The J-OSDI questionnaire
480 contains 12 questions divided into three subscales.

481 **Supplemental Table 1: Factor matrix of each J-OSDI question.** Results of factor analysis of each J-OSDI
482 question. All three subscales were in accordance with the subscales in the original version.

483 **Supplemental Table 2: Sensitivity analysis of the internal consistency of the vision-related function score.** The
484 total Cronbach's alpha was calculated by removing one item from a certain domain of the subscale of vision-related
485 function.

486 **Supplemental Table 3: J-OSDI total score sensitivity and specificity analysis results.** Full results of the
487 sensitivity and specificity analysis. Our reported cut-off value for suspecting dry eye disease was 36.3.

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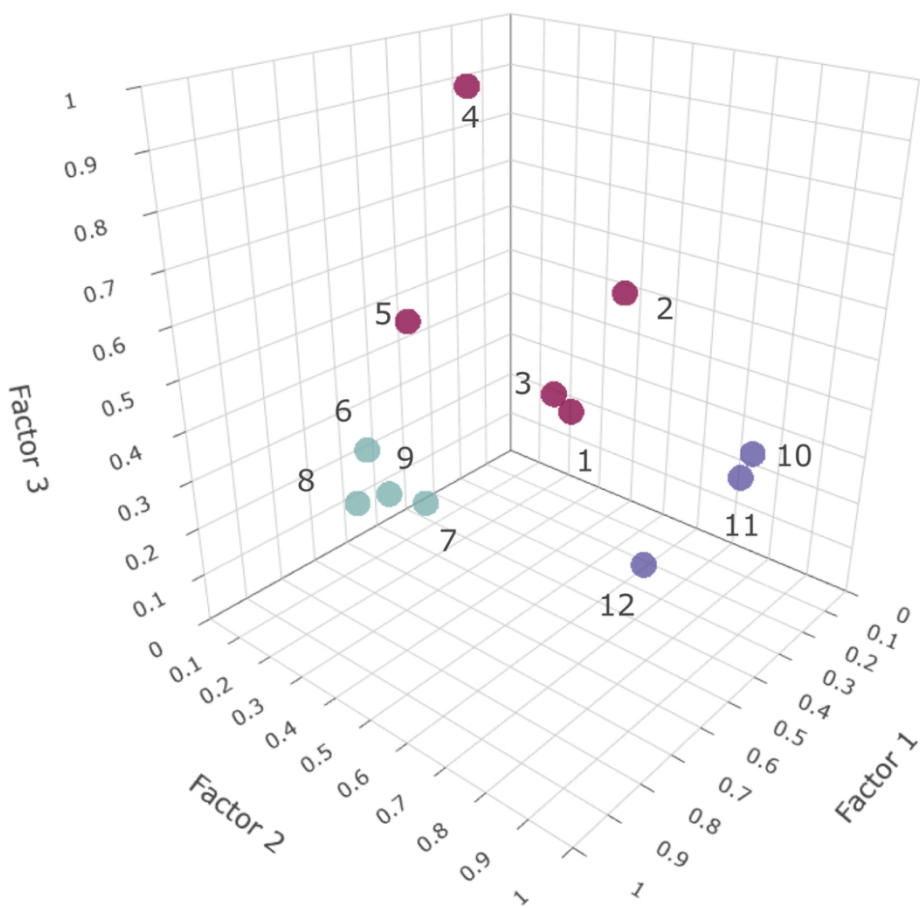


Figure 1

99x97mm (300 x 300 DPI)

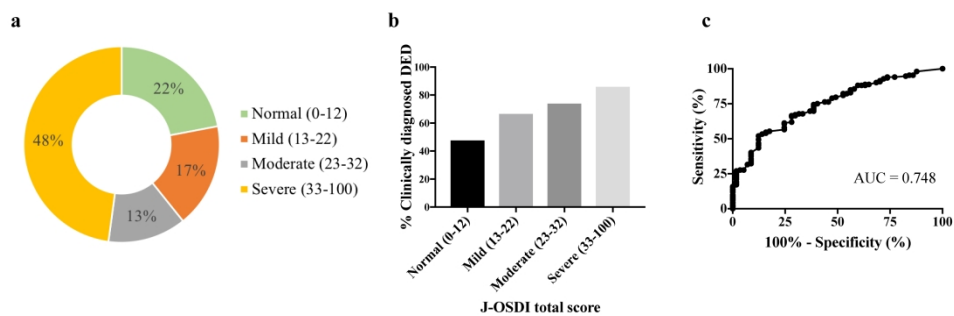


Figure 2

ドライアイ質問紙票 (J-OSDI)

氏名： _____ ID： _____

ご記入日 _____ 年 _____ 月 _____ 日

下記の設問のあてはまる数字に○をつけてください。

この一週間で下記の症状をどのくらい感じましたか？	いつも	ほとんど	半々	ときどき	全くない
1. まぶしさ	4	3	2	1	0
2. 目がゴロゴロする	4	3	2	1	0
3. 目の痛み	4	3	2	1	0
4. 目のかすみ	4	3	2	1	0
5. 見づらさ	4	3	2	1	0

この一週間で目の症状が原因で、下記の行動はどのくらい制限されましたか？	いつも	ほとんど	半々	ときどき	全くない	該当せず
6. 読書	4	3	2	1	0	—
7. 夜間の運転	4	3	2	1	0	—
8. パソコンや銀行ATMの使用	4	3	2	1	0	—
9. テレビ鑑賞	4	3	2	1	0	—

この一週間で次の環境において、目の不快感を感じましたか？	いつも	ほとんど	半々	ときどき	全くない	該当せず
10. 風が強いとき	4	3	2	1	0	—
11. 湿度が低い(乾燥している)場所	4	3	2	1	0	—
12. エアコンの効いている場所	4	3	2	1	0	—

Supplemental Information

From: Reliability and Validity of the Japanese version of the Ocular Surface Disease Index for Dry Eye Disease

Akie Midorikawa-Inomata RN, MPH, Takenori Inomata MD, PhD, MBA, Soko Nojiri, MPH, Masahiro Nakamura MD, PhD, Masao Iwagami MD, MPH, MSc, PhD, Keiichi Fujimoto MD, Yuichi Okumura MD, Nanami Iwata, Atsuko Eguchi, Hitomi Hasegawa MD, Hikaru Kinouchi, Akira Murakami MD, PhD, and Hiroyuki Kobayashi MD, PhD.

Table S1: Factor matrix of each J-OSDI question

Components	Factor		
	1	2	3
1	0.352	0.474	0.361
2	0.055	0.393	0.504
3	0.256	0.349	0.331
4	0.335	0.167	0.927
5	0.632	0.269	0.573
6	0.706	0.208	0.323
7	0.576	0.246	0.171
8	0.710	0.172	0.198
9	0.719	0.283	0.260
10	0.156	0.815	0.307
11	0.239	0.837	0.295
12	0.441	0.742	0.159

J-OSDI, Japanese version of the Ocular Surface Disease Index.

Extraction Method: Maximum likelihood method; Rotation Method: Equamax with Kaiser normalization

Table S2: Sensitivity analysis of the internal consistency of the vision related function score

	Cronbach α
Vision-related function	0.669
excluded 6. Reading?	0.529
excluded 7. Driving at night?	0.746
excluded 8. Working with a computer or bank machine (ATM)?	0.508
excluded 9. Watching TV?	0.497

Table S3: J-OSDI total score sensitivity and specificity analysis results

J-OSDI total score	Sensitivity (%)	Specificity (%)
> 1.05	98.03	12.28
> 2.2	95.39	14.04
> 2.4	95.39	15.79
> 3.35	94.74	17.54
> 4.9	94.08	22.81
> 5.95	94.08	26.32
> 6.55	92.76	28.07
> 6.95	91.45	29.82
> 7.3	90.79	29.82
> 7.9	90.13	31.58
> 9.15	88.82	35.09
> 10.2	88.82	36.84
> 10.9	88.16	38.6
> 11.95	88.16	40.35
> 13.05	84.87	42.11
> 14.1	84.21	43.86
> 14.8	82.24	43.86
> 15.3	81.58	45.61
> 15.75	81.58	47.37
> 16.3	80.26	47.37
> 17.45	78.95	50.88
> 18.5	78.29	52.63
> 19.1	75.66	54.39
> 19.7	75.66	56.14

> 20.25	74.34	59.65
> 20.65	73.68	61.4
> 21.35	72.37	61.4
> 22.05	71.05	61.4
> 22.35	70.39	61.4
> 22.6	69.08	61.4
> 23.85	69.08	63.16
> 26.15	67.11	66.67
> 27.4	67.11	68.42
> 27.8	66.45	70.18
> 28.65	65.79	70.18
> 29.35	65.13	71.93
> 29.75	61.18	71.93
> 30.3	60.53	75.44
> 30.95	59.87	75.44
> 31.55	57.24	75.44
> 32.55	55.92	75.44
> 33.7	54.61	82.46
> 34.55	53.95	84.21
> 35.2	53.29	84.21
> 35.75	52.63	85.96
> 36.25	51.32	87.72
> 36.95	48.68	87.72
> 38.55	46.05	87.72
> 39.8	44.74	87.72
> 40.85	42.76	87.72
> 42.1	39.47	91.23

> 42.85	38.82	91.23
> 43.5	38.16	91.23
> 44.4	36.84	91.23
> 45.4	34.87	91.23
> 46.5	33.55	91.23
> 47.35	32.89	91.23
> 47.6	32.24	91.23
> 47.8	31.58	91.23
> 48.95	30.92	92.98
> 51.05	27.63	94.74
> 52.2	26.97	98.25
> 52.4	25.66	98.25
> 53.35	25	98.25
> 54.35	23.03	98.25
> 55.4	21.71	98.25
> 56.55	21.05	98.25
> 57.15	20.39	98.25
> 57.9	18.42	98.25
> 58.7	17.11	98.25
> 59.75	16.45	98.25
> 61.45	15.79	100
> 63.05	15.13	100
> 63.75	13.82	100
> 64.25	13.16	100
> 66.05	11.84	100
> 67.7	9.868	100
> 68.35	9.211	100

> 69.65	8.553	100
> 70.65	7.895	100
> 71.85	7.237	100
> 75	6.579	100
> 77.2	5.921	100
> 78.25	4.605	100
> 82.1	3.947	100
> 85.7	2.632	100
> 87.5	1.974	100
> 89.3	1.316	100

J-OSDI, Japanese version of the Ocular Surface Disease Index

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1,2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	17
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	8
	(c) Explain how missing data were addressed	8	
	(d) If applicable, describe analytical methods taking account of sampling strategy	N/A	
	(e) Describe any sensitivity analyses	N/A	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9, 10
		(b) Indicate number of participants with missing data for each variable of interest	9
Outcome data	15*	Report numbers of outcome events or summary measures	9-11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A

		(b) Report category boundaries when continuous variables were categorized	5
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	16
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.