How useful are EQ-5D and ZBI in assessing the impact of caring for people with Alzheimer’s disease?

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Caring for a person with Alzheimer’s disease (AD) can have a physical, emotional, social and financial impact that may be reflected in health-related quality of life (HRQoL).

However when measured using the EQ-5D, one of the most widely used generic scales, caregiver HRQoL does not always vary by AD severity and has poor associations with HRQoL in people with AD.

Caregiver burden is an alternative multidimensional construct (e.g. Zarit Burden Interview) that has been associated with AD severity.

As the available studies of caregiver HRQoL and burden have inconsistent results, further understanding of the relationship between these caregiver measures is needed.

Objectives

♦ To examine correlations between EQ-5D scores with ZBI and caregiver T-IADL, and assess longitudinal changes in ZBI scores and T-IADL by changes within EQ-5D domains over 18 months within the caregiver population in the GERAS study
Methods

Study Design

♦ GERAS was an 18-month, prospective, multicentre, observational cohort study designed to evaluate the costs and resource use associated with AD dementia for people with AD and their caregivers in Germany, France and the UK\(^1\)

♦ Inclusion criteria were community-dwellers aged ≥55 years with probable AD according to NINCDS-ADRDA criteria\(^2\), who presented during the normal course of care and had a Mini-Mental State Examination (MMSE) score\(^3\) of ≤26 and with an informal caregiver

♦ Stratification was according to MMSE score at baseline: mild (21–26 points), moderate (15–20 points) or moderately severe/severe (MS/S) AD dementia (≤14 points)

♦ Data were collected at baseline and at 6, 12 and 18 months during routine care visits

## EuroQoL (EQ-5D)

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

### Mobility
- I have no problems in walking about
- I have some problems in walking about
- I am confined to bed

### Self-Care
- I have no problems with self-care
- I have some problems washing or dressing myself
- I am unable to wash or dress myself

### Usual Activities (e.g. work, study, housework, family or leisure activities)
- I have no problems with performing my usual activities
- I have some problems with performing my usual activities
- I am unable to perform my usual activities

### Pain/Discomfort
- I have no pain or discomfort
- I have moderate pain or discomfort
- I have extreme pain or discomfort

### Anxiety/Depression
- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed
To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.
### Zarit Burden Interview (ZBI)

Please circle the response that best describes how you feel.

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Quite Frequently</th>
<th>Nearly Always</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you feel that your relative asks for more help than he/she needs?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>2. Do you feel that because of the time you spend with your relative that you don’t have enough time for yourself?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>3. Do you feel stressed between caring for your relative and trying to meet other responsibilities for your family or work?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>4. Do you feel embarrassed over your relative’s behaviour?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>5. Do you feel angry when you are around your relative?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>6. Do you feel that your relative currently affects our relationships with other family members or friends in a negative way?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>7. Are you afraid what the future holds for your relative?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>8. Do you feel your relative is dependent on you?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>9. Do you feel strained when you are around your relative?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>10. Do you feel your health has suffered because of your involvement with your relative?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>11. Do you feel that you don’t have as much privacy as you would like because of your relative?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>12. Do you feel that your social life has suffered because you are caring for your relative?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>13. Do you feel uncomfortable about having friends over because of your relative?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

1.1.2 Caregiver Time

1a). On a typical care day during the last month, how much time per day did you assist the patient with tasks such as toilet visits, eating, dressing, grooming, walking and bathing? __________ hours per day

1b). During the last month, how many days did you spend providing these services to the patient? __________ days

2a). On a typical care day during the last month, how much time per day did you assist the patient with tasks such as shopping, food preparation, housekeeping, laundry, transportation, taking medication, and managing financial matters? __________ hours per day

2b). During the last month, how many days did you spend providing these services to the patient? __________ days

3a). On a typical care day during the last month, how much time per day did you spend supervising (that is, prevent dangerous events) the patient? __________ hours per day

3b). During the last month, how many days did you spend providing these services to the patient? __________ days

Statistical Analyses

♦ Baseline characteristics and EQ-5D domains of caregivers at baseline and 18 months were summarised using descriptive statistics based on non-missing observations.

♦ Comparisons between AD severity groups for caregiver EQ-5D (index score and VAS), ZBI and T-IADL used analysis of variance (ANOVA) with country and baseline MMSE severity as independent factors.

♦ Spearman correlation coefficients examined associations between EQ-5D (index score and VAS), ZBI and T-IADL at baseline and 18 months, and the change from baseline to 18 months.

♦ The change in caregiver ZBI total score or T-IADL over 18 months was examined by any change in each of the EQ-5D domains, categorised as better, stable or worse.
### Characteristics at Baseline by AD Severity

**Caregivers**

<table>
<thead>
<tr>
<th></th>
<th>Overall N=1495</th>
<th>Mild AD N=566</th>
<th>Moderate AD N=472</th>
<th>MS/S AD N=457</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>958 (64.2)</td>
<td>387 (68.5)*</td>
<td>305 (64.6)*</td>
<td>266 (58.3)*</td>
</tr>
<tr>
<td>Age, mean (SD) years</td>
<td>67.3 (12.0)</td>
<td>68.1 (11.6)</td>
<td>66.7 (11.7)</td>
<td>67.0 (12.9)</td>
</tr>
<tr>
<td>Relationship to pAD, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spouse</td>
<td>984 (65.9)</td>
<td>399 (70.6)*</td>
<td>298 (63.1)*</td>
<td>287 (62.9)*</td>
</tr>
<tr>
<td>Child</td>
<td>405 (27.1)</td>
<td>133 (23.5)</td>
<td>136 (28.8)</td>
<td>136 (29.8)</td>
</tr>
<tr>
<td>Other</td>
<td>104 (6.9)</td>
<td>33 (5.8)</td>
<td>38 (8.1)</td>
<td>33 (7.2)</td>
</tr>
<tr>
<td>Lives with pAD, n (%) yes</td>
<td>1135 (76.0)</td>
<td>429 (75.9)*</td>
<td>341 (72.2)*</td>
<td>365 (80.0)*</td>
</tr>
<tr>
<td>Caregivers with medical conditions, n (%)</td>
<td>875 (58.6)</td>
<td>344 (60.8)</td>
<td>272 (57.6)</td>
<td>259 (56.8)</td>
</tr>
<tr>
<td>Number of medical conditions, mean (SD)</td>
<td>1.1 (1.2)</td>
<td>1.2 (1.2)*</td>
<td>1.0 (1.1)*</td>
<td>1.0 (1.2)*</td>
</tr>
<tr>
<td>Working for pay, n (%)</td>
<td>355 (23.8)</td>
<td>133 (23.5)</td>
<td>120 (25.4)</td>
<td>102 (22.4)</td>
</tr>
</tbody>
</table>

**People with AD**

<table>
<thead>
<tr>
<th></th>
<th>N=1495</th>
<th>N=566</th>
<th>N=472</th>
<th>N=457</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>819 (54.8)</td>
<td>271 (47.9)*</td>
<td>269 (57.0)*</td>
<td>279 (61.1)*</td>
</tr>
<tr>
<td>Age, mean (SD) years</td>
<td>77.6 (7.6)</td>
<td>77.3 (6.9)</td>
<td>77.8 (8.0)</td>
<td>77.6 (8.1)</td>
</tr>
<tr>
<td>Time since diagnosis of AD, mean (SD) years</td>
<td>2.2 (2.2)</td>
<td>1.7 (2.0)*</td>
<td>2.1 (2.0)*</td>
<td>3.1 (2.4)*</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td>1101 (73.6)</td>
<td>426 (75.3)</td>
<td>345 (73.1)</td>
<td>330 (72.2)</td>
</tr>
<tr>
<td>Number of comorbidities, mean (SD)</td>
<td>1.4 (1.2)</td>
<td>1.5 (1.2)</td>
<td>1.4 (1.2)</td>
<td>1.4 (1.3)</td>
</tr>
</tbody>
</table>

*P<0.05 for differences between AD severity groups (ANOVA with country and AD severity as factors for continuous variables; Cochran-Mantel Haenzsel test with stratification by country for categorical variables)

AD = Alzheimer’s disease; MS/S = moderately severe/severe; SD = standard deviation

Baseline characteristics of caregivers and pADs were summarised based on non-missing observations.
Baseline EQ-5D Shows Only Small Changes with Greater AD Severity

<table>
<thead>
<tr>
<th>Caregiver Measure</th>
<th>n</th>
<th>Mean (SD)</th>
<th>Median (Q1, Q3)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQ-5D index score</td>
<td>1483</td>
<td>0.84 (0.20)</td>
<td>0.89 (0.79, 1.00)</td>
<td>0.043</td>
</tr>
<tr>
<td>Mild AD</td>
<td>560</td>
<td>0.86 (0.18)</td>
<td>0.89 (0.79, 1.00)</td>
<td></td>
</tr>
<tr>
<td>Moderate AD</td>
<td>469</td>
<td>0.85 (0.19)</td>
<td>0.89 (0.79, 1.00)</td>
<td></td>
</tr>
<tr>
<td>Moderately severe/severe AD</td>
<td>454</td>
<td>0.82 (0.23)</td>
<td>0.89 (0.73, 1.00)</td>
<td></td>
</tr>
<tr>
<td>EQ-VAS</td>
<td>1483</td>
<td>75.1 (17.5)</td>
<td>80.0 (65.0, 90.0)</td>
<td>0.013</td>
</tr>
<tr>
<td>Mild AD</td>
<td>560</td>
<td>75.8 (16.6)</td>
<td>80.0 (69.0, 89.0)</td>
<td></td>
</tr>
<tr>
<td>Moderate AD</td>
<td>469</td>
<td>76.3 (16.5)</td>
<td>80.0 (69.0, 90.0)</td>
<td></td>
</tr>
<tr>
<td>Moderately severe/severe AD</td>
<td>454</td>
<td>72.9 (19.2)</td>
<td>79.0 (60.0, 89.0)</td>
<td></td>
</tr>
<tr>
<td>ZBI total score</td>
<td>1485</td>
<td>29.0 (15.1)</td>
<td>28.0 (17.0, 40.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mild AD</td>
<td>560</td>
<td>24.6 (14.2)</td>
<td>22.0 (14.0, 33.0)</td>
<td></td>
</tr>
<tr>
<td>Moderate AD</td>
<td>471</td>
<td>29.4 (14.8)</td>
<td>29.0 (18.0, 39.0)</td>
<td></td>
</tr>
<tr>
<td>Moderately severe/severe AD</td>
<td>454</td>
<td>34.1 (14.8)</td>
<td>33.0 (22.0, 45.0)</td>
<td></td>
</tr>
<tr>
<td>Time for instrumental ADL (hours/month)</td>
<td>1493</td>
<td>79.3 (89.5)</td>
<td>60.0 (20.0, 120.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mild AD</td>
<td>565</td>
<td>61.0 (83.1)</td>
<td>36.0 (8.0, 90.0)</td>
<td></td>
</tr>
<tr>
<td>Moderate AD</td>
<td>472</td>
<td>77.5 (79.2)</td>
<td>60.0 (24.0, 120.0)</td>
<td></td>
</tr>
<tr>
<td>Moderately severe/severe AD</td>
<td>456</td>
<td>103.8 (101.1)</td>
<td>90.0 (40.0, 120.8)</td>
<td></td>
</tr>
</tbody>
</table>

*Comparisons between AD severity groups for caregiver EQ-5D, ZBI and caregiver time used analysis of variance (ANOVA) with country and baseline MMSE severity as independent factors.
Small Worsening in EQ-5D Index Score but not Significantly Different by AD Severity

-0.10
-0.08
-0.06
-0.04
-0.02
0.00
0.02
0.04
0.06

Change in EQ-5D Index Score from Baseline

Mild AD (n=396)

Moderate AD (n=304)

MS/S AD (n=233)

AD = Alzheimer’s disease; MS/S = moderate-severe/severe
EQ-5D index score uses a UK population-based preference weight. Data are presented as least square means with 95% CIs from ANCOVA of change from baseline. n value represents number of respondents. Change from baseline data missing for 10–12% of pAD across AD severity groups. EQ-5D Index score range = 0 (death) to 1.0 (perfect health).
Small Worsening in EQ-5D VAS but not Significantly Different by AD severity

AD = Alzheimer's disease; MS/S = moderate-severe/severe; VAS = visual analogue scale
Data are presented as least square means with 95% CIs from ANCOVA of change from baseline. n value represents number of respondents. Change from baseline data missing for 10–12% of pAD across AD severity groups. EQ-5D VAS score range = 0–100
Worsening ZBI Score Significantly different by AD Severity at Baseline

AD = Alzheimer’s disease; MS/S = moderate-severe/severe; VAS = visual analogue scale; ZBI = Zarit Burden Interview

Data are presented for all caregivers as least square means with 95% CIs from repeated measures analysis. Change from baseline data missing for 6–7%, 8–10% and 9–12% of caregivers across AD severity groups at 6, 12 and 18 months, respectively. New caregivers (n=9) were excluded. ZBI score range = 0–88.
Weak Correlations Between Caregiver EQ-5D Index Scores and EQ-VAS, ZBI, and T-IADL

<table>
<thead>
<tr>
<th>EQ-5D Country Specific Index score</th>
<th>EQ-5D VAS</th>
<th>ZBI total score</th>
<th>T-IADL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Correlation coefficient (95% CI)</td>
<td>p-value</td>
<td>Correlation coefficient (95% CI)</td>
</tr>
<tr>
<td>Baseline vs baseline&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.50 (0.46, 0.54)</td>
<td>&lt;0.001</td>
<td>-0.21 (-0.25, -0.16)</td>
</tr>
<tr>
<td>18 months vs 18 months&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.51 (0.46, 0.55)</td>
<td>&lt;0.001</td>
<td>-0.21 (-0.27, -0.15)</td>
</tr>
<tr>
<td>Change score vs change score&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.31 (0.25, 0.36)</td>
<td>&lt;0.001</td>
<td>-0.09 (-0.15, -0.03)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Spearman's correlation coefficients, 95% confidence intervals (CI) and p-values

<sup>b</sup>Change in score from baseline to 18 months
Most Caregivers Had No Problems at Baseline and at 18 Months

Baseline n=1483 (data missing for 11 caregivers); 18 months n=934 (data missing for 113 caregivers)
Caregivers with Worsening EQ-5D Had Largest Increases in Burden Score

- **Caregivers**
  - Mobility: 78 (81%) 755 (81%) 95 (10%)
  - Self-care: 25 (3%) 841 (90%) 62 (7%)
  - Usual activities: 67 (7%) 738 (79%) 123 (13%)
  - Pain/discomfort: 126 (14%) 637 (68%) 165 (18%)
  - Anxiety/depression: 113 (12%) 660 (71%) 155 (17%)

**Mean change in ZBI score**

- **Caregivers**
  - Better: Mobility 25 (3%) 755 (81%) 95 (10%)
  - Stable: Mobility 78 (81%) 841 (90%) 62 (7%)
  - Worse: Mobility 67 (7%) 738 (79%) 123 (13%)
  - Better: Self-care 25 (3%) 841 (90%) 62 (7%)
  - Stable: Self-care 78 (81%) 755 (81%) 95 (10%)
  - Worse: Self-care 67 (7%) 738 (79%) 123 (13%)
  - Better: Usual activities 67 (7%) 738 (79%) 123 (13%)
  - Stable: Usual activities 78 (81%) 755 (81%) 95 (10%)
  - Worse: Usual activities 67 (7%) 738 (79%) 123 (13%)
  - Better: Pain/discomfort 126 (14%) 637 (68%) 165 (18%)
  - Stable: Pain/discomfort 78 (81%) 755 (81%) 95 (10%)
  - Worse: Pain/discomfort 67 (7%) 738 (79%) 123 (13%)
  - Better: Anxiety/depression 113 (12%) 660 (71%) 155 (17%)
  - Stable: Anxiety/depression 78 (81%) 755 (81%) 95 (10%)
  - Worse: Anxiety/depression 67 (7%) 738 (79%) 123 (13%)

**EQ-5D domain**

- Mobility
- Self-care
- Usual activities
- Pain/discomfort
- Anxiety/depression

**95% confidence intervals**
No Clear Pattern with Time Spent on IADLs

Median change in T-IADL from baseline (hours/month)

EQ-5D domain

<table>
<thead>
<tr>
<th>Mobility</th>
<th>Self-care</th>
<th>Usual activites</th>
<th>Pain/discomfort</th>
<th>Anxiety/depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>76 (8%) 759 (77%) 93 (9%)</td>
<td>26 (3%) 840 (86%) 62 (6%)</td>
<td>68 (7%) 737 (75%) 123 (13%)</td>
<td>129 (13%) 635 (65%) 164 (17%)</td>
<td>111 (11%) 663 (68%) 154 (16%)</td>
</tr>
</tbody>
</table>

n (%) caregivers

95% confidence intervals
Study Strengths and Limitations

**Strengths**

- Longitudinal study of a large sample of caregivers and community-dwelling people with a wide range of AD dementia severity, with assessments made in the naturalistic setting.
- Use of standardised instruments for caregiver outcome measures (EQ-5D, ZBI, RUD).

**Limitations**

- Caregiver sample may not be representative of all caregivers for AD because GERAS study enrolled from memory clinics those who were willing and able to participate in the study (i.e. a high proportion of caregivers had no problems on physical EQ-5D domains).
- Analysis is based only on those caregivers with available data at 18 months and the analysis of changes in caregiver outcomes over 18 months is descriptive only.
- Changes in ZBI and T-IADL are continuous scores, versus categorical EQ-5D domain changes.
- Assessment of T-IADL may be subject to recall bias.
Conclusions

♦ Weak correlations between caregiver EQ-5D scores, burden and caregiver hours in this real-world population

♦ Assessment of the domain structure suggests the EQ-5D index score may not be the best measure of the impact of caring for people with AD dementia due to its focus on caregiver physical health ability

♦ ZBI, as a caregiver-specific instrument of perceived burden, is sensitive to change and may better reflect the impact on caregivers, but further research is needed
The GERAS study was supported by Eli Lilly and Company

Thanks to:

- GERAS advisory board
- GERAS investigators and study staff
- Participating people with AD and their carers

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