Development and Validation of a Patient-Centered Outcome Measure for use in Dementia Drug Trials

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SUMMARY

- We developed SymptomGuide® Dementia, a clinical outcome measure (COA) based on Goal Attainment Scaling (GAS) theory.
- SymptomGuide® Dementia lets patients and care partners use a semi-standardized menu to choose and track symptoms important to them.
- SymptomGuide® Dementia operates as a valid and responsive endpoint in clinical trials.

INTRODUCTION

- Are modest changes in traditional endpoints from dementia drug trials clinically meaningful to patients, their caregivers, regulators and payers?
- Tracking personalized symptoms robustly allows identification of relevant and non-arbitrary treatment effects.

AIM

- To review the development and validation of an endpoint that allows for individualized symptom tracking in dementia drug trials by caregivers.

METHODS

The SymptomGuide® Dementia (SG-D) menu was developed from qualitative analysis of goals set by patients, caregivers and clinicians using GAS (**Figure 1**) in:

- The Video Imaging Synthesis of Treating Alzheimer disease (VISTA) galantamine trial,
- Atlantic Canada Alzheimer Disease Investigation of Expectations (ACADIE) donepezil trial and,
- Patients from a memory clinic in Halifax, Nova Scotia

The final SG-D **contained a menu of 61 dementia symptoms, each with 8-12 descriptions**.

The SG-D was used in:

- An online platform (www.dementiaguide.com)
- A memory clinic in Halifax, Nova Scotia
- The VASPECT clinical trial

These data allowed us to test for feasibility, validity and responsiveness.

RESULTS

Evidence for Validity

Content Validity:
The SG-D content was reviewed by:

- Alzheimer's Society group leaders,
- Memory clinic nurses,
- Geriatricians, and
- Geriatric psychiatrists

Face Validity:
SG-D was used as a secondary outcome measure in VASPECT, a phase IV trial of donepezil in mild-moderate Vascular or mixed Alzheimer's disease/Vascular dementia.
By using semi-standardized menus, respondents in all three data sets often tracked multiple symptoms (**Table 1**), the most common of which being "Recent Memory" (**Figure 2**).

Feasibility:
Of the 108 subjects with SG-D scores who completed the VASPECT trial, 102 had valid SG-D data (completion rate 94.4%) vs. 97.5% for other measures (range 94.0-100%).

Construct Validity:
The mean SG-D symptom rating correlated with global change in VASPECT. SG-D total scores correlated notionally with change in other outcome measures (**Figure 3**).

- Clinical Global Impression-Improvement (CGI-I): rho=-0.64
- Mini-Mental State Examination (MMSE): r=0.37
- Neuropsychiatric Inventory-Questionnaire (NPI-Q): r=-0.38
- Disability Assessment for Dementia (DAD): r=0.30

Sensitivity to Change:
Compared to other measures, the SG-D showed the same or better responsiveness in VASPECT (**Figure 4**).
Standardized Response Means

- SG-D: 0.30
- MMSE: 0.22
- NPI-Q: -0.29

CONCLUSIONS

SymptomGuide® Dementia is an inherently clinically meaningful outcome measure that is valid and responsive. SymptomGuide® Dementia is feasible for use as an endpoint in dementia trials.

Figure 1. SymptomGuide® Dementia menu development

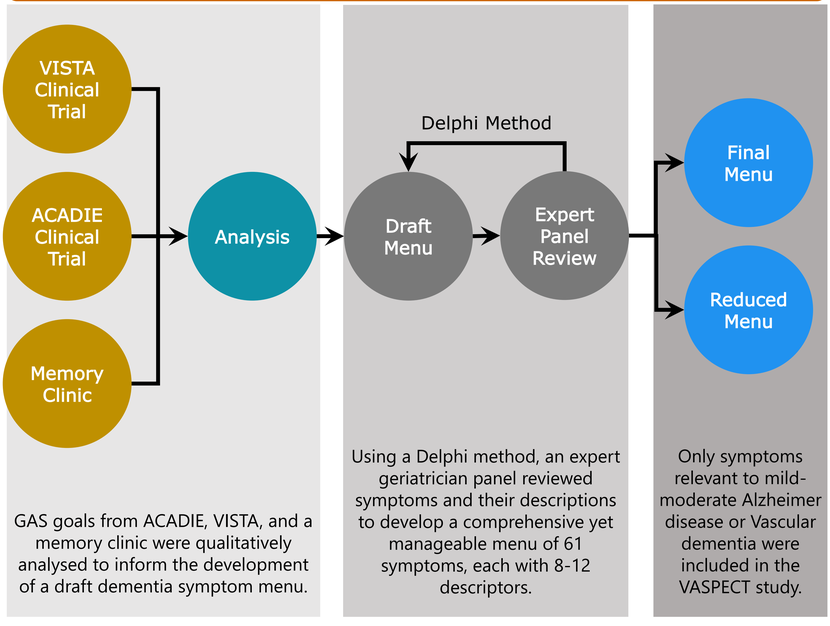


Table 1. SymptomGuide® Dementia user characteristics

Characteristic	Online	Clinic	VASPECT[1]
Sample size (N)	3740	422	148
Mean (SD) **Age**	75.3 (13.3)	74.9 (11.5)	75 (9.4)
% **Women**	63%	55%	55%
% **Alzheimer disease**	72%	83%	48%
Mean (SD) **MMSE**	N/A	22.4 (6.4)	23.4 (4.4)
Mean (SD) symptoms tracked	5.5 (5.1)	4.8 (2.2)	6.7 (5.4)

[1]VASPECT: six-month open-label trial of donepezil in mild-moderate Vascular dementia or mixed Alzheimer disease/Vascular dementia
Abbreviations: Mini-Mental State Examination (MMSE), standard deviation (SD)

Figure 2. Most commonly reported SymptomGuide® Dementia symptoms

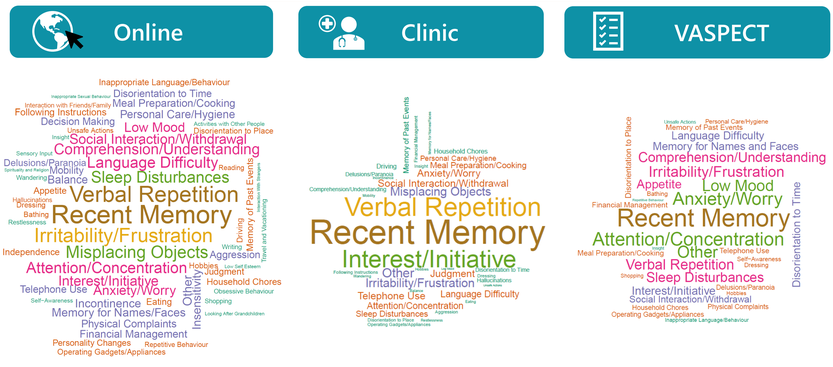


Figure 3. In VASPECT, SymptomGuide® Dementia change scores were highly correlated with six-month change in other outcome measures.

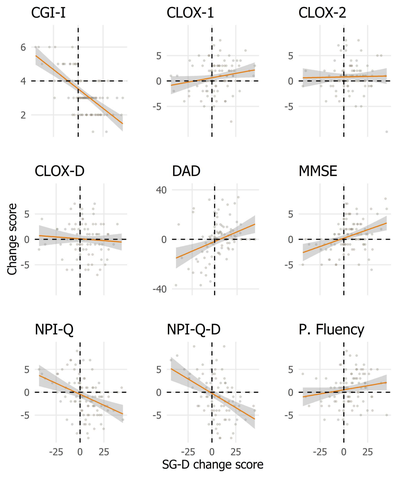
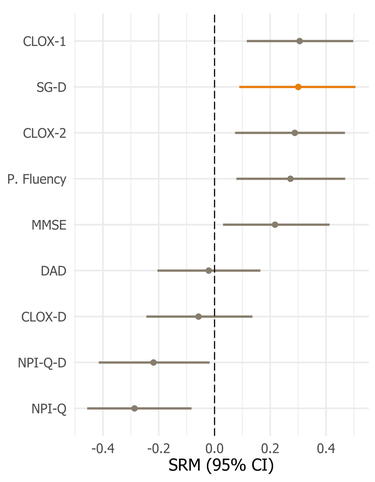


Figure 4. SymptomGuide® Dementia was responsive (six-month Standardized Response Mean; SRM).



Left: lines indicate best-fit linear relationship (95% CI) between change scores at six months.
Right: error bars indicate 95% CI from 2000 bootstrap resamples.
Abbreviations: Clinical Global Impression scale (CGI-I), Executive Clock Drawing Task (CLOX-1, CLOX-2 and CLOX-D), Disability Assessment for Dementia (DAD), Mini-Mental State Examination (MMSE), Neuropsychiatric Inventory (NPI-Q and NPI-Q-D), and Phonetic Fluency (P. Fluency).