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(Article begins on next page)

33 **Abstract**

34 **Introduction:** The early and rapid identification of psychosomatic symptoms is crucial to
35 prevent harmful outcomes in patients with human papillomavirus (HPV) infection in busy
36 comprehensive clinics. This study aimed to explore the prevalence and rapid screening
37 method of the Diagnostic Criteria for Psychosomatic Research-Revised (DCPR) syndromes in
38 patients with HPV infection.

39 **Methods:** A total of 504 participants underwent a clinical assessment, that included DCPR,
40 Diagnostic and Statistical Manual of Mental (DSM)-5, the Social Support Rating scale (SSRS),
41 the Simplified Coping Style Questionnaire (SCSQ), fear of disease, sociodemographic and
42 clinical characteristics. The prevalence of DCPR syndromes and DSM-5 diagnoses were
43 compared between the HPV-positive and negative patients using chi-square tests. We
44 explored the rapid screen indicator through multiple logistic regression analyses of the
45 participants' psychosocial factors, sociodemographic and clinical characteristics.

46 **Results:** The incidence of DCPR syndromes in HPV-positive patients (56.6%) was significantly
47 greater than that in HPV-negative patients (17.3%) and DSM-5 diagnoses (8.5%) in the HPV
48 positive group. **Health anxiety, irritable mood, type A behavior and demoralization were the**
49 **most common psychosomatic syndromes in HPV-positive patients.** As the degree of fear
50 increased from 0 to 5 to 10, the risk of DCPR increased from 1.27 (95% CI: 0.21-7.63) to 3.24
51 (score range: 1-5, 95% CI: 1.01-10.39) to 9.91 (score range: 6-10, 95% CI: 3.21-30.62) in
52 the HPV-positive group.

53 **Conclusion:** The degree of fear, as an independent risk factor, could be used to quickly screen
54 outpatients with a high risk of DCPR syndrome among women with HPV infection.

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66 **Introduction**

67 Human Papillomavirus (HPV) is a sexually transmitted virus that is very common and is
68 responsible for causing more than 99% of cervical cancers [1]. In recent years, studies using
69 self-rated scales have shown that there are psychosocial factors that affect HPV-positive
70 patients [2,3], and only one study used a structured clinical interview to assess mental
71 disorders (e.g., DSM) [4]. However, these studies did not assess psychosomatic symptoms or
72 provide specific guidance for clinical interventions.

73 The Diagnostic and Statistical Manual of Mental Disorders (DSM) is considered as the
74 gold standard in psychiatry [5,6]. However, it may not always be effective at detecting
75 psychological problems that are less severe, known as “subclinical” problems [7]. A new
76 Diagnostic Criteria for Psychosomatic Research (DCPR) assessment tool was developed in
77 1995 [8] to address this issue. 2017, a revised DCPR version was released, including a
78 semi-structured interview [9]. Reports have shown that the DCPR has clinical utility in (1)
79 subtyping medical patients, (2) identifying undetected syndromes, (3) evaluating the burden
80 of somatic syndromes, and (4) predicting treatment outcomes and identifying risk factors
81 [10]. The DCPR has been used to supplement DSM diagnosis in oncology [11], dermatology,
82 endocrinology, cardiology [12–15], and gastroenterology studies [16,17]. Its reliability and
83 advantages relative to the DSM were previously verified [18], and its clinimetric properties
84 were confirmed [19].

85 It is essential to assess the psychological health of patients who are HPV-positive.
86 However, routine assessment can be time-consuming (i.e., more than 30 minutes) and
87 require a specialized psychological clinic referral. Structured interviews require specialized
88 clinical experience and skills [20]. Therefore, doctors who do not have specialized
89 psychological training can use a more rapid screening method. In this study, we investigated
90 the prevalence and psychosocial factors that contribute to DCPR syndromes in patients with
91 HPV infection. We used multivariate analysis to develop a rapid screening method to help
92 doctors quickly identify patients at high risk of DCPR syndromes. This is the first study to
93 examine DCPR syndromes in obstetric and gynecological illnesses worldwide.

94 **Materials and Methods**

95 *Study design and Participants*

96 This cross-sectional study investigated risk factors **associated with DCPR syndromes in**
97 **HPV infection patients**. The study enrolled patients who visited the HPV Special Disease Clinic
98 of the Cervical Diseases Department of Changzhou Maternal and Child Health Care Hospital
99 consecutively from January 2022 to December 2022 and met the following criteria: (1) aged

100 20–66 years; (2) positivity for one or more HPV types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53,
101 56, 58, 59, 66, 68, or 82; (3) normal or abnormal cytological type; (4) Chinese maternal
102 history; and (5) primary school education or above. Patients who had cervical cancer or any
103 other cancer, hysterectomy, acute or fatal cardiovascular, kidney, liver, nervous system
104 disease, or immune system disease were excluded. **Participants in the control group were**
105 **without HPV infection, the other inclusion criteria and exclusion criteria were the same as**
106 **the HPV positive group.**

107 *Procedures and outcomes*

108 The primary measure to evaluate psychosomatic syndromes was through
109 semi-structured interviews using the DCPR tool [21]. In addition to this, other measures like
110 DSM-5 diagnoses [22], Social Support Rating Scale (SSRS) [23], Simplified Coping Style
111 Questionnaire (SCSQ) [24], and the level of fear was also evaluated (instruments available
112 within the online supplement). The sociodemographic and clinical data were collected by a
113 trained psychologist independently.

114 *Statistical analyses*

115 The statistical analyses were conducted using Empower Stats software version 2.2 (X&Y
116 Solutions, Inc., USA) and R (version 3.4.2; <http://www.R-project.org>). We compared the
117 sociodemographic and clinical characteristics, including age, educational level, income,
118 occupation status, marital status, infection duration, DCPR, DSM-5, degree of fear, medical
119 history, coping styles, SSRS, and incidence knowledge between HPV-positive and
120 HPV-negative groups using independent t-tests or Kruskal–Wallis tests. Similarly, we used the
121 same method to compare DCPR = 0 with DCPR \geq 1. **Chi-square test was used to analyze the**
122 **prevalence of DCPR syndromes and DSM-5 diagnoses. The age, education, income, SSRS,**
123 **degree of fear, HPV positivity, active coping, passive coping and infection duration were used**
124 **to evaluate the associations of psychosocial factors with DCPR syndromes (DCPR \geq 1) using**
125 **univariate and multivariate logistic regression analyses.** We also assessed the potential effect
126 of advanced fear on the relationship between DCPR risk and HPV positivity by interaction
127 analysis and obtained odds ratios (ORs) and 95% confidence intervals (CIs). We considered a
128 two-tailed $P < 0.05$ to indicate statistical significance.

129 **Results**

130 A total of 504 (249 HPV-positive and 255 negative) patients were enrolled in the study,
131 **as detailed in online supplementary Fig. 1.** The demographic and clinical characteristics of
132 the patients were analyzed to determine the risk factors associated with **DCPR syndromes in**
133 **HPV infection patients.**

134 Age, infection duration, degree of fear, DSM-5 diagnoses, and DCPR syndromes showed
135 significant differences between the HPV-positive and HPV-negative groups (all P values <
136 0.05), as detailed in online supplementary Table 1. Among the participants, 141 patients
137 (56.6%) reported at least one diagnosed DCPR syndrome, with the most common syndromes
138 being health anxiety (30.9%, n = 77), irritable mood (26.5%, n = 66), type A behavior (22.5%,
139 n = 56), and demoralization (16.7%, n = 33). Conversely, 44 individuals who tested negative
140 for HPV reported at least one DCPR syndrome, constituting 17.3% of the study population. In
141 contrast, 21 individuals who tested positive for HPV were diagnosed with at least one mental
142 disorder by DSM-5 criteria, accounting for 8.4% of the participants. **The incidence of DCPR**
143 **syndromes was significantly higher in HPV-positive patients than the incidence of DSM-5**
144 **diagnoses ($\chi^2 = 131.75, P < 0.001$).** For further details, please refer to the (supplemental)
145 Table 2.

146 The study revealed significant differences between participants with at least one DCPR
147 syndrome and those without regarding age, degree of fear, coping styles, educational levels,
148 income levels, and infection duration (all P values < 0.05–0.001), as indicated in Table 1.
149 Further analysis demonstrated that age (33–39 years: OR: 2.37, 95% CI: 1.15–4.90), SSRS
150 score (OR: 0.95, 95% CI: 0.92–0.99), degree of fear (6–10: 4.43, 95% CI: 1.86–10.53), and HPV
151 positivity (OR: 3.51, 95% CI: 2.04–6.04) were independent influencing factors of DCPR
152 syndrome (all P values < 0.05), as outlined in Table 2.

153 We found a significant relationship between fear and HPV positivity when it comes to
154 the risk of presenting at least one DCPR syndrome (see online suppl. Table 3). Our analysis
155 showed that as the degree of fear increased from zero to 1–5 to 6–10, the risk of DCPR
156 syndrome also increased from (95% CI: 0.59 to 14.54, P=0.1877) to 6.48 (95% CI: 2.35-17.84,
157 P= 0.003) to 18.94 (95% CI:7.05-50.91, P<0.0001) respectively, in the crude model. However,
158 after considering various factors such as age, education level, duration, income, coping style,
159 and SSRS score, the risk of DCPR syndrome still increased in the adjusted model from 1.27
160 (95% CI=0.21 to 7.63, P=0.7918) to 3.24 (score range=1-5, 95% CI=1.01 to 10.39, P=0.0477)
161 to 9.91 (score range=6-10, 95% CI=3.21 to 30.62, P<0.0001) respectively.

162 **Discussion**

163 Patients with HPV, the most common sexually transmitted disease, are increasingly
164 aware of the link between HPV infection and cervical cancer. In addition to worrying about
165 their health, patients also fear disclosing their test results to their partners, family, or friends
166 due to the stigma associated with the infection. This has led to an increase in anxiety, distress,
167 and shame among patients [27, 28, 29]. In this study, it was found that both depressive

168 disorder and anxiety disorder were more common in HPV-positive patients compared to
169 negative ones. However, the differences were not statistically significant. According to the
170 DSM-5, only 8.5% of the patients displayed symptoms that indicated a psychiatric diagnosis.
171 However, a much higher percentage of patients (56.6%) met the criteria for DCPR syndrome.
172 This suggests that the DCPR can identify subthreshold or subsyndromal disorders related to
173 HPV that may have gone undiagnosed by DSM-5 alone. This finding is consistent with
174 previous research in other medical settings [30,31].

175 The prevalence of DCPR syndromes has been studied in patients with various illnesses,
176 revealing different syndromes as the most common. In congestive heart failure patients, the
177 three most common syndromes were irritable mood (12.9%), illness denial (22.9%), and
178 demoralization (15.7%) [31]. In primary care patients, the main DCPR syndromes were
179 maladaptive illness behavior (26.5%), allostatic overload (15.5%), and demoralization (15%)
180 [30]. Patients who underwent coronary artery bypass grafting surgery had type A behavior
181 (14.7%), irritable mood (14.7%), and health anxiety (11.8%) [14]. For migraine, the most
182 frequent syndromes were allostatic overload (29%), type A behavior (10.5%), and persistent
183 somatization (8%) [18]. In HPV-positive patients, the most common DCPR syndromes were
184 health anxiety (30.9%), irritable mood (26.5%), type A behavior (22.5%), and demoralization
185 (16.7%) [33]. These three, along with demoralization, were among the four major
186 psychosocial aspects of a medical disorder in the biopsychosocial model based on clinimetric
187 methods of classification [32].

188 Health anxiety is a condition where an individual experiences excessive and persistent
189 worrying about their health, often accompanied by intense bodily preoccupations and an
190 inclination to amplify physical sensations [20]. Fortunately, several effective treatments have
191 been identified for this condition, including Cognitive-behavioral therapy (CBT) [33], imagery
192 techniques [34], mindfulness training, and acceptance and commitment therapy. These
193 treatments can be administered individually or in group settings, both in-person or virtually
194 over the Internet, and be efficacious in the short and long term [35].

195 Demoralization is a term used to describe the feelings of helplessness, despair, and
196 subjective incompetence that people experience when they believe they are not meeting
197 their or others' expectations while coping with difficulties [36, 37]. Identifying demoralization,
198 which can also manifest as hopelessness in severe cases, can help identify patients who are
199 more susceptible to nonspecific elements of treatment [38]. CBT combined with WBT,
200 bedside psychotherapy [39], and existential inquiry [40] can be effective in addressing
201 demoralization based on preliminary findings [41].

202 In this research, it was found that HPV-positive women with a fear level ranging from 6
203 to 10 had a risk of DCPR that was up to 9.91 times greater than that of HPV-negative women,
204 even when other factors were taken into account [42]. According to the hypnosis theory of
205 Milton Erickson, each person responds to questions based on their inner needs. The degree
206 of fear reported by the participants was influenced by their personality traits, coping styles,
207 and cognitive levels. This, in turn, reflected their attitudes and behaviors toward the disease.
208 As the literature suggests, listening to the patient’s beliefs about the illness and its treatment
209 can help identify inadequate expectations and convictions that may lead to health-damaging
210 behaviors [20]. Therefore, self-reported fear levels could be used as a quick method to screen
211 for DCPR syndrome in outpatients with HPV infection. Further research is needed to
212 determine whether this approach could be applied to other diseases

213 The current study has a few limitations that should be considered. First, it was a
214 single-center cross-sectional study that may not accurately represent the general population.
215 Thus, the conclusions drawn from this study need to be validated before being extended.
216 Second, the focus of this study was on the Chinese population, and since HPV-positive rates
217 vary according to race, further well-designed multicountry studies are required. Lastly, this
218 study only examined one illness; future studies should determine if these findings apply to
219 other diseases.

220 **Conclusion**

221 The DCPR tool clinicians administer requires proper training and familiarity with the
222 literature on DCPR. It also requires prior knowledge of a patient’s medical and psychiatric
223 diagnosis, disease course, and treatment history. A joint psychiatric assessment is
224 recommended. This study aimed to fill the gap in knowledge on the use of DCPR syndrome in
225 obstetrics and gynecology illnesses. It also explored a rapid screening method for doctors
226 with no special psychological training rather than simplifying assessment scales or training
227 more psychiatrists, as done in previous research. The findings showed that over 85% of
228 patients with a fear score of 6–10 had at least one DCPR syndrome, and the detection
229 efficiency improved significantly when applying the results of this experiment to the clinic.

230 We need to investigate further whether the correlation between the level of fear and
231 the incidence of DCPR syndrome applies to other diseases. Furthermore, this method can aid
232 clinicians in rapidly identifying outpatients at a greater risk of developing DCPR syndrome.
233 This would promote efficient and systematic DCPR assessment in various clinical
234 environments.

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237 nonauthor team members Wang Li, Hu Huiwen and Zhu Haiyan, for collection and
238 preparation of the data presented herein.

239 **Statement of Ethics**

240 The authors assert that all of the procedures contributing to this work comply with the
241 ethical standards of the relevant national and institutional committees on human
242 experimentation and with the Helsinki Declaration of 1975 as revised in 2008. All of the
243 participants provided written informed consent, and all procedures for the study were
244 approved by the Ethics Committee of Nanjing Medical University (Approval number
245 2022(491)).

246 **Statement of Ethics**

247 The study was conducted ethically in accordance with the World Medical
248 Association Declaration of Helsinki. All participants gave their written informed
249 consent to participate in the study. The Ethics Committee of Nanjing Medical University
250 approved the study with Approval Number 2022-491.

251 **Conflict of Interest Statement**

252 The authors have no conflicts of interest to declare.

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257 **Author Contributions**

258 X. Cui, L. Ding, and Y. Xu designed the study. X. Cui, L. Ding and Q. Zhang extracted the
259 data, conducted, and wrote the first draft of the manuscript. X. Yuan cross-checked the
260 statistical analyses. C. Rafanelli and S. Gostoli critically reviewed and interpreted the
261 manuscript. Z. Liu and J. Cao are the principal investigators, providing resources and
262 supervising all steps of this project. All authors contributed to the interpretation, review, and
263 editing the manuscript, and approved the submission of the final version.

264 **Data Availability Statement**

265 The data cannot be shared due to patient confidentiality and privacy concerns. Further
266 enquiries can be directed to the corresponding author.

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- 379

380 Table1 Psychosocial factors and health-related information of DCPR syndromes

Characteristics	DCPR		P
	0 (n=319)	≥ 1 (n=185)	
Age (year)	33.8±8.5	37.4±9.2	< 0.001
20-27	72 (22.6)	20 (10.8)	< 0.001
28-32	112 (35.2)	45 (24.3)	
33-39	68 (21.4)	52 (28.1)	
40-66	67 (21)	68 (36.8)	
Education			
High school or below	112 (35.1)	98 (53)	< 0.001
College or above	207 (64.9)	87 (47)	
Income (RMB)			
<5,000	43 (13.5)	42 (22.7)	0.018
5000-10,000	133 (41.7)	76 (41.1)	
>10,000	143 (44.8)	67 (36.2)	
Occupation			
Unemployed	80 (25.1)	44 (23.8)	0.745
Employed	239 (74.9)	141 (76.2)	
Marital Status			
Unmarried	9 (2.8)	12 (6.5)	0.112
Married	301 (94.4)	166 (89.7)	
Divorce	9 (2.8)	7 (3.8)	
Degree of fear			
0	53 (16.6)	8 (4.3)	< 0.001
1-5	176 (55.2)	61 (33)	
6-10	90 (28.2)	116 (62.7)	
Medical history			
0	258 (80.9)	148 (80)	0.810
1	61 (19.1)	37 (20)	
High incidence			
Known	199 (62.4)	99 (53.5)	0.051
Unknown	120 (37.6)	86 (46.5)	
Duration(month)	0 (0-0.6)	1 (0.1-12)	< 0.001
HPV			
Positive	108 (33.9)	141 (76.2)	< 0.001
Negative	211(66.1)	44 (23.8)	
Active coping	37.4±6.6	33.8±7.5	< 0.001
Passive coping	17.2±3.7	17.4±4.1	< 0.001
SSRS	43.0±6.5	38.8±7.1	< 0.001

381 DCPR, Diagnostic Criteria for Psychosomatic Research-revised; SSRS, Social Support Rating
382 Scale; DSM-5, Diagnostic and Statistical Manual of Mental Disorder, fifth edition; HPV,
383 human papillomavirus. High incidence, people whether know the lifetime risk of HPV
384 infection is nearly 80%. Duration, the time that people have been diagnosed with
385 HPV-positive.

386

387 Table 2 Regression analysis of influencing factors of DCPR syndromes

Characteristics	DCPR			
	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Age (year)				
20-27	1		1	
28-32	1.45(0.79, 2.65)	0.231	1.70 (0.85, 3.42)	0.135
33-39	2.75 (1.49, 5.08)	0.001	2.37 (1.15, 4.90)	0.020
40-66	3.71 (2.04, 6.76)	< 0.001	1.69 (0.80, 3.56)	0.170
Education				
High school or below	1		1	
College or above	0.48 (0.33, 0.69)	< 0.001	1.04 (0.62, 1.74)	0.895
Income (RMB)				
<5,000	1		1	
5000-10,000	0.59 (0.35, 0.97)	0.039	1.31 (0.71, 2.39)	0.385
>10,000	0.48 (0.29, 0.80)	0.005	1.32 (0.69, 2.54)	0.399
SSRS	0.91 (0.89, 0.94)	< 0.001	0.95 (0.92, 0.99)	0.010
Degree of fear				
0	1		1	
1-5	2.30 (1.03, 5.10)	0.041	1.74 (0.74, 4.12)	0.206
6-10	8.54 (3.86, 18.87)	< 0.0001	4.43 (1.86, 10.53)	0.001
HPV				
Negative	1		1	
Positive	6.26 (4.15, 9.44)	< 0.0001	3.51 (2.04, 6.04)	< 0.0001
Active Coping	0.93 (0.91, 0.96)	< 0.0001	1.01 (0.95, 1.06)	0.846
Passive Coping	1.92 (1.89, 1.95)	< 0.0001	1.95 (0.90, 1.01)	0.132
Duration	1.02(1.01,1.04)	0.000	1.00(0.99, 1.02)	0.757

388 DCPR, Diagnostic Criteria for Psychosomatic Research-revised; SSRS, Social Support Rating

389 Scale; DSM-5, Diagnostic and Statistical Manual of Mental Disorder, fifth edition; HPV,

390 human papillomavirus

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