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The Pregnancy-Unique Quantification of Emesis: Its Clinical Correlates and Severity Ranking Among Japanese First Trimester Pregnant Women

Running head: PUQE severity ranking

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Abstract

Background: Nausea and vomiting (emesis) is one of the commonest symptoms during pregnancy. The Pregnancy Unique Quantification of Emesis (PUQE: Koren et al., 2002) is one of the most widely used measures of emesis. **Aim:** To validate the 24-hour version of the PUQE (PUQE-24) in a population of pregnant Japanese women. A second aim was to identify the severity ranking of PUQE-24 scores. **Methods:** Approximately 1,500 pregnant women at gestational weeks before 20 were recruited for antenatal checkups at a general hospital and five private clinics in the Tokyo metropolitan area and Kagoshima Prefecture in Japan from January 2017 to May 2019. About a quarter (n = 378) of the participants responded to the questionnaire. They were distributed a set of questionnaires, including the PUQE-24. **Results:** PUQE-24 scores significantly correlated with younger gestational age, scores on the Health-Related Quality of Life for Nausea and Vomiting during Pregnancy, reduced changes in fluid and meal intake, Sheehan Disability Scale, and depression scores. A two-step cluster analysis with a fixed number of clusters at 4 yielded four groups: Severe, Moderate, Mild, and No Symptoms. Receiver operating characteristic (ROC) analysis produced the best cutoff points for these four groups (3/4, 6/7, and 7/8). They reported excellent specificity, sensitivity, and positive and negative predictive values. **Conclusion:** Our findings indicate that a cutoff point of 6/7 may be suitable for clinical uses in pregnant women.

Keywords: pregnancy-unique quantification of emesis (PUQE); validity; severity

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Introduction

Nausea and vomiting (also known as emesis) is one of the commonest symptoms during pregnancy. The prevalence of emesis, as reported by a prospective study in England, was 80%, with 28% experiencing only nausea and 52% experiencing both nausea and vomiting (Gadsby et al., 1993). The quality of life of pregnant women is substantially reduced (Attard et al., 2002; Hada et al., 2022). Hyperemesis gravidarum (HG) is a severe form of emesis; however, its diagnostic criteria have not yet reached an agreement (Koot et al., 2018). A quarter of HG cases persist throughout pregnancy (Fejzo et al., 2009). Emesis and HG in particular are associated with poor delivery outcomes such as premature birth (Fejzo et al., 2009) and termination of pregnancy (Poursharif et al., 2007) as well poor child development (Nijsten et al., 2022). Emesis is also associated with higher prevalence of mental health problems before and during pregnancy as well after childbirth such as depression (Aksoy et al., 2015; Hizli et al., 2012; Kjeldgaard et al., 2017a; Mitchell-Jones et al., 2016, 2020; Muchanga et al., 2020; Pirimoglu et al., 2009; Seng et al., 2007), anxiety (McCormack et al., 2011; Mitchell-Jones et al., 2016; Pirimoglu et al., 2009; Seng et al., 2007), obsessive-compulsive disorder (Pirimoglu et al., 2009), tokophobia (Poursharif et al., 2008), posttraumatic stress disorder (Christodoulou-Smith et al., 2011; Kjeldgaard et al., 2019: Mullin et al., 2012) and others (Fell et al., 2006; Kjeldgaard et al., 2017b)

Among several self-report measures of emesis (Lacasse & Bérard, 2008; Magee et al., 2002; Munch & Schmitz, 2007; Power et al., 2010; Rhodes et al., 1984), the Pregnancy Unique Quantification of Emesis (PUQE: Koren et al., 2002) is one of the most widely used tools (e.g., Birkeland et al., 2015; Koren & Cohen, 2020; Yilmaz et al., 2022). The PUQE was recommended by the American College of Obstetricians and Gynecologists (2018), National Institute for Health and Care Excellence (2021), French College of Gynecologists and Obstetricians (Deruelle et al., 2022), and Society of Obstetric Medicine of Australia and New Zealand (Lowe et al., 2019). Its 24-hour version PUQE-24 (Ebrahimi et al., 2009) has only three items with a 5-point scale: nausea, vomiting and retching for the previous 24 hours. Its total score ranges from 3 to 15 with higher scores indicating more severe emesis. The PUQE-24 was translated into Japanese by Kitamura and colleagues after obtaining the permission from the original author and Hada et al. (2021) reported its configural, measurement, and structural invariance between nulliparas and multiparas and across two measurement time points. There may be no debatable points about content validity of the PUQE-24 because emesis consists of nausea and vomiting together with retching when there is no food or fluid to vomit. However, its criterion validity is yet to be studied in details. Criterion validity is based on correlations with an accepted standard. In this study, we expected that the PUQE-24 score would be associated with other measures of emesis such as the Health-Related Quality of Life for Nausea and Vomiting during Pregnancy (NVPQOL; Magee, et al., 2002) as well as clinical measures including reduced water and meal intake, reduced urinary frequency, and treatment for emesis as well social dysfunctioning. Construct validity is based on the conceptual variable underlying a test. We expected, in this study, that the PUQE-24 scores would be associated with the severity of psychiatric symptoms including depression and insomnia. The first aim of this study is, thus, to study the validity of the PUQE-24 among Japanese pregnant women.

A conventional ranking suggests 3–6 points as ‘mild’, 7–12 points as ‘moderate’, and 13–15 points as ‘severe’ (Lacasse et al., 2008). Classification of pregnant women into a small number of categories is a clinical convention that is useful in practice. These findings provide guidelines for perinatal healthcare professionals. However, whether these cutoff points are applicable to the Japanese population remains unknown. Suitable cutoff points for patient-rated symptom measures may differ between countries and cultures. A second aim of the present study is to identify severity rankings of the instrument in a Japanese population. We used a cluster analysis with a fixed number of clusters of four. Reasonable cutoff points for the total PUQE-24 scores may be identified using receiver operating characteristic (ROC) curve analysis.

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Methods

Study Procedures and Participants

Data used in this study were obtained from previous studies (Hada et al., 2021; Hada et al., 2022; Shinohara et al., 2022; Wakamatsu et al., 2021; Yamada et al., 2022). Emesis typically has its onset between the 4th and 7th week of pregnancy, peaks around the 9th week and results in cessation of symptoms in 90% of women by the 20th week (RCOG Green-top Guideline No. 69; Nelson-Piercy et al., 2024). For this study, approximately 1,500 pregnant women at gestational weeks before age 20 were recruited for antenatal checkups at a general hospital and five private clinics in the Tokyo metropolitan area and Kagoshima Prefecture in Japan from January 2017 to May 2019. The exclusion criteria for recruitment were: (a) insufficient fluency in Japanese, (b) age < 20 years, (c) history of an eating disorder, (d) symptoms of vaginal bleeding or abdominal pain, (e) history of subchorionic haematoma, and (f) recurrent miscarriages.

Measurements

24 hour-Pregnancy-unique Quantification of Emesis and Nausea (PUQE-24; Ebrahimi Maltepe, Bournissen, & Koren, 2009): The PUQE-24 has three items to measure nausea, vomiting, and retching. The scores were rated as the daily number of vomiting episodes, duration of nausea per day in hours, and number of retching episodes per 24 h. The PUQE-24 score ranged from 1 to 5 for each category. The total score ranged from 3 to 15. Higher scores indicated more severe symptomatology. The PUQE-24 was translated into Japanese by M.M. and T.K. after obtaining permission from the original author. The bilingual author (T.K.) back-translated the text and compared it with the original English.

Health-Related Quality of Life for Nausea and Vomiting during Pregnancy (NVPQOL; Magee, et al., 2002): The NVPQOL is a specific measure shown to be reliable and valid in a population of women reporting emesis during pregnancy. The NVPQOL contains 30 items and measures the QOL in the previous week. The scores ranged from 1 to 7 for each item. The total NVPQOL scores ranged from 30 to 210. Lower scores corresponded to better QOL. Yamada et al. (2020) examined the psychometric properties of the Japanese version of the NVPQOL and identified a one-factor structure.

Fluid and food intake and urinary frequency: Daily fluid intake was asked by a single item: "How much fluid did you drink each day in the past week?" in millilitres.

Change in fluid or meal intake was assessed by a single item: "How does your fluid or food intake in the past week compare with your pre-pregnancy intake?" This was rated on a 7-point scale (1=extremely reduced, 2=reduced, 3=slightly reduced, 4=unchanged, 5=slightly increased, 6=increased, and 7=extremely increased). Urinary frequency in the past week was assessed using a single item: "How many times did you urinate in a day in the past week?".

Treatment of emesis: We asked about the outpatient visits and inpatient admissions for emesis. We scored 1= none, 2=outpatient visits, and 3=inpatient admissions.

The Sheehan Disability Scale (SDS; © Copyright 1983–2020 Sheehan DV. All rights reserved. May be reproduced only with the permission of Dr. David V. Sheehan, copyright holder. For permission contact davidsheehan@gmail.com). The SDS is a self-report measure consisting of three items. The SDS measures disabilities in the following three domains: (a) work and schoolwork, (b) social and leisure activities, and (c) family life and home responsibilities. Each item was rated from 0 to 10. Higher scores indicate better adjustment. We used the Japanese version of the SDS (Yoshida et al., 2004). Hada et al. (2022) used the Japanese version of the SDS to measure pregnancy-related disabilities in expectant Japanese women.

Patient Health Questionnaure-9 (PHQ-9; Spizer, 1999): The PHQ-9 is a self-report measure of depression. Nine items check for the frequency of depressive symptoms over the previous two weeks and are rated on a four-point Likert scale from 0 to 3. Higher scores indicated more severe symptomatology. The Japanese version of the PHQ-9 (Inagaki et al., 2013; Muramatsu et al., 2009) was used for assessing depression. The Japanese version of the PHQ-9 has a two-factor bifactor structure (i.e., the first, second, and general factors). The first factor reflected sleep change, fatigue,

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and appetite change. Thus, it was considered a somatic factor. The second factor reflected loss of interest, depressed mood, self-blame, concentration difficulty, psychomotor symptoms, and suicidality. Thus, it was considered a non-somatic factor. The general factor includes all items and reflects depression severity (Wakamatsu et al., 2021).

Insomnia Severity Index (ISI; Bastien et al., 2001). The ISI was used to measure insomnia severity. The ISI is a self-reported measure consisting of seven items rated from 0 (no problem) to 4 (very severe). The total scores ranged from 0 to 28. Shinohara et al. (2022) reported the two-factor structure of the ISI in a sample of pregnant Japanese women. The first factor represents early, middle, and late insomnia and sleep dissatisfaction. The second factor represents interference of insomnia-induced difficulties with daytime functioning, noticeable sleep problems, and concerns about sleep problems. The measurement invariance was also confirmed.

Data Analysis

First, Little's Missing Completely at Random (MCAR) test was used to examine the characteristics of the missing values across all variables. Thereafter, the mean, standard deviation (SD), and skewness for continuous variables, and frequencies for nominal variables were calculated. All cases were classified into the severity ranking categories of the PUQE-24 according to original classification (i.e., None=3, Mild=4-6, Moderate=7-12, and Severe=13-15) scores, of which mean (SD) scores were calculated. The PUQE-24 score also correlated with other variables.

Next, we performed a two-step cluster analysis of the participants using their scores on the three PUQE-24 items. Cluster analysis divides cases into groups that are internally homogeneous and externally heterogeneous based on relevant characteristics (Borgen & Barnett, 1987). The three items of the PUQE-24 were used as indicators for two-step cluster analysis. The cluster number was set to four because our aim was to identify the severity rankings of the instrument corresponding to the conventions of None, Mild, Moderate and Severe. To clarify the characteristics of the emerging clusters, those belonging to the four clusters were compared in terms of the variables studied. We set the alpha level (possibility of a Type I error) at $p < .001$ because of multiple comparisons.

To identify the most suitable cutoff points for the total PUQE-24 scores (between None and Mild/Moderate/Severe, None/Mild and Moderate/Severe, and None/Mild/Moderate and Severe), we performed a receiver operating characteristic (ROC) analysis (Grener et al., 2000; Zwaig & Campbell, 1993). The accuracy of prediction based on the PUQE-24 score was examined in terms of specificity, sensitivity, and positive and negative predictive values with a range of cutoff points. The optimal cutoff points balanced psychometric properties and clinical utility.

Results

Of the pregnant women eligible for the study, 382 (approximately 25%) women participated in this study. Three cases were missing gestational weeks, and one case was at 22 weeks of gestation. Therefore, these four cases were excluded from the statistical analyses ($N = 378$). Of these, 139 (37%) were nulliparae, and 239 (63%) were multiparae. Parity was unknown in only four cases. Approximately half of the participants were employed (Supplementary Table S1). Eighty-four (22%) had experiences with assisted reproductive technology. The mean, SD, skewness, and kurtosis of the continuous variables are shown in Table 1. While skewness for the SDS total score (7.06) and kurtosis for the vomiting item of the PUQE-24 (9.64) were high, the other variables were within an acceptable range, indicating a normal distribution of the variables (Table 1). Little's Missing Completely at Random (MCAR) test showed that the data were missing completely at random: χ^2 (df) = 2737.479 (2679) (p = .211). Therefore, missing values were treated with listwise deletions (see n in each Table).

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Table 1. Mean, SD, skewness, and kurtosis for continuous variables (*N* = 378).

variable	*n*	Mean	SD	Skewness	Kurtosis
Demographics					
Age	374	31.9	4.9	0.01	−0.10
Husband's age	370	33.4	5.4	0.03	−0.25
Body mass index (BMI)	370	21.1	3.1	1.29	1.82
Gestational week	374	11.0	1.6	0.4	2.08
PUQE-24					
Nausea	376	3.09	1.45	−0.37	−1.35
Vomiting	377	1.26	0.64	2.92	9.64
Richling	377	2.14	1.26	1.01	0.02
total	376	6.50	2.71	0.53	−0.38
NVP-QOL					
NVP-QOL total	348	104.85	42.94	−0.04	−0.85
Daily fluid intake	357	904.34	391.95	0.94	−1.19
Predictive validity measures					
Changes fluid intake	379	4.00	1.44	−0.38	−0.51
Changes meal intake	377	3.24	1.62	0.49	−0.57
Urinary frequency	369	7.09	2.69	0.94	1.19
Emesis treatment	377	1.02	0.18	9.22	90.7
SDS					
SDS total	375	8.34	7.08	7.06	−0.15
PHQ-9					
Somatic	376	7.63	2.56	0.08	−1.00
Non-somatic	375	8.80	3.18	1.39	1.58
General	375	16.43	5.16	0.80	0.26

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ISI					
ISI 1st factor	374	9.22	19.00	0.56	−0.29
ISI 2nd factor	368	5.91	13.00	0.60	−0.51

Note. PUQE-24, Pregnancy-Unique Quantification of Emesis and Nausea; SDS, Sheehan Disability Scale; PHQ-9, Patient Health Questionnaure-9; Somatic, Somatic subscale score; Non-somatic, Non-somatic subscale score; General, total score; ISI, Insomnia Severity Index; ISI 1st, ISI first factor score, ISI 2nd, ISI second factor score.

Pregnant women were distributed from the lowest (i.e., 3) to the highest (i.e., 15) PUQE-24 scores (Supplementary Table S1) with low skewness and kurtosis (Table 1). The women's gestational weeks ranged from 4 to 19 weeks (Supplementary Table S1), with a mean (SD) of 11.0 (1.6). Almost all other variables in women showed low skewness and kurtosis (Table 1 and Supplementary Table S1).

The PUQE-24 scores were correlated with neither the women's age nor body mass index (BMI). However, it was slightly significantly ($p < .05$) correlated with gestational age ($r = -.17$). As expected, the PUQE-24 scores were significantly correlated with the NVP-QOL scores ($r = .71$, $p < .001$), and reduced changes of fluid ($r = -.22$, $p < .001$) and meal ($r = -.34$, $p < .001$) intake (Supplementary Table S2). It was, however, not correlated with daily fluid intake, urinary frequency, or emesis treatment.

The PUQE-24 scores were also correlated with the scores of the SDS ($r = -.39$, $p < .001$), PHQ-9 ($r = -.36$, $-.38$, $-.42$, for Somatic, Non-somatic, and General factors respectively. $p < .001$) and ISI ($r = -.29$ and $-.29$ for the 1st and 2nd factors, respectively, $p < .001$) (Supplementary Table S2).

Two-step cluster analysis yielded four clusters: Cluster 1 ($n = 69$ [18.4 %]), Cluster 2 ($n = 153$ [40.7 %]), Cluster 3 ($n = 85$ [22.6 %]), and Cluster 4 ($n = 69$ [18.4 %]). The silhouette coefficient was 0.4. Women in Cluster 1 scored higher than those in the other three groups in terms of nausea, vomiting, and retching (Table 2). Hence, we named this cluster Severe. Women belonging to Clusters 2 and 3 scored the same in terms of vomiting, and higher than those in Cluster 4 in nausea and retching. Those women belonging to Cluster 2 were scored higher than those belonging to Cluster 3 in terms of nausea and retching. Hence, we named these Clusters Moderate, and Mild, respectively. Women in Cluster 4 scored 1 (the lowest score) for nausea, vomiting, and retching. Hence, we named this Cluster No Symptoms.

Table 2. Mean scores of PUQE-24 by each cluster and the construct validity ($n = 376$).

	Cluster 1: Severe nausea and vomiting $n = 69$ (18.4%)	Cluster 2: Moderate nausea and retching $n = 153$ (40.7%)	Cluster 3: Mild nausea and retching $n = 85$ (22.6%)	Cluster 4: No symptoms $n = 69$ (18.4%)	One-Way ANOVA F (df)	Effect size η^2	Tukey post hoc comparison
PUQE-24							
Nausea	4.13	3.64	2.96	1.00	142.366 (3, 372)***	.534	1>2>3>4
Vomiting	2.43	1.00	1.00	1.00	389.137 (3, 372)***	.758	1>2=3=4

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Retching	2.90	2.39	2.00	1.00	38.724 (3, 372)***	.238	1>2>3>4
total	9.49	7.03	5.96	3.00	155.988 (3, 372)***	.557	1>2>3>4
Demographic							
Age	31.26	32.76	31.52	31.92	2.738 (3, 368)*	.022	1=2=3=4
Husband's age	32.91	34.41	32.63	32.88	2.694 (3, 364)*	.022	1=2=3=4
Gestational weeks	10.80	10.77	11.02	11.70	6.016 (3, 372)***	.046	1=2=3<4
Body mass index (BMI)	21.64	20.74	21.59	20.72	2.390 (3, 364)*NS*	.019	
NVP-QOL							
total	138.75	115.13	105.41	49.79	92.972 (3, 342)***	.449	1>2=3>4
Predictive validity measures							
Daily fluid intake	806.45	864.09	982.32	1006.20	4.413 (3, 351)**	.036	1=2=3=4
Changes fluid intake	3.45	3.88	4.34	4.42	7.592 (3, 372)***	.058	1=2=3=4
Changes meal intake	2.43	3.15	3.43	4.06	13.321 (3, 371)***	.097	1<2=3=4
Urinary frequency	6.51	7.23	7.55	6.88	2.170 (3, 363)*NS*	.018	
Emesis treatment	1.04	1.03	1.01	1.00	0.801 (3,371)*NS*	.006	
SDS							
total	10.91	9.05	8.25	4.31	11.739 (3, 369)***	.087	1=2=3>4
PHQ-9							
Somatic	8.30	7.96	7.63	6.19	10.280 (3, 370)***	.077	1=2=3>4
Non-somatic	10.07	9.14	8.51	7.12	11.747 (3, 369)***	.087	1=2=3>4
General	18.38	17.10	16.14	13.31	13.772 (3, 372)***	.101	1=2=3>4
ISI							

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ISI 1st	10.22	9.38	9.34	7.73	7.413 (3, 368)***	.057	1=2=3>4
ISI 2nd	6.35	6.05	6.04	5.02	3.874 (3, 362)**	.031	1=2=3=4

*, $p < .05$; **, $p < .01$; *** $p < .001$; *NS*, not significant. PUQE-24, Pregnancy-Unique Quantification of Emesis and Nausea; SDS, Sheehan Disability Scale; PHQ-9, Patient Health Questionnaure-9; Somatic, PHQ-9 Somatic subscale score; Non-somatic, PHQ-9 Non-somatic subscale score; General, PHQ-9 total score; ISI, Insomnia Severity Index; ISI 1st, ISI first factor score, ISI 2nd, ISI second factor score.

As expected, the women with No Symptoms were significantly older in terms of gestational age. Women in all the four Clusters did not differ in terms of their age or BMI. The NVP-QOL scores were in the order of Clusters, but not significantly different between the Moderate and Mild Clusters. The four Cluster women did not differ significantly in terms of daily fluid intake, changes in fluid intake or urinary frequency. Women belonging to Cluster 1 were characterised by greater reduction of meal intake. The four Cluster women did not differ in terms of emesis treatment. The Clusters 1, 2, and 3 were scored significantly higher in social disability. Women in the Severe, Moderate, and Mild Cluster did not differ in terms of all PHQ-9 subscales and ISI scores, but they were significantly higher than the No Symptoms Cluster women except for the second subscale of the ISI.

ROC analyses were performed to determine the optimal cutoff points for the total PUQE-24. We performed ROC analyses for discrete No symptoms (Cluster 4) versus Mild, Moderate, and Severe clusters (Clusters 3+2+1); No symptoms and Mild clusters (Clusters 4+3) versus Moderate and Severe cluster (Clusters 2+1), and No symptoms, Mild, and Moderate clusters (Clusters 4+3+2) versus Severe cluster (Cluster 1). The specificities, sensitivities, and positive and negative predictive values with a range of cut-off points were calculated. The best clinical cut-off point for No symptoms vs. Mild/Moderate/Severe was judged as 3/4 with perfect accuracy (Table 3). For No Symptoms/Mild vs. Moderate/Severe, the best clinical cut-off point was 6/7. The best clinical cut-off point for No Symptoms/Mild/Moderate vs. Severe was 7/8.

Table 3. PUQE-24 Cut off scores for four Clusters.

Comparisons	Optimal cut-off points	Sensitivity	Specificity	Positive predictive value	Negative predictive value
No Symptoms vs. Mild, Moderate, and Severe	3/4	1.000	1.000	1.000	1.000
No Symptoms and Mild vs. Moderate and Severe	6/7	.671	.844	0.844	0.671
No Symptoms, Mild, and Moderate vs. Severe	7/8	.783	.779	0.783	0.779

Discussion

Among currently pregnant women, the scores of the PUQE-24 were widely distributed. The scores of the three items were normally distributed, except for vomiting which had high skewness and kurtosis. Among the present Japanese pregnant women, approximately 82% had emesis. The prevalence of emesis as well as distribution of emesis scores are in line with or virtually the same as those reported in other countries (although using different measures) such as England (Gadsby et al., 1993), Canada (Lacasse et al., 2009), China (Li et al., 2023), and Finland (Ellilä et al., 2018).

The PUQE-24 scores were moderately correlated with those of the NVPQOL, another widely used measure of emesis, showing concurrent validity. Pregnant women with high PUQE-24 scores

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were more likely to experience reduced fluid and meal intakes during pregnancy, supporting criterion validity. The lack of a strong link between the experience of emesis treatment and current PUQE-24 scores was not unexpected because we distributed the questionnaire exclusively to outpatients. Even if they had previously received treatment for severe nausea and vomiting, they were asked about emesis just for the last 24 h when their emesis may have subsided. Further studies should include pregnant women currently undergoing treatment for emesis (such as those admitted). It is of note that there is no consensus about the definition of HG (Koot et al., 2018) and its treatment varies (Abramowitz et al., 2017; Buckwalter & Simpson, 2002; Di Iorio et al., 2025; Grooten et al., 2015). As expected, pregnant women with high PUQE-24 scores were more likely to be socially disabled and have psychological symptoms, such as depression and insomnia. These findings were in line with previous literature (see Introduction).

Clinicians require a ranking inventory to categorise pregnant women into classes based on the severity of emesis. The clinical convention proposes four categories: None (PUQE-24, 3), Mild (PUQE-24, 4-6), Moderate (PUQE-24, 7-12), and Severe (PUQE-24, 13-15). Applying this convention to the present sample, however, only nine women (2%) were categorised as Severe. However, this approach was impractical. Our two-step cluster analysis with a fixed number of clusters at 4 was aimed at providing a more evidence-based categorisation of emesis cases. About a quarter of the women (Cluster 4) were free from symptoms of emesis. The remaining patients exhibited symptoms of emesis. This is consistent with the results of a previous epidemiological study on emesis. The three Clusters with emesis symptoms differed in that Cluster 1 women had both nausea and vomiting/retching, whereas Clusters 2 and 3 women mainly had nausea. Clusters 2 and 3 differed in terms of nausea and retching severity. ROC analysis revealed excellent or acceptable validity (sensitivity, specificity, and positive and negative predictive values) at cutoff points of 3/4, 6/7, and 7/8, respectively. Taking into consideration clinical utility, we think that the distinction between Moderate and Severe may be of little use because women of Moderate Cluster scored only 7 on the PUQE-24. Hence, we recommend the use of No Symptoms/Mild and Moderate/Severe symptoms for clinical use.

Our study was not without drawbacks and limitations. We used a questionnaire survey with limited data on biological features (e.g., electrolytes). Psychological symptoms were rated using self-report measures. Therefore, clinician-rated interview data will provide detailed insights for future studies. Second, we collected data at a single time point. The trajectory of emesis symptoms during pregnancy may cast light on emesis research. It may be argued that the PUQE-24 covers emesis symptoms only for the previous 24 hours and that the time covered by the measure should be expanded to a week or two weeks. The latter recommendation, however, is subject to memory bias (e.g., women accurately remember yesterday's vomiting but forget about the last week's one).

Despite these drawbacks, our study showed that the PUQE-24 is a valid and useful tool for measuring emesis in pregnant Japanese women. We recommend using a cut-off point of 6/7 for the detection of cases for treatment of emesis. It also highlights the multiple aspects of emesis, including gastrointestinal symptoms, psychosocial disability, and psychological maladjustment.

Supplementary Materials: The following supporting information can be downloaded at Preprints.Org.

Ethics Approval and Consent to Participate: This study was approved by the Research Ethics Committees of Kitamura Institute of Mental Health Tokyo, Tokyo, Japan (no. 2015052301) and Kagoshima University (no. 170247). Study participants were anonymous. Therefore, all participants provided informed consent after understanding the study's rationale and procedures. The authors assert that all procedures contributing to this study complied with the ethical standards of the national and institutional committees on human experimentation and the Declaration of Helsinki of 1975, as revised in 2008.

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Conflict of Interests: The authors declare that they have no conflict of interests.

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