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# Polish version of the Acute Cystitis Symptom Score for patients with acute uncomplicated cystitis

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**Introduction** The Acute Cystitis Symptom Score (ACSS) is a self-reporting questionnaire to evaluate the symptoms and quality of life in women with uncomplicated acute cystitis (AC). The aim of the current study was the additional cognitive and clinical validation of the Polish version.

**Material and methods** Professional forward and backward translations from original Russian to Polish were performed by Mapi SAS. For cognitive assessment, women with different ages and educational levels were asked to comment on each item of the Polish ACSS to establish the final study version. The clinical validation was performed as a prospective, non-interventional cohort study. Women with AC (Patients) and those without (Controls) filled in the Polish ACSS during their visits to a physician's office and at a follow-up visit. Statistical analysis included ordinary descriptive values, calculation of reliability, validity, discriminative ability, responsiveness (sensitivity, specificity), and comparative analysis.

**Results** The cognitive assessment was performed in 60 women with a median (range) age of 44.5 (21–88) years and different educational levels: grade school (n = 8), high school (n = 25), college (n = 22), and postgraduate education (n = 5). Forty-three patients were recruited for the clinical validation study along with 34 controls. Statistical analyses resulted in excellent values of internal consistency, discriminative ability, and validity for diagnosis of AC. At a summary score of 6 and higher in the ´Typical´ domain, positive and negative predictive values were 97% and 79%, and sensitivity and specificity were 79% and 97%, respectively.

**Conclusions** The Polish version of the ACSS has demonstrated benefits for diagnosis and patient-reported outcome assessment. It is objective, fast, and cost-effective, and it may help to easily confirm the accurate diagnosis of AC. The Polish ASCSS can now be recommended for use in clinical and epidemiological studies, in clinical practice, or for self-diagnosis and patient-reported outcome in women with symptoms of AC.

Key Words: acute cystitis ‹› acute cystitis symptom score ‹› questionnaire ‹› clinical study ‹› patient-reported outcome ‹› clinical results

## INTRODUCTION

Urinary tract infections (UTIs) are among the most prevalent infectious diseases in general practice [1], and of these, 80% are classified as uncomplicated UTIs (uUTIs). Although current guidelines recommend the use of antibiotics (ABs) as the first choice of treatment for the acute phase of uUTIs [2, 3], several prospective, randomized, placebo-controlled studies have been performed already comparing antibiotic therapy with symptomatic therapy [4–7]. These results were compelling enough for the updated German Clinical Guidelines [3] to encourage the use of the non-AB symptomatic treatment in selected cases of acute lower uUTIs with mild-to-moderate symptoms.

If symptomatic therapies are compared with antibiotic therapies in clinical studies, the patient-reported clinical outcome at end of therapy, test of cure, and an assessment for the maintenance of clinical response at approximately 21 to 28 days after randomization conducted in the intention-to-treat population, and not the elimination of bacteriuria, should become the main study aims. In such a study it could be demonstrated that the recurrence rate within 28 days after start of treatment is not correlated with the patient receiving an effective non-antibiotic or antibiotic therapy; it depends only on the patient's history, i.e. whether the patient has experienced recurrent UTI in the past or not [8].

If the clinical outcome becomes the most important study aim, well defined clinical inclusion as well as patient-reported outcome criteria need to be established, for which the Acute Cystitis Symptom Score (ACSS) questionnaire was developed, originally in Uzbek and Russian language [9, 10, 11] and now translated and validated in many other languages.

The aim of the current study was the additional cognitive and clinical validation of the Polish version of the ACSS.

## MATERIAL AND METHODS

The linguistic validation of the Polish ACSS was already performed earlier in 2014 by Mapi SAS, Lyon, France using the procedures outlined by MAPI guidelines [12, 13]. From the original Russian language [9, 10, 11] two forward translations into Polish language were performed by a professional translator. After reconciliation one backward translation to the original language was performed, again by a qualified translator, to exclude any discrepancies. The final Polish version was then validated by a cognitive interview with 5 women with cystitis symptoms. This version has already been used in a phase III study [7].

For the additional cognitive assessment of the Polish ACSS, female subjects with different ages and educational levels were asked to comment on each item of the ACSS, about whether they had any difficulties in understanding and/or answering the specific questions. All comments were discussed within the scientific committee, which consisted of the authors and local investigators. If needed, small linguistic adaptations or explanations in the form of footnotes were made to finally establish the study version.

The final study version of the Polish ACSS was then used in a prospective, non-interventional, comparative, clinical cohort study including female patients with symptoms suspected of AC as compared to female subjects (controls) who were either healthy or with other diseases not related to UTI. The patients and controls were asked to fill in part A (diagnostics) of the ACSS questionnaire during their first visit to the physician's office and part B (patient-reported outcome) during the follow-up visit at about 1–2 weeks to determine the clinical outcome.

### Statistical methods

The psychometric abilities of the domains of the Polish ACSS were measured by the strength of internal consistency using Cronbach's alpha and split-half reliability [14]. The diagnostic values of the domains of the Polish ACSS were tested by means of calculation of the sensitivity, specificity, diagnostic accuracy, diagnostic odds ratio (DOR), Youden index, positive and negative predictive values, likelihood ratios of the positive and negative test results, and the proportions of the false positive and false negative tests. For the representation of the sensitivity and specificity of the selected items and domains of the Polish ACSS, we used Receiver Operating Characteristic (ROC) curve analysis with the calculation of the area under the curve (AUC).

The numerical variables were presented in averages and dispersions (such as 95% confidence intervals), depending on the normality of distribution, which was in turn assessed both visually (using histograms and Q-Q Plots) and mathematically (using statistical tests such as Shapiro-Wilks) [15].

Non-normally distributed and interval variables (such as scores of the items and summary scores of the domains of the ACSS) are presented as medians and interquartile ranges (IQR). Categorical and dichotomous variables are presented as integers and proportions. Comparative analysis between

**Table 1.** *Demographic characteristics of study population, risk factors for complicated urinary tract infection (ORENUC) and recurrent urinary tract infection (LUTRIE nomogram), and additional conditions according to the Acute Cystitis Symptom Score (ACSS)*

| Parameter | Total | Patients | Controls | P-values* |
|---|---|---|---|---|
| Number of subjects, n (%) | 77 (100) | 43 (55.8) | 34 (44.2) | n.a. |
| Age of subjects, median (IQR) | 41.0 (35.0–58.0) | 46.0 (36.5–65.0) | 35.0 (33.0–53.0) | 0.029 |
| Sexually active, n (%) | 38 (46.8) | 24 (55.8) | 14 (41.2) | 0.219 |
| Sexually inactive, n (%) | 19 (24.7) | 9 (20.9) | 12 (35.3) | 0.219 |
| No answer about sexual life, n (%) | 18 (23.4) | 10 (23.3) | 8 (23.5) | 1.000 |
| Antimicrobial therapy in preceding 3 months, n (%) | 6 (7.8) | 5 (11.6) | 1 (2.9) | 0.302 |
| Number of acute episodes within the last year, median (IQR) | 1.0 (0.0–2.0) | 1.5 (0.8–3.0) | 0.0 (0.0–0.0) | <0.001 |
| Number of acute episodes within the last 6 mo., median (IQR) | 0.0 (0.0–1.0) | 1.0 (0.0–1.0) | 0.0 (0.0–0.0) | <0.001 |
| Age, when first episode of an acute UTI was noted, median (IQR) | 28.0 (19.0–33.5) | 28.5 (20.5–38.0) | 20.0 (16.0–30.0) | 0.115 |
| Employment | | | | |
| Full-time, n (%) | 53 (68.8) | 30 (69.8) | 23 (67.6) | 0.821 |
| Retired, n (%) | 3 (3.9) | 2 (4.7) | 1 (2.9) | 1.000 |
| Not working/unemployed, n (%) | 1 (1.3) | 1 (2.3) | 0 (0.0) | 1.000 |
| Other, n (%) | 15 (19.5) | 9 (20.9) | 6 (17.6) | 1.000 |
| Not answered, n (%) | 5 (6.5) | 1 (2.3) | 4 (11.8) | 0.229 |
| Level of education | | | | |
| Grade school, n (%) | 7 (9.1) | 5 (11.6) | 2 (5.9) | 0.614 |
| High school, n (%) | 17 (22.1) | 11 (25.6) | 6 (17.6) | 0.541 |
| College, n (%) | 31 (40.3) | 13 (30.2) | 18 (52.9) | 0.088 |
| Postgraduate, n (%) | 21 (27.3) | 13 (30.2) | 8 (23.5) | 0.644 |
| Not answered, n (%) | 1 (1.3) | 1 (2.3) | 0 (0.0) | 1.000 |
| Risk factors, according to ORENUC system [25] | | | | |
| O: No known risk factor, n (%) | 61 (79.2) | 36 (83.7) | 25 (73.5) | 1.000 |
| R: Risk factors for recurrent urinary tract infection but no risk of more severe outcome, n (%) | 4 (5.2) | 4 (9.3) | 0 (0.0) | 0.244 |
| E: Extra-urogenital risk factors with risk of more severe outcome, n (%) | 1 (1.3) | 1 (2.3) | 0 (0.0) | 1.000 |
| N: Nephropathic diseases with risk of more severe outcome, n (%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | n.a. |
| U: Urologic risk factors with risk of more severe outcome, which can be resolved during therapy, n (%) | 4 (5.2) | 2 (4.7) | 2 (5.9) | 1.000 |
| C: Permanent urinary catheter and unresolvable urologic risk factors with risk of more severe outcome, n (%) | 2 (2.6) | 0 (0.0) | 2 (5.9) | 0.310 |
| No available data, n (%) | 5 (6.5) | 0 (0.0) | 5 (14.7) | 0.033 |
| Risk factors for reinfection, according to LUTIRE nomogram [25] | | | | |
| Number of sexual partners within the last year, median (IQR) | 1.0 (0.0–1.0) | 1.0 (0.0–1.0) | 1.0 (0.0–1.0) | 0.521 |
| Hormonal status: fertile, n (%) | 41 (53.2) | 21 (48.8) | 20 (58.8) | 0.415 |
| Hormonal status: postmenopausal, n (%) | 18 (23.4) | 12 (27.9) | 6 (17.6) | 0.432 |
| Hormonal status: no answer, n (%) | 18 (23.4) | 10 (23.3) | 8 (23.5) | 1.000 |
| Bowel function: normal, n (%) | 51 (66.2) | 27 (62.8) | 24 (70.6) | 0.634 |
| Bowel function: diarrhoea, n (%) | 2 (2.6) | 1 (2.3) | 1 (2.9) | 1.000 |
| Bowel function: constipation, n (%) | 6 (7.8) | 5 (11.6) | 1 (2.9) | 0.325 |
| Bowel function: no answer, n (%) | 18 (23.4) | 10 (23.3) | 8 (23.5) | 1.000 |
| Additional conditions according to ACSS | | | | |
| Menstruation, n (%) | 3 (3.9) | 2 (4.7) | 1 (2.9) | 1.000 |
| Premenstrual syndrome, n (%) | 1 (1.3) | 1 (2.3) | 0 (0.0) | 1.000 |
| Symptoms of the menopause, n (%) | 6 (7.8) | 4 (9.3) | 2 (5.9) | 0.898 |
| Pregnancy, n (%) | 1 (1.3) | 1 (2.3) | 0 (0.0) | 1.000 |
| Known sugar diabetes, n (%) | 2 (2.6) | 2 (4.7) | 0 (0.0) | 0.580 |

ACSS – Acute Cystitis Symptom Score; n – number of patients; n.a. – not applicable; IQR – interquartile range; UCI – urinary tract infection
Note: *Parameters are compared between the groups using a two-sided independent sample t-test with the Welch correction in cases of inequality of variances for continuous variables, the chi-square test for categorical variables, and Wilcoxon-Mann-Whitney test for interval variables.

**Table 2.** *Comparison between patients and controls concerning the Acute Cystitis Symptom Score (ACSS) features. A. ACSS typical and differential symptoms and quality of life (n, %), B. summary scores of different ACSS domains (median, IQR), and C. age versus summary scores of 'Typical' domain (median, IQR)*

| A. Symptoms/discomfort | | Patients (n = 43) | Controls (n = 34) | p-value* |
|---|---|---|---|---|
| 'Typical' domain | Frequency, n (%) | 42 (97.7) | 5 (14.7) | <0.001 |
| | Urgency, n (%) | 37 (86.0) | 6 (17.6) | <0.001 |
| | Painful urination (dysuria), n (%) | 38 (88.4) | 3 (8.8) | <0.001 |
| | Incomplete bladder emptying, n (%) | 37 (86.0) | 5 (14.7) | <0.001 |
| | Suprapubic pain, n (%) | 33 (76.7) | 5 (14.7) | <0.001 |
| | Visible blood in urine, n (%) | 12 (27.9) | 1 (2.9) | 0.009 |
| 'Differential' domain | Flank pain, n (%) | 25 (58.1) | 7 (20.6) | 0.002 |
| | Vaginal discharge, n (%) | 18 (41.9) | 2 (5.9) | <0.001 |
| | Urethral discharge, n (%) | 16 (37.2) | 1 (2.9) | <0.001 |
| | Feeling fever, n (%) | 15 (34.9) | 1 (2.9) | 0.002 |
| 'Quality of Life' (QoL) domain | General discomfort, n (%) | 42 (97.7) | 6 (17.6) | <0.001 |
| | Everyday activities/work, n (%) | 42 (97.7) | 5 (14.7) | <0.001 |
| | Social activities, n (%) | 41 (95.3) | 5 (14.7) | <0.001 |
| B. Summary scores of ACSS domains | | Patients (n = 43) | Controls (n = 34) | p-value* |
| 'Typical' domain (median, IQR) | | 10.0 (6.5–13.0) | 0.0 (0.0–1.0) | <0.001 |
| 'Differential' domain (median, IQR) | | 2.0 (0.0–4.0) | 0.0 (0.0–0.8) | <0.001 |
| 'QoL' domain (median, IQR) | | 5.0 (4.0–7.0) | 0.0 (0.0–0.0) | <0.001 |
| 'Typical' + 'QoL' domain (median, IQR) | | 16.0 (12.5–19.0) | 0.0 (0.0–2.8) | <0.001 |
| C. Number and summary score of typical symptoms according to age: n patients (n controls) >50 years: 17 (9); <50 years: 26 (25) | | | | |
| Number of typical symptoms | | >50 years | <50 years | p-value* |
| Controls (median, IQR) | | 0.0 (0.0–0.0) | 0.0 (0.0–1.0) | 0.605 |
| Patients (median, IQR) | | 5.0 (3.0–5.0) | 5.0 (5.0–5.0) | 0.188 |
| Summary score of typical symptoms | | >50 years | <50 years | p-value* |
| Controls (median, IQR) | | 0.0 (0.0–0.0) | 0.0 (0.0–1.0) | 0.672 |
| Patients (median, IQR) | | 10.0 (9.0–12.0) | 11.0 (6.2–13.8) | 0.517 |

*two-sided Wilcoxon-Mann-Whitney test
n – number of patients; ACSS – Acute Cystitis Symptom Score; IQR – interquartile range; QoL – quality of life

independent variables was performed depending on the nature of the variable: a two-sided independent sample t-test with the Welch correction in cases of inequality of variances was used for continuous variables, the chi-square test for categorical variables, and the Wilcoxon-Mann-Whitney test for interval variables [16, 17, 18]. The statistical significance for all measures was set at the P-value of 0.05.

R-Studio with the R version 4.1.0 (2021-05-08) software with built-in and additional packages was used for the statistical analysis and graphical representation of the study results [19–23].

### Ethical considerations

This non-interventional study was performed in accordance with good clinical practice (GCP) as defined in the International Council for Harmonization (ICH), and in keeping with the regulations of the Declaration of Helsinki and applicable European regulations and standard operating procedures (SOPs) for clinical investigation and documentation, and national and local laws and regulations. Before including any female subjects in the study, ethical approval of the protocol was received for the study in Poland by the Bioethical Commission of the Medical University of Silesia in Katowice, Poland, KNW/0022/KB/168/19 dated 12.06.2019. Women who were willing to participate signed a consent form, and a three-digit code was assigned to them that was used for the analysis of data.

## RESULTS

In Poland the additional cognitive assessment was performed in 8 urological centres including a total of 60 female subjects with mean (SD) and median (range) ages of 47.5 (18.0) and 44.5 (21–88) years, respectively, with different educational levels: grade school (n = 8), high school (n = 25), college (n = 22), and postgraduate education (n = 5).

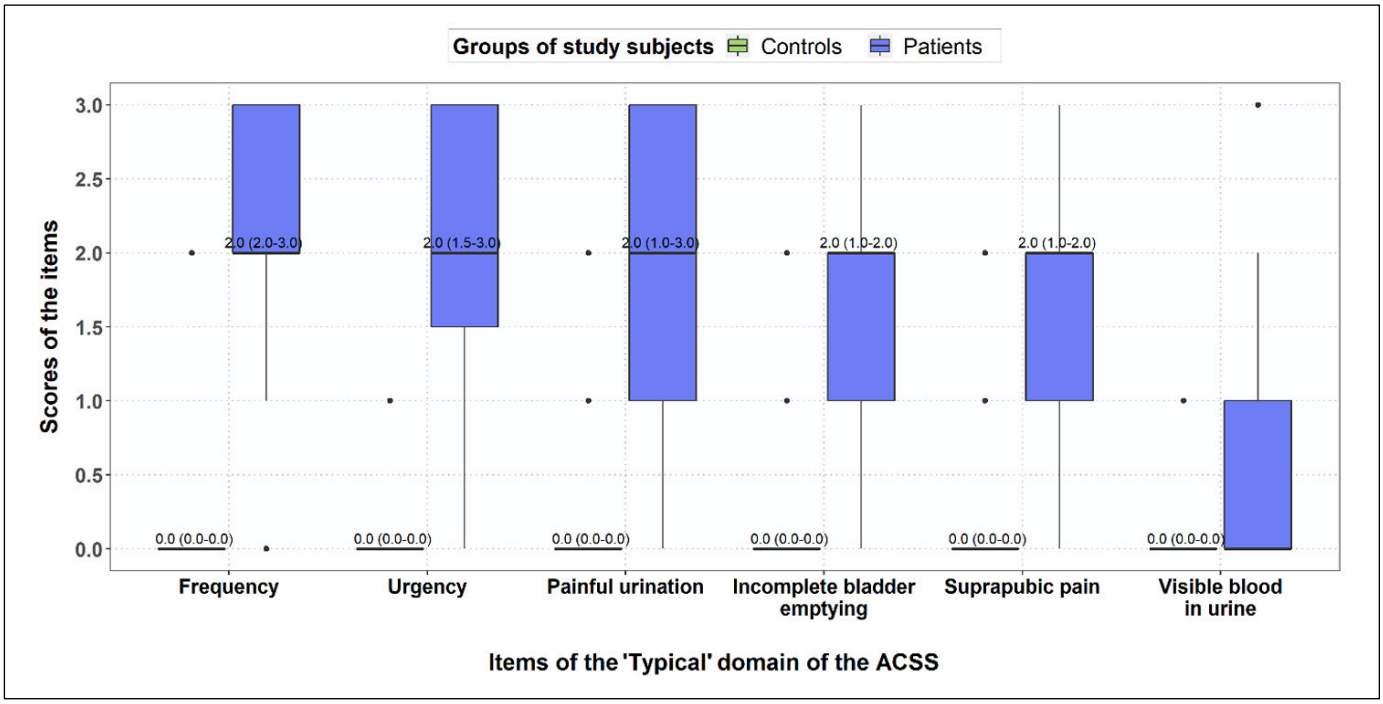


**Figure 1.** *Boxplots with typical symptom scores (median, IQR) for patients with acute cystitis (n = 43) and controls (n = 34) at baseline visit.*

ACSS – Acute Cystitis Symptom Score; IQR – interquartile range

After all comments were discussed within the scientific committee, the final study version of the Polish ACSS parts A and B could be established [24].

Nine urological centres participated in a clinical study using the final study version of the Polish ACSS. A total of 43 female patients diagnosed by their physicians with AC and 34 controls were included in the study. Table 1 shows the demographics of the patients and controls. The median age of the controls (35.0) was 11 years lower than that of the patients (46.0), and the patients more often reported recurrent UTIs than the controls. Otherwise, there were no statistically significant differences ($p < 0.5$) concerning sexual activity, employment status, level of education, risk of recurrence measured by the LUTIRE nomogram [25], complicated UTI measured by the ORENUC system [26], and additional conditions according to the ACSS questionnaire, between patients and controls.

The median score for all 5 typical symptoms in the patients (2, moderate) was significantly higher than in the controls (0, not present). Only 12 (27.9%) patients and one (2.9%) control claimed visible blood in the urine (Figure 1, Table 2A). The summary scores of the ACSS domains ('Typical', 'Differential', 'Quality of Life' (QoL), and cumulative 'Typical & QoL') of the patients were also significantly higher than in the controls (Figure 2, Table 2B).

**Table 3.** *Coefficients of reliability of the Acute Cystitis Symptom Score (ACSS) domains (mean; 95% CI)*

| Domain | Cronbach's alpha mean (95% CI) | Split-half reliability mean (95% CI) |
|---|---|---|
| 'Typical' domain | 0.90 (0.87; 0.93) | 0.91 (0.86; 0.91) |
| 'Differential' domain | 0.62 (0.48; 0.75) | 0.57 (0.55; 0.71) |
| 'QoL' domain | 0.95 (0.94; 0.97) | 0.85 (0.85; 0.86) |
| Cumulative 'Typical' & 'QoL' domains | 0.94 (0.92; 0.96) | 0.94 (0.90; 0.96) |
| Entire ACSS, excluding 'Additionals' | 0.93 (0.90; 0.95) | 0.93 (0.86; 0.96) |

ACSS – Acute Cystitis Symptom Score; QoL – Quality of Life; CI – confidence intervals

If the patients and controls were split according to age (>50 and <50 years of age), there was no indication that the number or severity of symptoms differed according to age in the group of patients or in the controls (Table 2C).

Cronbach's alpha of the entire ACSS (excluding 'Additionals') was 0.93 and the split-half reliability was 0.93, and for the 'Typical' domain they were 0.90 and 0.91, respectively (Table 3). The ROC analysis shows the best balance between sensitivity and specificity and the highest area under the curve (AUC) for the 'Typical' domain and the cumulative 'Typical & QoL' domain as compared to the individual typical symptoms or the 'QoL' domain (Figure 3).

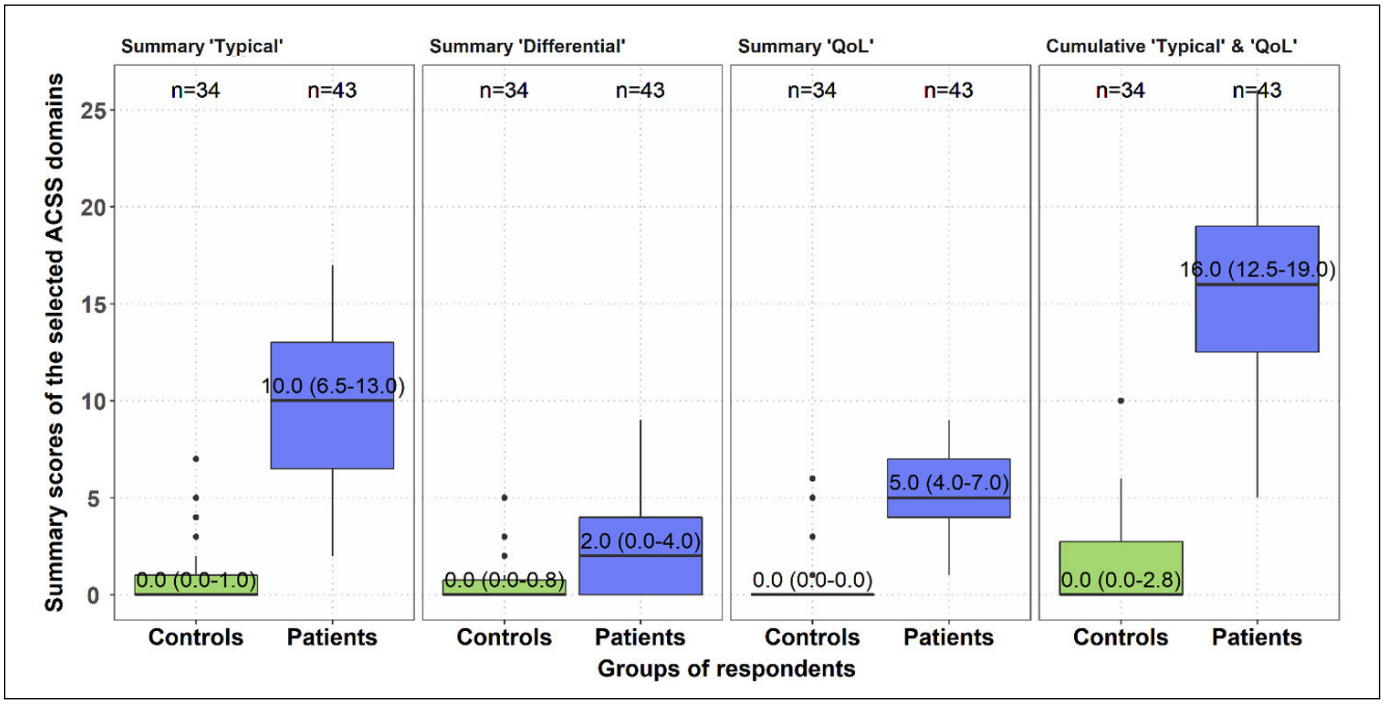


**Figure 2.** *Boxplots with the Acute Cystitis Symptom Score domains (median, IQR) for patients with acute cystitis (n = 43) and controls (n = 34) at baseline visit.*

IQR – interquartile range

Table 4 shows the diagnostic value of the Polish ACSS for acute uncomplicated cystitis in women at different cut-off levels of the summary score for the 'Typical' domain. At a cut-off of 6 and higher a median specificity of 97% was achieved, which was as high as at a cut-off of 7 and higher, but higher than at a cut-off of 5 and higher. However, the sensitivity at a cut-off of 6 and higher was only 79%, but this was similar to [27] or somewhat lower than other ACSS versions [10, 28].

In 42 of the 43 patients there was a follow-up (visit 2) between Day 6 and Day 13. In all ACSS domains a significant ($p < 0.05$) reduction of summary scores could be observed (Figure 4). There was also a significant ($p < 0.05$) correlation at the follow-up visit between the assessment in the 'Dynamics' domain and the summary scores of most of individual symptoms/discomfort and domains except for 'visible blood in urine' and for 3 of the 'differential' symptoms (vaginal and urethral discharge, and fever), as expected (Figure 5 and Table 5).

Using part B of the ACSS as a patient-reported outcome measure, the treatment could be rated as successful according to different thresholds [29]. Of the 42 patients who filled in part B of the ACSS at the follow-up visit, 33 (78.6%) rated the therapeutic outcome as successful according to the 'Dynamics' domain (all or most symptoms disappeared).

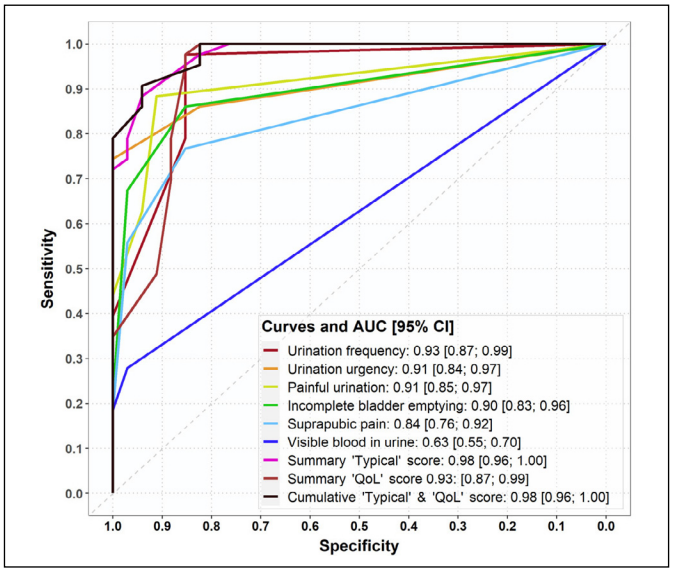


**Figure 3.** *Receiver Operating Characteristic (ROC) analysis on each of the typical symptoms, of typical symptoms domain (Typical), of quality of life domain (QoL), and the cumulative 'Typical & QoL' domain.*

AUC – area under the curve; CI – confidence intervals

Using other thresholds (B-E) the treatment could be rated as successful in 73.8–78.6% of the patients (Table 6).

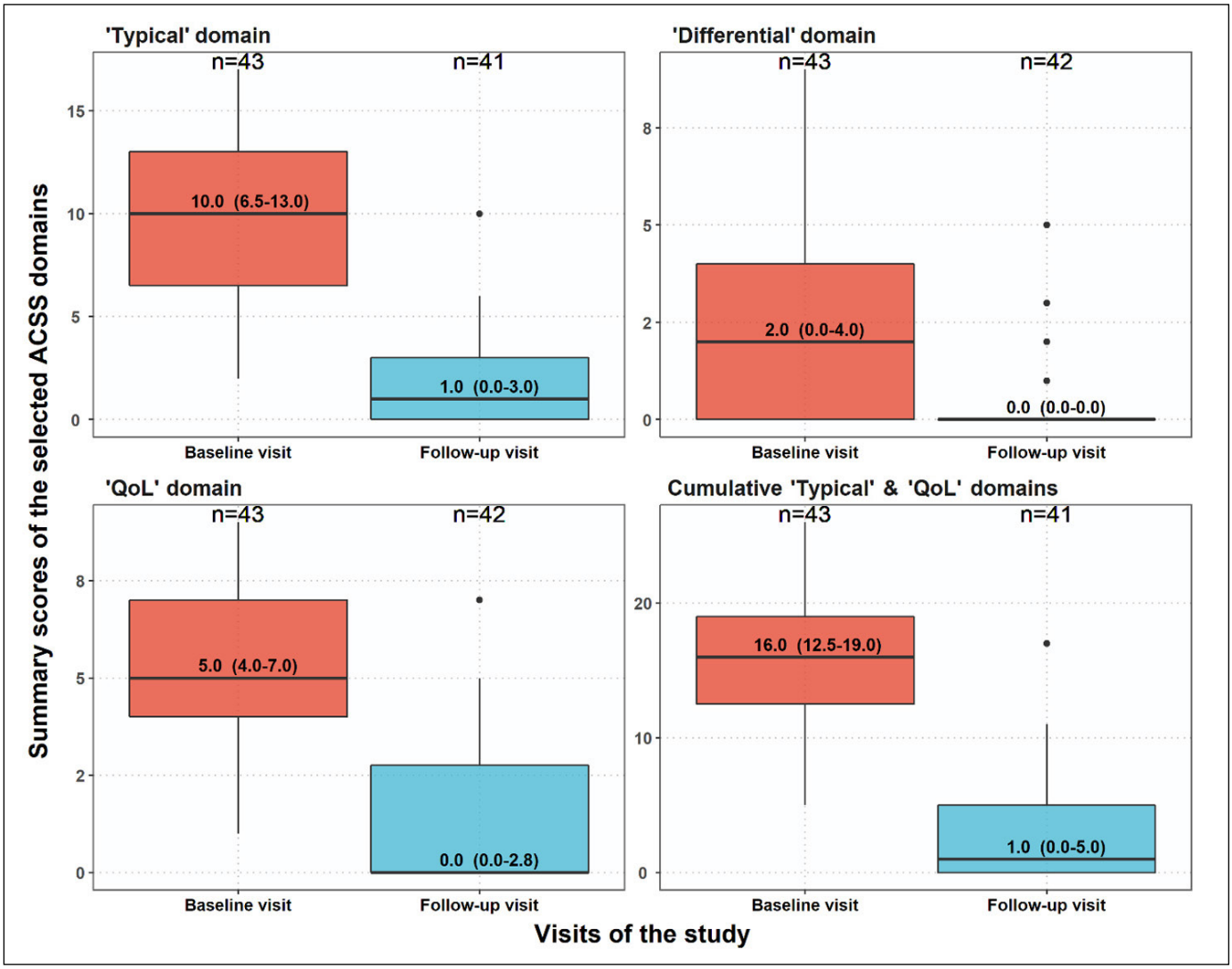


**Figure 4.** *Boxplots of the Acute Cystitis Symptom Score domains (median, IQR) at baseline and follow-up visit for patients with acute cystis.*

n – number of patients; IQR – interquartile range; QoL – quality of life

**Table 4.** *Diagnostic value of the Polish Acute Cystitis Symptom Score for acute uncomplicated cystitis in women*

| Parameter | Sum TS ≥4 mean (95% CI) | Sum TS ≥5 mean (95% CI) | Sum TS ≥6 mean (95% CI) | Sum TS ≥7 mean (95% CI) |
|---|---|---|---|---|
| Sensitivity | 0.95 (0.84; 0.99) | 0.88 (0.75; 0.96) | 0.79 (0.64; 0.90) | 0.74 (0.59; 0.86) |
| Specificity | 0.85 (0.69; 0.95) | 0.94 (0.80; 0.99) | 0.97 (0.85; 1.00) | 0.97 (0.85; 1.00) |
| Diagnostic accuracy | 0.91 (0.82; 0.96) | 0.91 (0.82; 0.96) | 0.87 (0.77; 0.94) | 0.84 (0.74; 0.92) |
| Diagnostic odds ratio | 119 (21.6; 656) | 122 (22.1; 670) | 125 (15.0; 1039) | 96.0 (11.7; 787) |
| Youden index | 0.81 (0.53; 0.94) | 0.82 (0.55; 0.95) | 0.76 (0.49; 0.90) | 0.71 (0.44; 0.86) |
| Positive predictive value | 0.89 (0.76; 0.96) | 0.95 (0.83; 0.99) | 0.97 (0.85; 1.00) | 0.97 (0.84; 1.00) |
| Negative predictive value | 0.94 (0.79; 0.99) | 0.86 (0.71; 0.95) | 0.79 (0.63; 0.90) | 0.75 (0.60; 0.87) |
| Likelihood ratio of a positive test | 6.48 (2.88; 14.6) | 15.0 (3.90; 57.9) | 26.9 (3.87; 187) | 25.3 (3.64; 176) |
| Likelihood ratio of a negative test | 0.05 (0.01; 0.21) | 0.12 (0.05; 0.28) | 0.22 (0.12; 0.39) | 0.26 (0.16; 0.44) |
| Proportion of false positive result | 0.15 (0.05; 0.31) | 0.06 (0.01; 0.20) | 0.03 (0.00; 0.15) | 0.03 (0.00; 0.15) |
| Proportion of false negative result | 0.05 (0.01; 0.16) | 0.12 (0.04; 0.25) | 0.21 (0.10; 0.36) | 0.26 (0.14; 0.41) |

n – number of patients; CI – confidence intervals

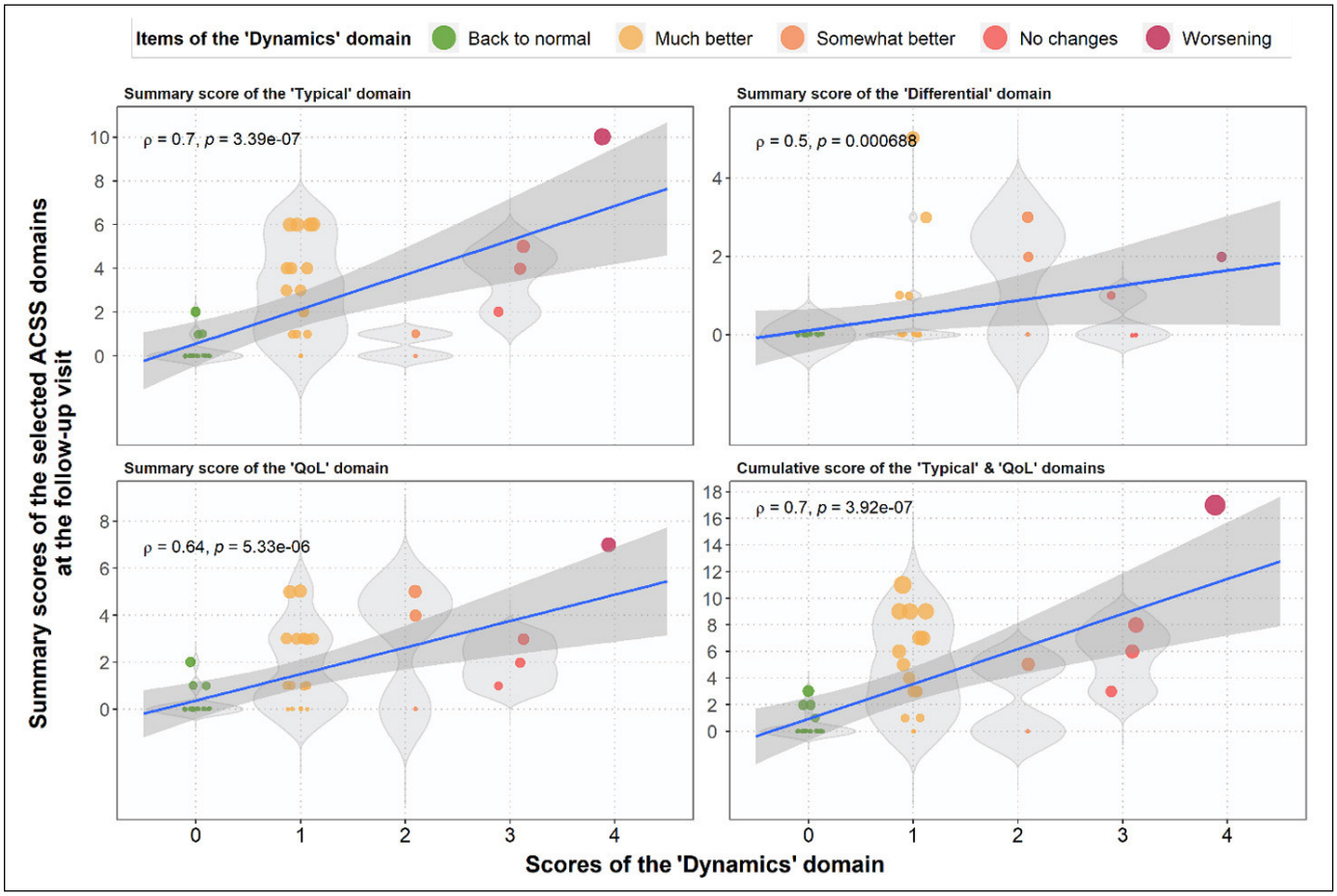


**Figure 5.** *Summary scores of the selected the Acute Cystitis Symptom Score domains at the follow-up visit versus scores of the 'Dynamics' domain.*

ACSS – Acute Cystitis Symptom Score; QoL – quality of life

## DISCUSSION

The ACSS was developed as a self-reporting questionnaire for the clinical diagnosis of AC based on complaints. It combines graded assessment of the severity of symptoms and their effect on the quality of life. The ACSS consists of 2 parts: diagnostic (part A) and follow-up (part B) forms. Both parts include 4 identical domains: a) 6 items for 'typical' symptoms of AC, b) 4 items for differential diagnoses, c) 3 items for the quality of life, and d) 5 items for additional conditions. Part B contains in addition domain, called 'Dynamics', to monitor changes in the condition of the patient during follow-up.

There are already other questionnaires developed for patients with acute UTI [30–34] but, unlike the ACSS, none of these are validated for diagnostics, for differential diagnosis, or for assessing severity, quality of life, and treatment efficacy in these patients. Other questionnaires in urology include, for example, chronic prostatitis [35] and overactive bladder syndrome [36].

If questionnaires for patients are used in different countries and languages, it is important to follow international guidelines with forward and backward translations, as was performed here earlier by the Mapi Group [7]. In addition, it is important to use such a linguistically validated translation for a cognitive assessment procedure to get feedback from women of different ages and with educational backgrounds, to ensure that it is well understood by all such individuals.

The final diagnostic value, however, can only be determined if patients suspected of AC are compared with controls – either healthy female subjects or those with diseases other than UTIs. The results of this clinical validation showed the same good results as obtained with the ACSS versions that have already been validated in other languages [27, 28, 37, 38, 39] and in 2 international studies including 139 and 285 patients and 147 and 232 controls,

**Table 5.** *Strength of associations between the scores of the 'Dynamics' domain and other item/domain scores of the Acute Cystitis Symptom Score at the follow-up visit*

| Item/domain | Correlation coefficient* | p-value |
|---|---|---|
| Frequency | 0.55 | <0.001 |
| Urgency | 0.54 | <0.001 |
| Painful urination (dysuria) | 0.42 | 0.006 |
| Incomplete bladder emptying | 0.52 | <0.001 |
| Suprapubic pain | 0.37 | 0.016 |
| Visible blood in urine | 0.10 | 0.556 |
| Summary score of 'Typical' domain | 0.70 | <0.001 |
| Flank pain | 0.47 | 0.002 |
| Vaginal discharge | 0.17 | 0.293 |
| Urethral discharge | 0.14 | 0.398 |
| Feeling fever | 0.10 | 0.556 |
| Summary score of 'Differential' domain | 0.47 | 0.002 |
| General discomfort | 0.60 | <0.001 |
| Impact on everyday activities | 0.51 | 0.001 |
| Impact on social activities | 0.51 | 0.001 |
| Summary score of 'QoL' domain | 0.62 | <0.001 |
| Cumulative score of 'Typical' & 'QoL' domains | 0.70 | <0.001 |

*Spearman's rho

**Table 6.** *Proportions of patients with the assessment of the treatment efficacy at follow-up (N = 42) according to different pre-defined thresholds*

| Successful treatment outcome | Success, n (%) | Non-success, n (%) |
|---|---|---|
| A) score of ACSS 'Dynamics' domain <1 | 35 (83.3%) | 7 (16.7%) |
| B) summary score of typical domain ≤ 5 scores, no item > 1 and 'visible blood in urine' = 0 | 32 (76.2%) | 10 (23.8%) |
| C) summary score of typical domain < 5 scores, no item > 1 and no item of QoL > 1 and 'visible blood in urine' = 0 | 31 (73.8%) | 11 (26.2%) |
| D) summary score of 4 FDA symptoms ≤ 4, no item > 1 and 'visible blood in urine' = 0 | 32 (76.2%) | 10 (23.8%) |
| E) summary score of 3 EMA symptoms ≤ 3, no item> 1 and 'visible blood in urine' = 0 | 33 (78.6%) | 9 (21.4%) |

n – number of patients; ACSS – Acute Cystitis Symptom Score; EMA – European Medicines Agency; FDA – Food and Drug Administration; QoL – Quality of Life

respectively [10, 40]. Again, the summary score of all typical symptoms showed the highest diagnostic value (AUC) as compared to any of the typical symptoms considered alone, whereas a threshold of 6 and higher showed the highest specificity (0.97) with reasonable high sensitivity (0.79). A similarly high diagnostic value (AUC) can be reached if the summary score of the typical symptoms is combined with the summary score of the 3 QoL categories. Therefore, either the scoring of the typical symptoms or the combination with the QoL categories should also be used as a patient-reported outcome measure [29]. Using such parameters clinical results could also be considered in the future for the main study aim comparing the clinical results in patient groups treated with different antibiotic or non-antibiotic modalities.

This non-interventional study has some limitations. Although all the investigators were asked to diagnose an episode of AC according to international and national guidelines, some patients were diagnosed with AC with very low severity of symptoms. A total of 5 patients had a summary score of 4 or lower in the 'Typical' domain, whereas in only one of these 5 patients at least the symptoms, frequency and urgency, were assessed as moderate with pyuria and positive bacteriuria with Escherichia coli justifying the diagnosis of AC. Unfortunately, for the remaining 4 patients the complete dataset is missing. Urinary culture was not performed in any of the 3 patients with a summary score of 5 in the 'Typical' domain, and only one of them had pyuria by dipstick. The relatively low summary scores of these 8 patients are the reason for the relatively low sensitivity for the diagnostic threshold using a summary score of 6 and higher in the 'Typical' domain. For clinical studies, however, the specificity is probably more important. Therefore, for the clinical diagnosis using the self-reporting Polish ACSS, a threshold using a summary score of 6 and higher in the 'Typical' domain should still be recommended, as has also been shown for the ACSS versions validated in other languages.

## CONCLUSIONS

In the current clinical validation study the Polish version of the ACSS professionally translated from the original languages and cognitively assessed showed similar favourable diagnostic values as in the original and the other, already validated languages. It could therefore be used for clinical studies, in clinical practice, and for clinical self-diagnosis, especially in patients with recurrent UTIs. It is objective, fast, and cost-effective, and it may help to easily confirm the accurate diagnosis of AC. Such a validated questionnaire could also be used for patient-reported outcome assessment in patient groups treated with different antibiotic or non-antibiotic modalities.

### CONFLICTS OF INTEREST

The authors have no competing financial interests relevant to this study to disclose. J.F.A, K.G.N., A.P., F.M.E.W. are copyright hold-

ers of the ACSS. K.G.N. is consultant of Adamed Pharma, Bionorica SE, BioMerieux, GlaxoSmithKline, OM Pharma, MIP/Rosen Pharma. JFA is consultant of Bionorica SE. F.M.E.W. declares personal fees and advisory board attendance and study participation from Achaogen, Astellas, AstraZeneca, Bionorica, MSD, Janssen, GSK, Klosterfrau Health Group, OM Pharma/Vifor Pharma, Pfizer, Rosen-Pharma and Shionogi.



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**AUTHORS' CONTRIBUTION**

J.F.A., K.G.N., A.P., and F.M.E.W. participated in the development of the study plan and design. The following coauthors contributed to the cognitive assessment (CA) and clinical validation (CV) of the Polish ACSS by including the female subjects into the study: T.B. (CA,CV), M.C. (CA,CV), W.G. (CA), J.K. (CA,CV), W.K. (CV), P.M. (CV), P.N. (CA,CV), M.P. (CA,CV), S.P. (CV), M.S. (CA,CV), M.Z. (CV). J.F.A. processed the study data and performed the statistical analysis. K.G.N. wrote the first draft of the manuscript and J.F.A., A.P., and F.M.E.W. contributed to the manuscript revision. All authors have read and agreed to the final version of the manuscript.

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