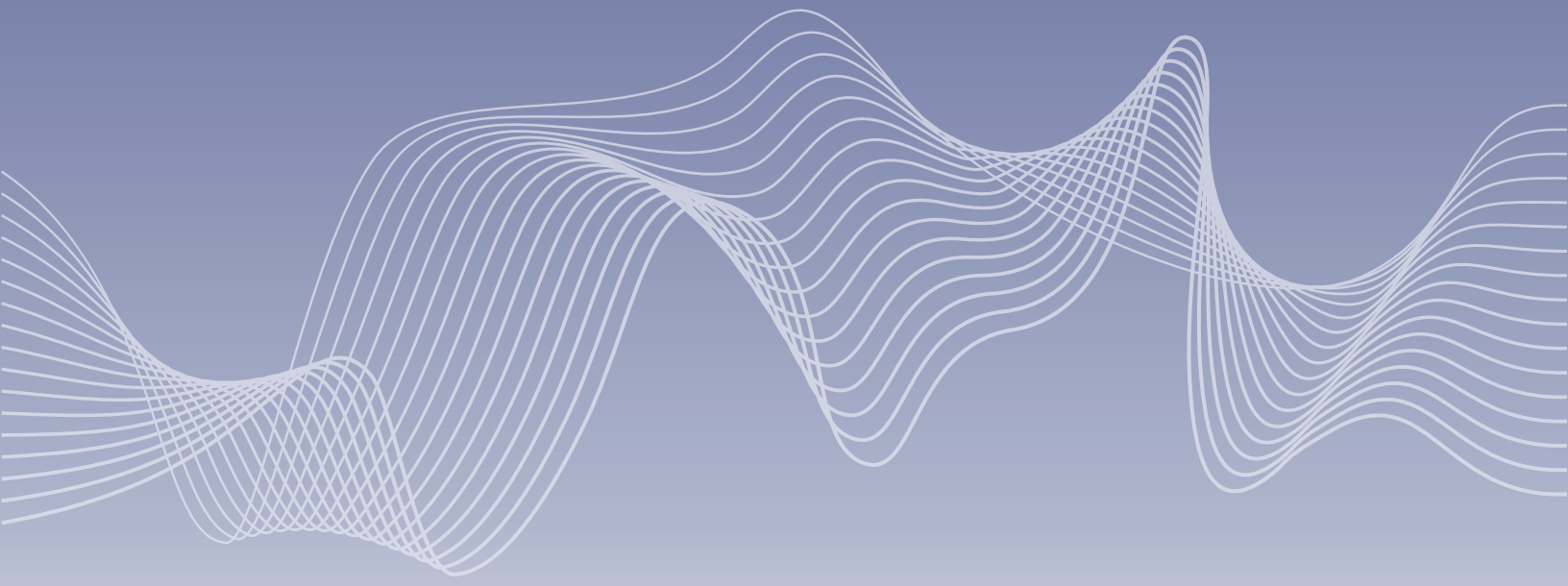
ARDEA OUTCOMES

White Paper

The Value of Personalized Outcome Assessment: Goal Attainment Scaling (GAS) in Patient-Focused Drug Development

Transforming Reimbursement Decisions in Alzheimer's Disease - A Case from Canada



Introduction

Pharmaceutical companies are increasingly investing in clinical development programs that hold promise for addressing complex and heterogeneous conditions. Yet, a persistent challenge remains: traditional clinical outcome assessments (COAs) often fail to capture changes that are meaningful to patients and their families. Standardized instruments, while valuable for comparability across trials, can miss individual priorities and dilute signals of treatment benefit by blending affected and unaffected symptoms.

Personalized outcome assessment—particularly Goal Attainment Scaling (GAS) offers a compelling solution. Unlike other endpoint strategies, GAS does not require identification of an endpoint for each aspect of health, selection of a multicomponent endpoint, or definition of thresholds. Instead, it anchors assessment in personal goals around impacted symptoms that matter most to individual patients, caregivers, and clinicians.

Several features highlight the unique value of GAS in patient-focused drug development:

- Clinically meaningful and patient-centric: GAS is inherently tailored to each patient's experience, ensuring outcomes are meaningful and directly relevant to the individual rather than arbitrary or externally imposed.
- Highly responsive: By centering evaluation on the specific areas identified at baseline, GAS avoids diluting the treatment effects across irrelevant symptoms. This responsiveness enhances sensitivity to change, even in small and heterogeneous patient populations.
- Flexible and scalable: GAS can be applied across diverse conditions and trial phases, reducing the burden of developing new disease-specific instruments while preserving rigor in outcome assessment.

In an era where regulatory agencies and stakeholders increasingly emphasize patient-focused drug development, GAS represents a practical and scientifically robust method to bridge the gap between clinical efficacy and real-world relevance.

What is Goal Attainment Scaling?

GAS is a personalized endpoint that quantifies the impact of an intervention on individualized goals. Clinicians, in partnership with the patient and/or caregiver, identify meaningful goals and develop unique scales tailored to each treatment goal. The process begins by defining what "treatment success" looks like from the patient's perspective and selecting priority goal areas.

For each goal area:

- Baseline status is recorded at –1
- The expected outcome (what success would reasonably look like) is set at 0
- Further levels are defined as +1 ("somewhat more than expected"), +2 ("much more than expected"), and -2 ("much less than expected")

This structured process ensures that goals are SMART (specific, measurable, achievable, realistic/relevant, and time-bound). Importantly, the scale is co-created through dialogue between the clinician and patient, embedding the patient perspective at the heart of outcome measurement.

Priority is given to treatment goals that are meaningful to the patient, relevant to the therapeutic area, and likely to be impacted by the intervention. In addition to being specific, measurable, realistic, and relevant to the patient's condition and treatment, these goals are aligned with the timeframe of the proposed investigation, and the goal scales possess appropriate psychometric properties.

At the prespecified follow-up visit or visits, goal attainment is scored using the 5-point scale for each goal area. At the end, a standardized formula is used to calculate attainment scores across multiple goals, accounting for the differing number of goals across patients.

How GAS Works?

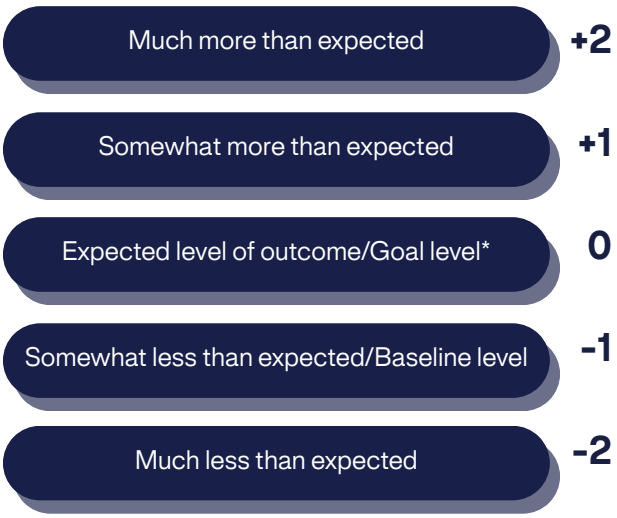
Goal Setting

Identify Goals: The clinician facilitates with the patient and/or caregiver

Build GAS Scales: Together they develop a 5-point goal attainment scale for each identified goal, starting with a baseline scaled at -1, the targeted goal at 0, followed by setting all the other outcomes.

Follow-Up: Scoring Goal Attainment

Obtain Current Status: The patient and clinician discuss the patient's current status concerning each goal area.
Measure Achievement: The patient and clinician rate the level of attainment for each goal.



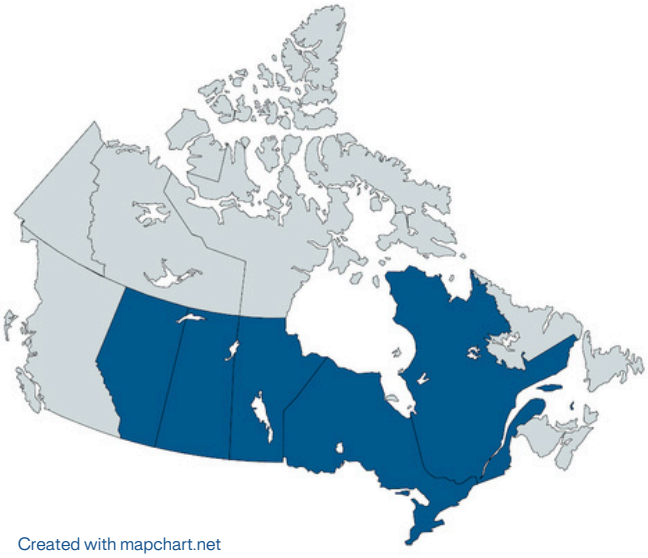
Advocating for Reimbursement Using Personalized Outcome Assessment: Goal Attainment Scaling

GAS and Drug Reimbursement Decisions: A Case Study on Alzheimer's Disease

Drug developers face two major hurdles in gaining market access for new treatments. Regulatory approval, granted by bodies like the FDA and EMA, requires extensive clinical testing and adherence to safety and efficacy standards, but does not guarantee market access alone. Companies must also be successful in health technology appraisals that demonstrate cost-effectiveness and secure reimbursement in each country. Recently developed disease-modifying therapies for Alzheimer's disease (AD) have faced challenges both with regulatory approval and reimbursement in different jurisdictions.

Whilst by no means unique to AD, the parallels to challenges faced during the development of symptomatic therapies for AD, and the evaluation of data from clinical outcome assessments in these reviews, is instructive. When cholinesterase inhibitors, including galantamine, were being assessed for their impact on patients with mild to moderate AD, while they eventually were deemed an evidence-based method to delay decline in cognitive function, the significance and clinical meaningfulness of these changes were questioned.

In Canada, the approval and reimbursement landscape for cholinesterase inhibitors was initially challenging. Donepezil became the first AD treatment approved in 1997, followed by rivastigmine and galantamine in subsequent years. However, early results on efficacy were met with skepticism, and by 2002, only five of Canada's ten provinces had agreed to reimburse these drugs.



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VISTA Trial

Between November 2001 and July 2004, the randomized controlled trial (RCT) of galantamine (VISTA: Video-Imaging Synthesis of Treated Alzheimer's disease) used Goal Attainment Scaling (GAS) to gauge treatment outcomes, revealing significant improvements in clinician-rated goal attainment, as well as cognitive measures such as ADAS-cog and CIBIC-plus.

These findings helped to demonstrate that galantamine not only produced statistically significant effects but also helped patients to meaningfully meet the treatment goals identified through a dialogue between the patients (their caregivers) and clinicians, offering a clearer picture of its benefit to patients.

Methods

Participants	130 patients with mild to moderate Alzheimer's
Sites	14 Canadian Sites
Study Type	Randomized Controlled Trial (RCT)
Groups	- Galantamine (n = 64) - Placebo (n = 66)
Duration	- 4 months: galantamine or placebo - 4 months: all received galantamine (open-label)
Primary Outcomes	Goal Attainment Scaling (GAS) by clinicians and patients/caregivers
Secondary Outcomes	ADAS-cog (to measure cognitive function), CIBIC-plus (clinician and caregiver impressions of change), DAD (daily functioning), CBS (caregiver burden)

Results

Sample size	Out of 130 patients, 128 were analyzed.
Primary Outcomes	Clinician ratings suggested that those taking galantamine improved more than placebo. Patient and caregiver ratings suggested that the galantamine group improved, but not statistically significant more than the placebo.
Secondary Outcomes	ADAS-cog and CIBIC-plus scores showed significant improvement to cognition and overall impression of change. No significant changes were found in daily functioning (DAD) or caregiver burden (CBS).

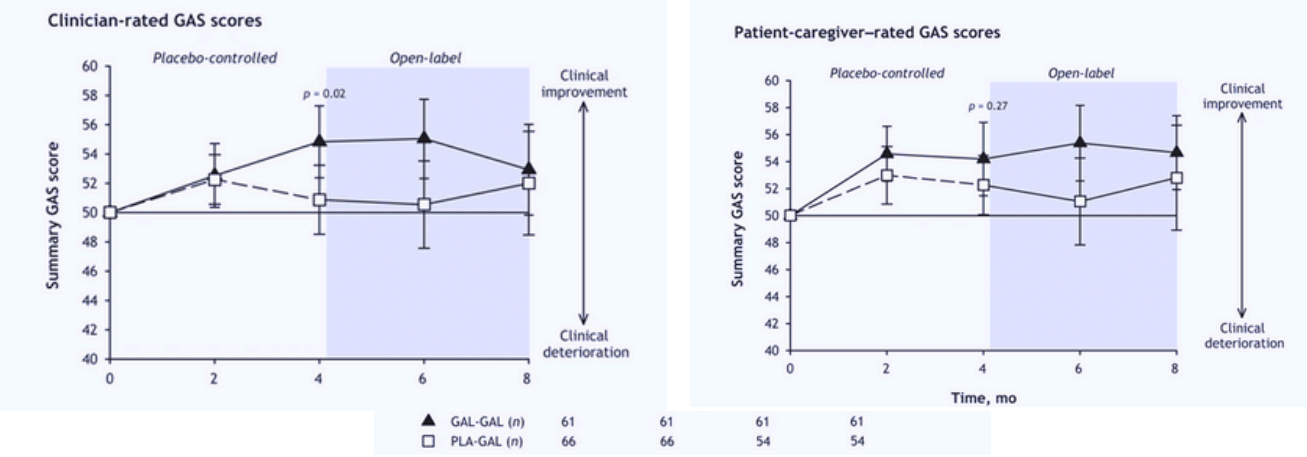

Fig.1 shows the Mean change in GAS (Goal Attainment Scaling) scores among patients with mild to moderate Alzheimer's disease, by treatment group. Top panel: clinician-rated GAS scores. Bottom panel: patient-caregiver-rated GAS scores. Error bars represent 95% confidence intervals. GAL-GAL (black triangles) = patients who received galantamine during both the placebo-controlled phase (months 0–4) and the open-label phase (months 4–8); PLA-GAL (white squares) = patients who received placebo during the placebo-controlled phase and galantamine during the open-label phase. (Missing data were imputed based on the last observation carried forward, excluding baseline data; for comparing groups in the open-label phase, only observations in the galantamine group during the placebo-controlled phase were carried forward.)

The VISTA trial helped prove the real-world value of treatment by using patient-centered goals.

ACADIE Trial

Conducted between 2002 and 2003, the ACADIE study was a 12-month, open-label trial assessing donepezil in real-world Alzheimer's patients using Goal Attainment Scaling (GAS). Patients, caregivers, and clinicians set individualized goals across five domains.

Early improvements were seen, especially in behavioral goals, but gains declined over time. While traditional measures showed only modest cognitive benefit, the study highlighted the importance of patient-centered outcomes in evaluating treatment success.

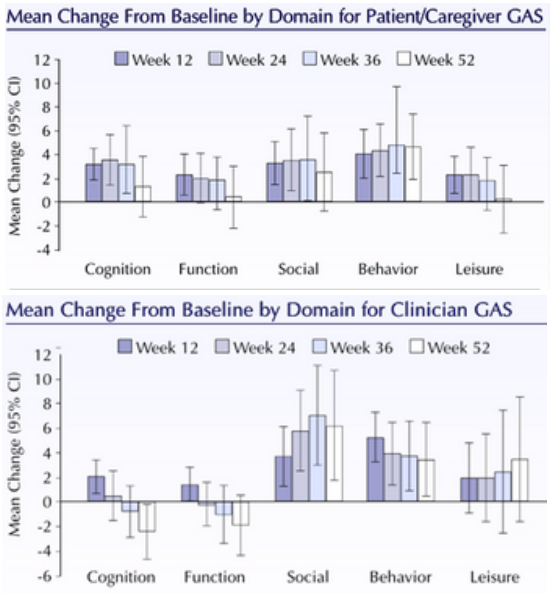

Fig 2. Shows mean change (95% CI) from baseline by domain for patient/caregiver rated GAS. Mean change (95% CI) from baseline by domain for clinician-rated GAS.

ACADIE Trial

Methods

Participants	108 patients with mild-to-moderate Alzheimer's disease
Sites	Six sites across Atlantic Canada
Study Type	Open-label, real-world trial (no placebo group)
Intervention	Donepezil: 5 mg/day for 12 weeks → 10 mg/day (82% of patients)
Duration	- 12 months, Phase IV Trial
Primary Outcomes	Goal Attainment Scaling (GAS) by patients, caregivers, and physicians
Secondary Outcomes	ADAS-cog, MMSE, CIBIC-plus, function, and depression assessments

Results

Sample size	Out of 130 patients, 128 were analyzed.
Primary Outcomes	Clinician ratings suggested that those taking galantamine improved more than placebo at Week 24, but this was not significant at Week 52. Patient and caregiver ratings suggested that the galantamine group improved more than the placebo group, especially in the first 6-9 months.
Secondary Outcomes	ADAS-cog and MMSE showed significant improvement in cognition at Week 12, and decline at Week 52. No significant lasting improvements were found in daily functioning (notably, IADLs declined after initial maintenance), standard cognitive scores after Week 12, and sustained clinician-rated outcomes beyond the early months

Impact on Reimbursement Decisions

Following the evidence from the VISTA RCT trial and the ACADIE open-label trial, the four provinces of Atlantic Canada (NS, PEI, NB, NL) revisited their stance. They made key decisions regarding reimbursement for AD treatments.

They established key criteria for reimbursement, which include:

- Patients who maintained a Mini-Mental State Examination (MMSE) scored greater than 12 out of 30
- Patients who exhibited symptomatic treatment effects, as assessed by their treating physician, at three months, six months, and annually thereafter, with a minimum of three specific goals. These goals could be reset annually.

These criteria, grounded in clinical data, provided a clear, structured framework that facilitated broader reimbursement coverage for patients with Alzheimer's disease. This ensured access to effective treatments for those who showed measurable improvements in goal attainment and cognitive function.

Paralleling these challenges, in the draft guidance for lecanemab produced by the National Institute for Health and Care Excellence (NICE), in England, substantial discussion was given to the meaningfulness of treatment effect on the Clinical Dementia Rating – Sum of Boxes (CDR-SB).

This included debate regarding the minimum clinically important difference (MCID), the impact of heterogeneity in disease progression as measured by the CDR-SB, its lack of sensitivity in early disease, the meaningfulness of delay in time to progression, and that the CDR is not used in clinical practice. Thus, comparable challenges remain for the current crop of AD disease-modifying therapies, some of which might also be addressed by GAS.

Conclusion

Adapting novel clinical outcome assessments, such as goal attainment scaling—a personalized outcome assessment that quantifies the impact of an intervention on individualized goals—may increase the chances of success for clinical development programs, inform reimbursement decisions, and ultimately improve health outcomes.

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