



Validation of the Colorado Adult Joint Assessment Scale in Adult Patients With Severe Hemophilia A

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INTRODUCTION

- In patients with hemophilia, repeated bleeding into joints can lead to irreversible hemophilic arthropathy.¹
- The efficacy of prophylaxis for preventing bleeding episodes and joint damage in pediatric patients is well established²; however, the role of prophylaxis in preventing the progression of hemarthropathy in adults is less clear.
- There is a need for validated joint health assessment measures for adults with hemophilia, particularly to gauge the effects of prophylaxis on joint structure and function.
- The Colorado Adult Joint Assessment Scale (CAJAS) is a clinician-reported outcome measure developed specifically to assess the range of joint health seen in adults with hemophilia; the CAJAS was derived from the World Federation of Hemophilia physical examination score (Gilbert Score).³
- The CAJAS was initially developed as an 11-item assessment measure⁴; 2 items (Pain, Splint/Orthotic) were subsequently removed in the final 9-item CAJAS.
- Assessment of joint status using the CAJAS was a key secondary endpoint of SPINART, a phase 3 randomized study that compared prophylaxis vs on-demand treatment with sucrose-formulated recombinant factor VIII (Kogenate[®] FS, Bayer, Berkeley, CA) in adults and adolescents with hemophilia A.⁵

OBJECTIVE

- To assess the content validity and reliability (test-retest and interrater reliability) of the CAJAS for use in adults with hemophilia A (CAJAS validation study) and to evaluate the psychometric properties of the CAJAS based on data collected from the CAJAS validation and SPINART studies

METHODS

Patients and Studies

- Data were obtained from the CAJAS validation and SPINART studies.
 - The CAJAS validation study was conducted at 4 US centers with 2 physical therapists (PTs) per site. It included male patients aged 18–50 years with moderate to severe hemophilia A (FVIII activity [FVIII:C], <1%–2%).
 - SPINART, a 3-year, randomized, controlled, parallel-group study, included patients aged 12–50 years with severe hemophilia A (FVIII:C <1%; 10% of patients could have FVIII:C of 1%–2% if they showed clinical severity).

Assessments

- The CAJAS involves physical evaluation of 6 joints (right and left elbows, knees, ankles) by PTs and clinicians experienced in hemophilia joint assessment.
 - It comprises 9 domains: Swelling, Muscle Atrophy, Axial Deformity, Crepitus, Range of Motion, Contracture, Instability, Strength, and Gait (Figure 1).
 - Within the domains, scoring was 0–2 (for Axial Deformity, Instability, and Gait), 0–3 (for Swelling, Muscle Atrophy, Crepitus, Range of Motion, and Contracture), or 0–4 (for Strength); higher scores indicate more severe joint problems.
 - The CAJAS total score was calculated as the average of the mean scores for each joint type.

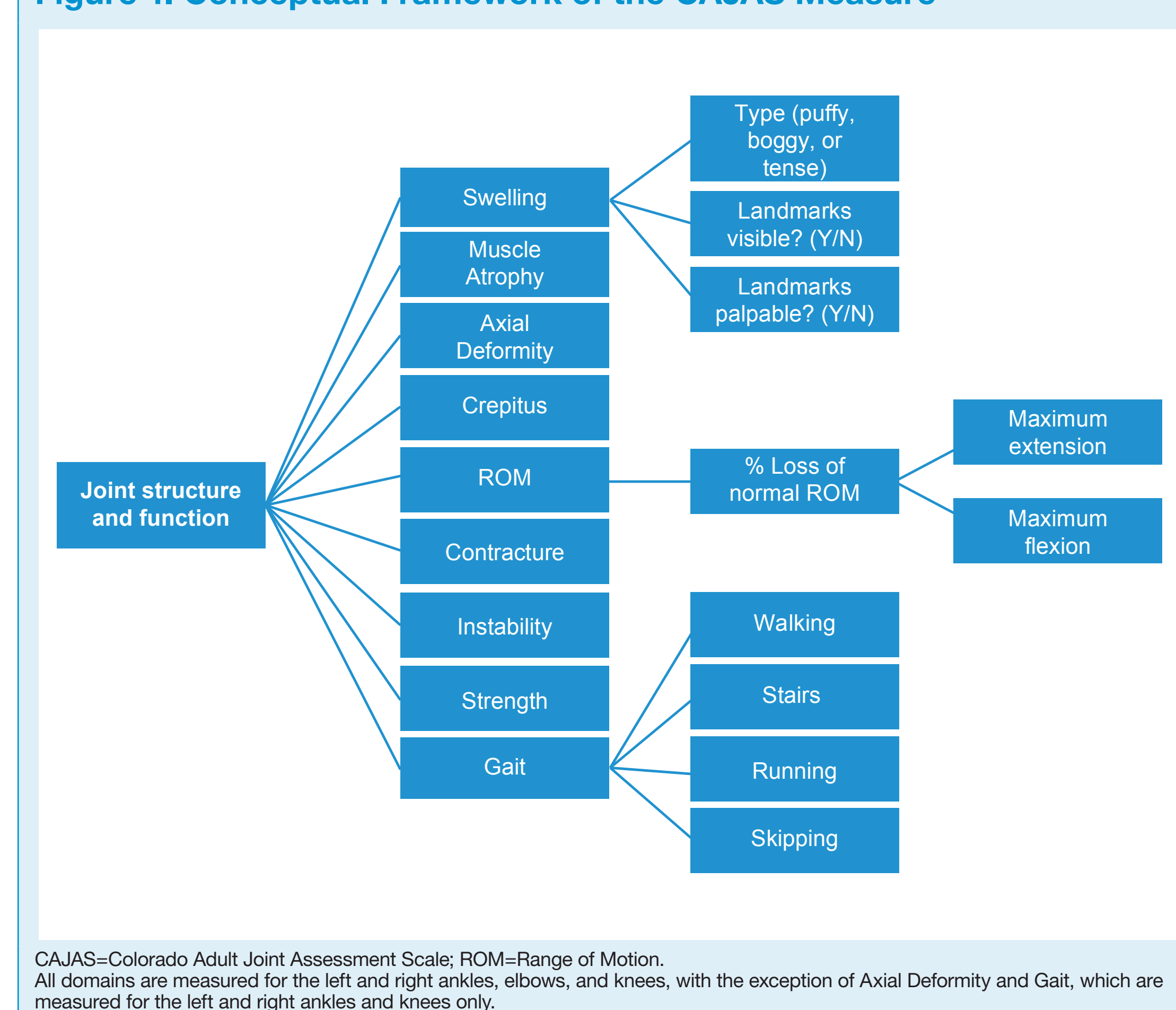
Content and Cultural Validity of the CAJAS

- Content validity was assessed using cognitive debriefing interviews conducted with 6 PTs who assessed a total of 12 patients from 3 different clinical sites in the United States during the CAJAS validation (content validity) study (2 PTs and 4 patients per site).
- Cultural equivalence was assessed by interviewing PTs and clinicians from Argentina, Bulgaria, and Romania (n=7; SPINART CAJAS evaluators) about their understanding of the CAJAS training, examination methods, and scoring.

Reliability/Psychometric Properties of the CAJAS

- Data to assess the CAJAS psychometric validity were obtained from the SPINART study. Test-retest and interrater reliability were assessed in the CAJAS validation study.
 - Test-retest reliability was evaluated by having the same PT perform the same examination in a single patient on 2 visits 7–10 days apart.
 - Interrater reliability was evaluated by comparing the CAJAS scores of 2 PTs performing separate examinations, 4 hours apart, at the same visit.
 - Baseline and final assessment (year 3) CAJAS data from SPINART were used to evaluate the following psychometric properties: internal consistency reliability (using Cronbach's alpha), construct validity (assessed by convergent/divergent validity and known-groups validity), and ability to detect change (responsiveness or sensitivity to change).
 - Minimally important difference (MID; clinically meaningful change at the group level) and responder definition (clinically meaningful change for an individual patient) were also calculated.

Figure 1. Conceptual Framework of the CAJAS Measure



CAJAS=Colorado Adult Joint Assessment Scale; ROM=Range of Motion. All domains are measured for the left and right ankles, elbows, and knees, with the exception of Axial Deformity and Gait, which are measured for the left and right ankles and knees only.

RESULTS

Patients

- Demographics and treatment regimens for the CAJAS validation and SPINART studies are shown in Table 1.
 - Patients in the CAJAS validation study were similar in age but slightly more ethnically diverse compared with those in SPINART.

Table 1. Demographics and Treatment Regimens of Patients From the CAJAS Validation and SPINART Studies

| | CAJAS Validation Study (N=30) | SPINART (N=80) |
|--------------------------|-------------------------------|------------------------|
| Age, y | | |
| Mean ± SD | 30.9±7.6 | 31.0±8.8 |
| Range | 18–47 | 17–50 |
| Race, n (%) | | |
| White | 20 (66.7) | 73 (91.2) |
| Black | 1 (3.3) | 0 (0) |
| Asian | 2 (6.7) | 2 (2.5) |
| Hispanic | 4 (13.3) | 5 (6.2) |
| Mixed ethnicity | 3 (10.0) | 0 (0) |
| Treatment regimen, n (%) | | |
| On-demand treatment | 2 (6.7) | 41 (51.3) [†] |
| Prophylaxis | 22 (73.3) [*] | 39 (48.8) [†] |
| Other | 6 (20.0) | 0 (0) |

CAJAS=Colorado Adult Joint Assessment Scale. ^{*}Prophylaxis dosing regimens included 1x/wk, 2x/wk, 3x/wk, or every other day. [†]Patients were randomized 1:1 to prophylaxis (3x/wk) or on-demand treatment regimens.

Content and Cultural Validity of the CAJAS

- Content validation indicated similar understanding of the CAJAS items, terms, instructions, methods, and scoring for each of the CAJAS domains by all PTs; there was minimal difficulty performing and scoring the joint assessments.
- Cultural validation of the interpretation and implementation of the CAJAS by non-US PTs indicated common understanding of the instructions and scoring of the CAJAS for all but one of the clinicians.

Psychometric Properties

- In the CAJAS validation study, the CAJAS test-retest reliability and interrater reliability were both high (Table 2).
- Analysis of the SPINART baseline data indicated that the CAJAS had good psychometric reliability and validity (Table 2).
 - Overall, the CAJAS demonstrated good convergent/divergent validity as shown by correlations between the CAJAS total scores and outcome measures used in SPINART (Table 2, Table 3).
 - Known-groups validity (the ability of the instrument to discriminate between identified groups who differ on a specific characteristic associated with the construct of relevance) was demonstrated with the CAJAS (Table 2).
 - Based on analysis of SPINART results, recommended values are provided for MID and responder definition of the CAJAS total score (Table 2).

Table 2. Summary of Psychometric Properties of the CAJAS Total Score

| Psychometric Property | Evidence |
|----------------------------------|---|
| Test-retest reliability | ICC, 0.92 (95% CI, 0.85–0.96) for 1 PT ICC, 0.91 (95% CI, 0.83–0.96) for a second PT |
| Interrater reliability | 0.87 (95% CI, 0.76–0.93) |
| Internal consistency reliability | Cronbach's alpha coefficient of 0.90 |
| Concurrent validity | Correlations observed for the CAJAS total scores and SPINART secondary outcomes such as Haemo-QoL-A physical functioning, EQ-5D, current activity level, and extended MRI |
| Known-groups validity | The scale scores differed significantly between participants grouped by <ul style="list-style-type: none"> Age: mean difference for patients aged 35–50 y (n=24) vs 17–26 y (n=28), 4.01 (95% CI, 1.90–6.12; P<0.001) IPSG MRI-17 scores[†]: mean difference between patients with moderate or severe joint damage (n=54) vs patients with little or no joint damage (n=16), 4.37 (95% CI, 2.93–5.81; P<0.001) |
| MID and responder definition | Based on analysis of SPINART results, an MID of 0.80 points and a responder definition of 1.0 point are recommended for the CAJAS total score; the responder definitions for individual joints are slightly higher |

CAJAS=Colorado Adult Joint Assessment Scale; EQ-5D=EuroQoL 5D; Haemo-QoL-A=Haemo-QoL questionnaire for adults; ICC=intra-class correlation coefficient; IPSG=International Prophylaxis Study Group; MID=minimally important difference; MRI=magnetic resonance imaging; PT=physical therapist. [†]MRI-17 is a scoring system that combines earlier progressive and additive MRI scoring methods (score range, 0–17 with higher scores indicating more severe joint damage).

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Disclosures

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Table 3. Correlation Between the CAJAS Total Score and SPINART Outcome Measures

| Outcome Measure | Correlation Coefficient |
|--|-------------------------|
| Haemo-QoL-A | |
| Physical functioning | −0.51 [*] |
| Role functioning | −0.23 [*] |
| Worry | −0.24 [†] |
| Consequences of bleeding | −0.20 |
| Emotional impact | −0.06 |
| Treatment concern | −0.31 [†] |
| Haemo-QoL-A total | −0.34 [‡] |
| EQ-5D | |
| Visual analog scale | −0.43 [*] |
| Short-Form McGill Pain Questionnaire | |
| Pain summary score | 0.19 |
| Pain (last 4 wk) | 0.28 [†] |
| Pain (current) | 0.07 |
| Activity List | |
| Change in physical activities or lifestyle | 0.10 |
| Current activity level | 0.25 [†] |
| Extended MRI scale | |
| Total score | 0.78 [*] |
| Ankle | 0.53 [*] |
| Elbow | 0.60 [*] |
| Knee | 0.65 [*] |

CAJAS=Colorado Adult Joint Assessment Scale; EQ-5D=EuroQoL 5D; Haemo-QoL-A=Haemo-QoL questionnaire for adults; MRI=magnetic resonance imaging. All coefficients were calculated using Pearson correlations except for the extended MRI scale, which was calculated using Spearman correlations. Higher scores for the CAJAS denote decreased joint functioning, higher Haemo-QoL-A scores denote better functioning, higher EQ-5D scores denote better health-related quality of life, higher pain scores represent a worse status, higher current activity level scores denote greater impairment, and higher extended MRI scores denote greater joint damage. Negative correlations with the CAJAS total scores are expected for Haemo-QoL-A and EQ-5D; positive correlations are expected for extended MRI scores, current activity level, and pain scores. ^{*}P<0.001. [†]P<0.05. [‡]P<0.01.

- The change in the CAJAS total scores from baseline to year 3 correlated with changes in other SPINART clinical outcomes measures for the same time frame; this demonstrates the scale's sensitivity to change (Table 4).

Table 4. Correlation Between Change in Scores From Baseline to Year 3 for the CAJAS Total Score and SPINART Outcome Measures

| Outcome Measure | Correlation Coefficient |
|--------------------------------------|-------------------------|
| Haemo-QoL-A | |
| Physical functioning | −0.34 [*] |
| EQ-5D | |
| Visual analog scale | −0.38 [*] |
| Short-Form McGill Pain Questionnaire | |
| Pain summary score | 0.27 [†] |
| Pain (last 4 wk) | 0.38 [*] |
| Pain (current) | 0.06 |
| Activity List | |
| Current activity level | 0.28 [†] |
| Extended MRI scale | |
| Total score | 0.04 |
| Ankle | −0.05 |
| Elbow | 0.05 |
| Knee | 0.13 |

CAJAS=Colorado Adult Joint Assessment Scale; EQ-5D=EuroQoL 5D; Haemo-QoL-A=Haemo-QoL questionnaire for adults; MRI=magnetic resonance imaging. All coefficients were calculated using Pearson correlations except for current pain and activity level, which were calculated using Spearman correlations. ^{*}P<0.01. [†]P<0.05.

CONCLUSIONS

- The CAJAS is the first physical joint exam scale to undergo comprehensive validation in adults with hemophilia.
- The CAJAS is reliable, valid, and reproducible across trained PTs in multinational sites and can be used in clinical practice for assessing joint function in adults with hemophilia.



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Hemophilia - clinical
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