Evaluating a Personalized Endpoint in Down Syndrome–Associated Alzheimer's Disease: Feasibility and Stakeholder Perspectives

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▶ Background

Assessing outcomes in Down syndrome–associated Alzheimer's disease (DS-AD) is challenging due to wide variability in baseline abilities and trajectories of decline. Standardized measures often miss meaningful change, highlighting the need for sensitive, valid tools that capture heterogeneous symptoms and treatment responses in individuals with DS-AD (Hartley et al., 2015; Lott & Head, 2019). Patient-centered outcome measures, such as Goal Attainment Scaling, are well-suited for this purpose (Morel & Cano, 2017;Knox et al., 2020).

However, the successful implementation of GAS in a clinical trial setting requires rigorous standardization to ensure consistency, transparency, and psychometric robustness. The primary objective of this study was to investigate the feasibility and acceptability of a standardized, inventory-facilitated GAS protocol as a patient-centric tool for evaluating treatment response in individuals with DS-AD.

▶ Methods

This was a prospective, 16-month, non-interventional study. We developed a defined protocol for goal identification, scaling, and utilized a DS-AD goal inventory (Knox et al., 2021) to guide the clinician-facilitated goal setting with caregivers of individuals with Down syndrome. A total of 46 participants with DS and their caregivers enrolled in the study and completed an initial goal-setting visit at baseline.

Each dyad established ≥3 personalized goals across **Behavior, Cognition, Daily Function, Executive Function, or Physical Manifestations** domains, with the option to add novel "other" goals.

How Goal Attainment Scaling Works

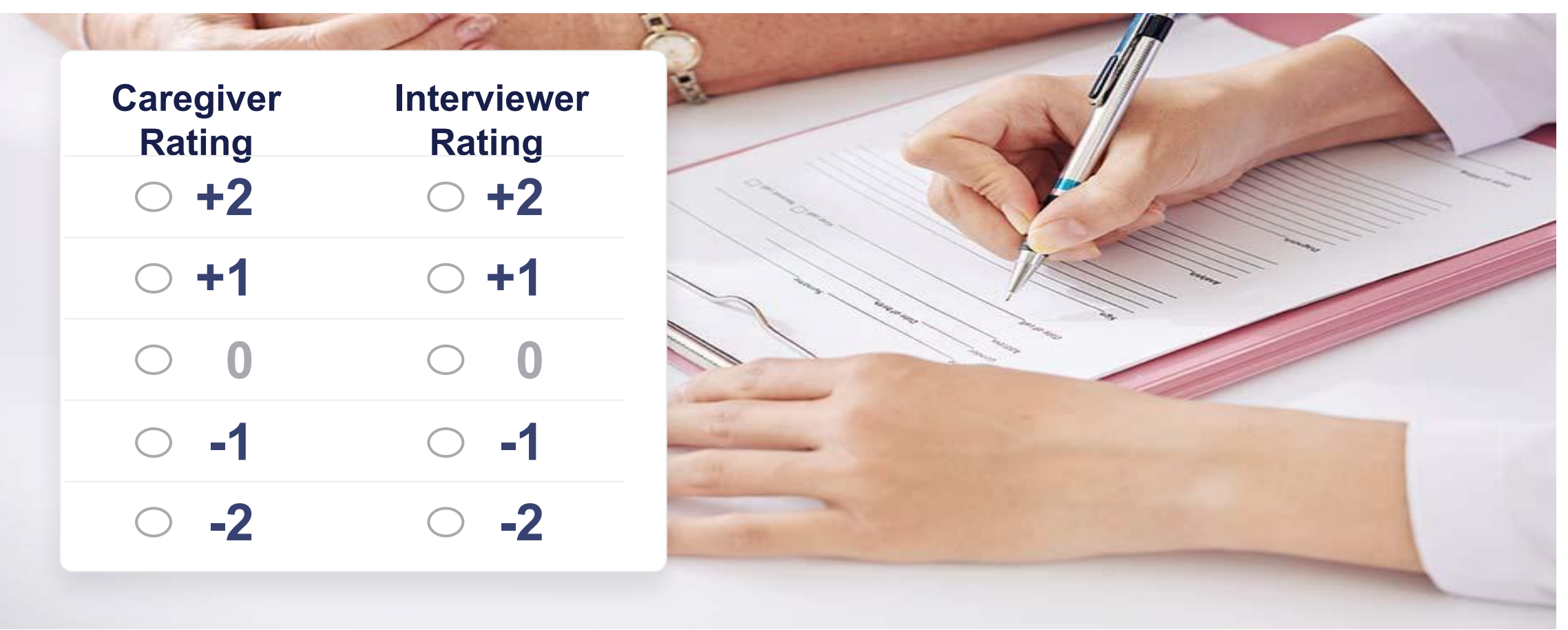
Identify Goals
Clinician facilitates interview with participant to identify goals

Build GAS Scales
Clinician and participant develop the 5-point scale for each identified goal

Measure & Score Attainment
Clinician and participant each rate at follow-up Calculate overall attainment.

Goal attainment was assessed during two subsequent follow-up interviews at Month 3 and Month 16.

The Follow-Up Visits



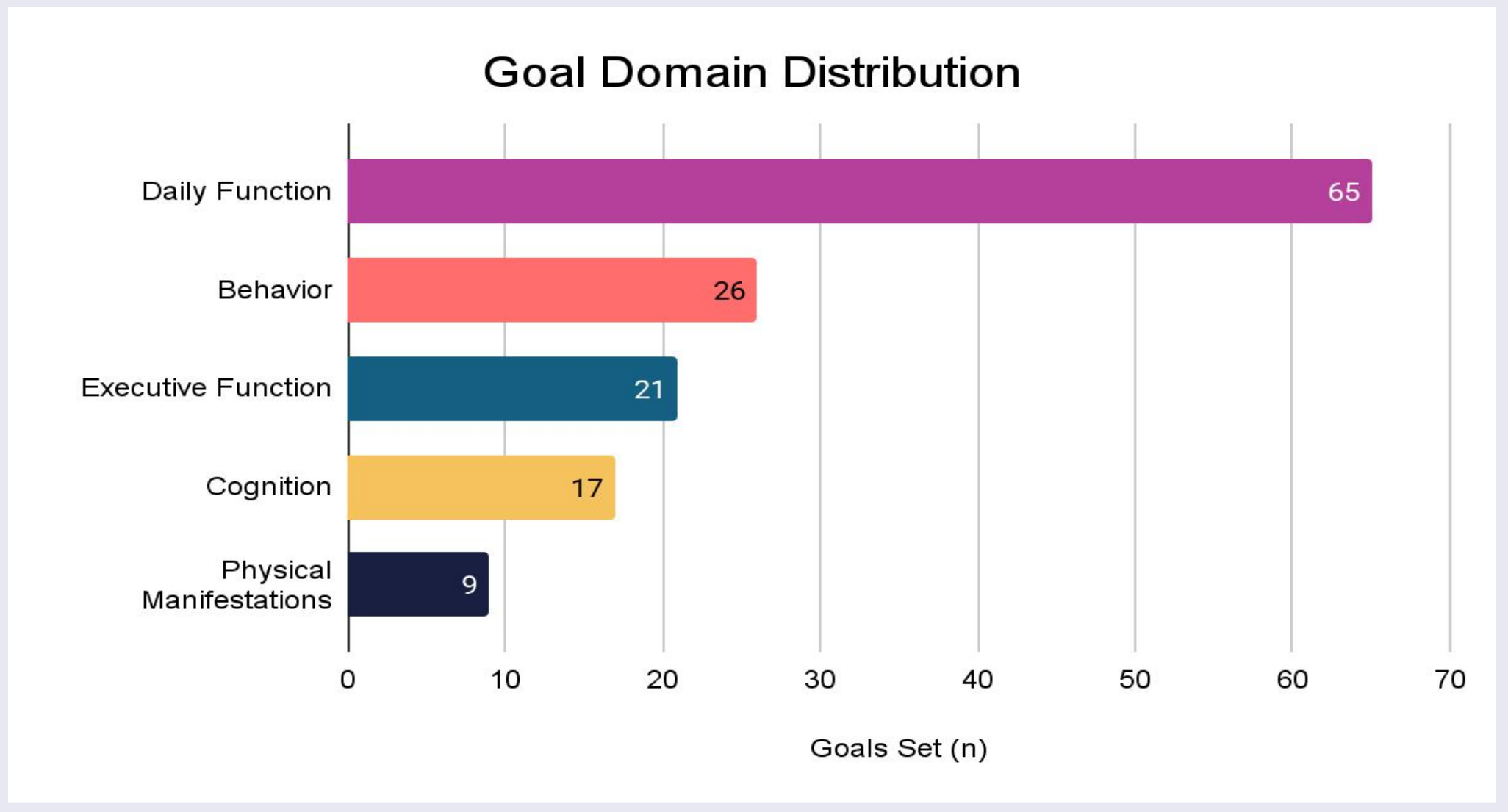
Feasibility indicators included the number of goals set, data completeness, and the time required to complete the GAS interviews. **Acceptability** was assessed via end-of-study surveys completed by caregivers and GAS interviewers.

▶ Results

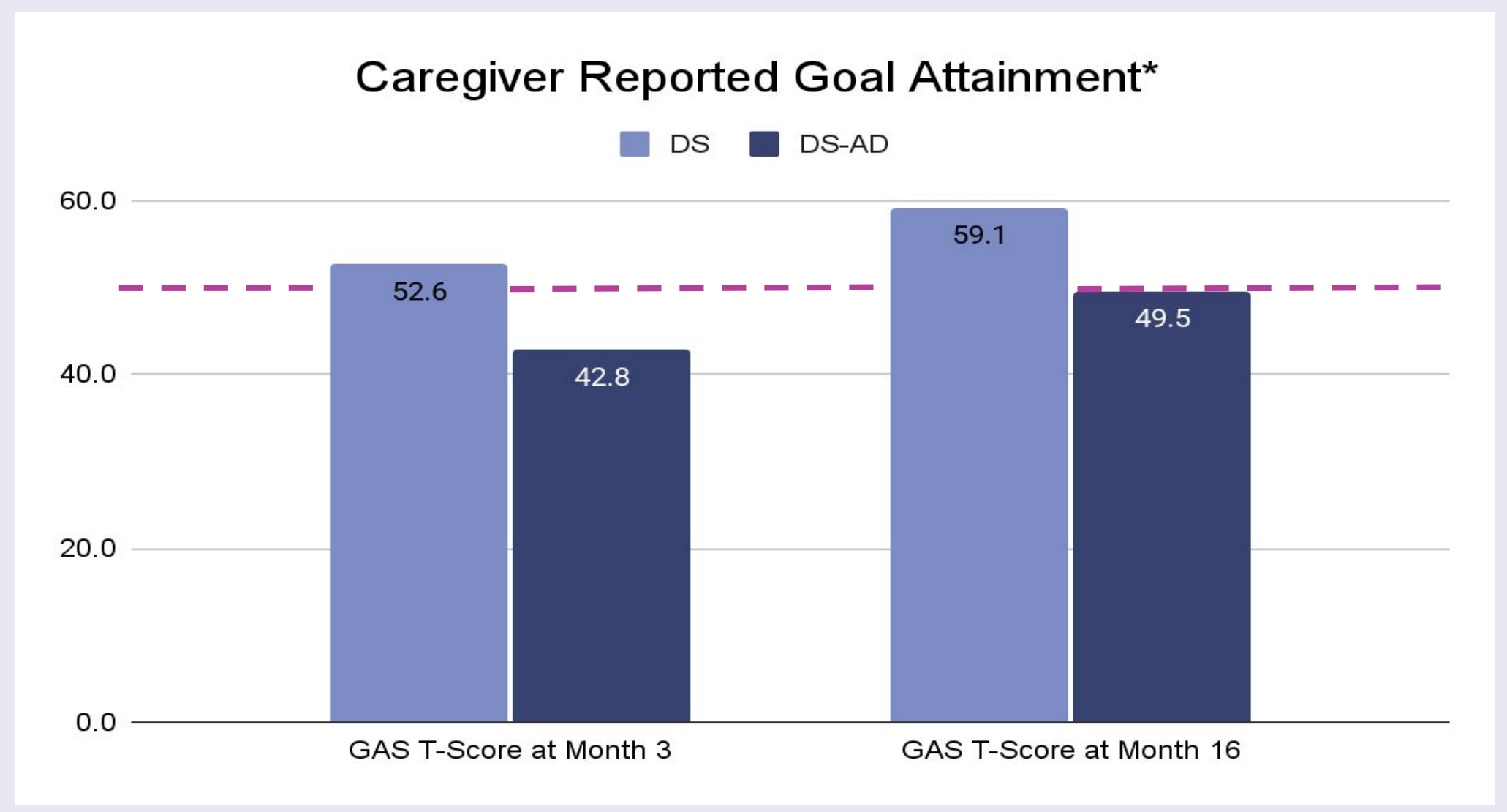
A total of 46 participants with DS and their caregivers enrolled in the study and completed the baseline visit at Month 0. Follow-up completion rates were high: 45/46 (Month 3) and 43/46 (Month 16), reflecting low attrition (2.2% and 6.5%).

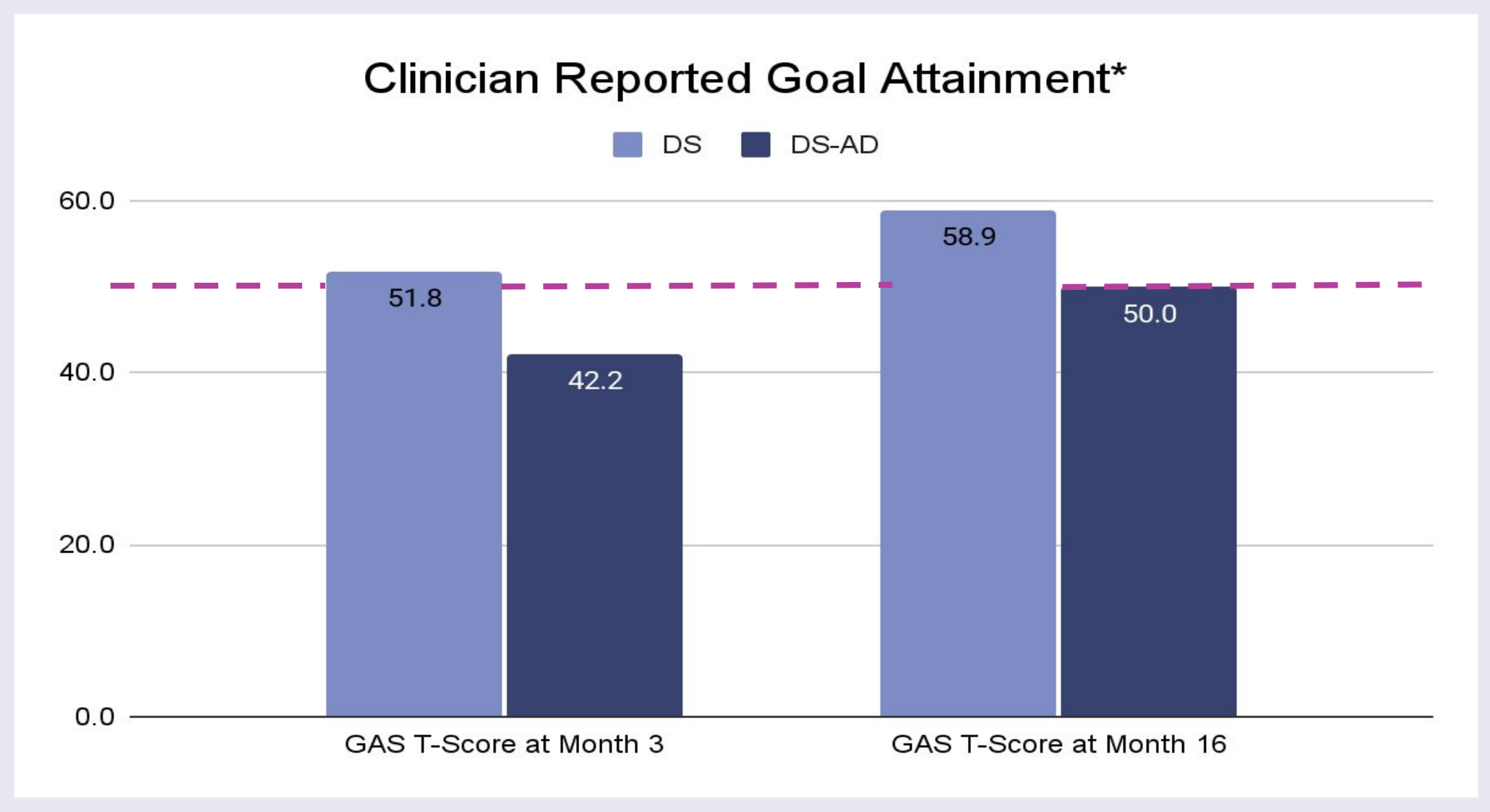
The mean time for the initial goal-setting interview was 38.6 (±10.4) minutes. Subsequent follow-up interviews required significantly less time, with mean times of 17.9 (±9.5) minutes at Month 3 and 14.5 (±4.7) minutes at Month 16.

Of the 46 enrolled participants, all caregivers (100%) successfully set a minimum of 3 goals, each with a 5-level scale.Participants set goals in all five domains, most frequently in daily function domain(n=65, 47%).



The number of individuals reporting an AD diagnosis increased from 7 at baseline to 10 at month 16. For those with DS-AD, caregiver reported GAS T-Scores indicated a lower rate of goal attainment (T% ≥50; 29% and 40%) compared to individuals with DS (T% ≥50; 68% and 79%) at Month 3 and Month 16, respectively. Similar trends were observed for Clinician-reported GAS T-scores; (T% ≥50; 14% and 40%) compared to individuals with DS (T% ≥50; 68% and 76%) at Month 3 and Month 16 respectively.





*A score of 50 represents goal achievement for all goals.

Survey results from 33 caregivers indicated a high degree of acceptability. A majority of caregivers reported positive experiences with the GAS process (n=31, 94%), found the goals they selected to be highly meaningful (n=31, 94%), and valued the improved communication with clinicians that the process facilitated (n=30, 91%). A significant number also reported gaining new perspectives and knowledge regarding their loved one's condition and care needs (n=10, %30).

▶ Results

Qualitative results sample: Caregiver Perspective

Theme 1: GAS Enhanced Communication and Fostered Shared Understanding with Clinicians

"It's helped us effectively communicate our child's needs and has helped us keep track of things that need improvement." (DSR2030057)

Theme 2: Goals Were Practical, Life-Relevant, and Aimed at Long-Term Well-Being

"Their everyday goals useful for [the subject]." (DSR2010052)

Theme 3: GAS was Informative, Enhancing Caregiver Understanding and Awareness

"Made [caregiver] look into how they care for participant, re-evaluate strategies." (DSR9060194)

Theme 4: GAS Helped Identify Priorities and Enhanced Caregiver Engagement

"Help us focus on what we should be working on." (DSR2010180)

Theme 5: A Sense of Achievement and Satisfaction Through GAS

"Was able to express the goals that [the participant] had and pursue it. Meaningful and rewarding to see them complete the goal." (DSR2010050)

*Clinician participation in the end-of-study surveys was too limited to allow for meaningful analysis and is therefore not reported here.

▶ Discussion & Conclusion

This study demonstrates that a standardized, inventory-facilitated Goal Attainment Scaling protocol is both feasible and acceptable for assessing patient-centric outcomes in the DS-AD population. The high rates of data completeness and strong positive feedback from caregivers suggest that this methodology can provide a robust and meaningful approach for measuring individualized treatment effects.

These findings support the use of GAS as a valuable outcome measure in future clinical trials aimed at evaluating the efficacy of new therapies for Down syndrome associated Alzheimer's disease.

▶ Acknowledgements & References

Hartley D et al. Alzheimers Dement 2015;11(6):700–709. doi:10.1016/j.jalz.2014.10.007

Knox K et al. Alzheimers Dement 2020;16:e043046. doi:10.1002/alz.043046

Knox K et al. J Patient Rep Outcomes 2021;5(1):5. doi:10.1186/s41687-020-00278-7

Lott IT, Head E. Nat Rev Neurol 2019;15(3):135–147. doi:10.1038/s41582-018-0132-6

Morel T, Cano SJ. Orphanet J Rare Dis 2017;12(1):171. doi:10.1186/s13023-017-0718-x