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The effect of functional capacity and concomitant medications on life expectancy in Alzheimer's disease

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Conclusions

Instrumental activities of daily living capacity (ADL), but not basic ADL, was an important predictor of life-span after diagnosis of Alzheimer's disease (AD) and should be considered by clinicians and community-based services when estimating prognosis in AD. Antidiabetic therapy was a strong risk factor for reduction in life expectancy among AD patients.

Background

An increased knowledge of the predictors of survival in AD patients treated with cholinesterase inhibitors (ChEIs) is important for clinicians and for the health services. Impairment in ADL, somatic diseases, and psychiatric symptoms may influence mortality in AD, in addition to male sex, older age, and lower cognitive ability, which are factors that are commonly associated with a shorter life-span. We aimed to study the impact of functional capacity and concomitant medications on the life expectancy of AD patients in clinical practice.

Methods

The Swedish Alzheimer Treatment Study (SATS) is a prospective, observational, multicenter study for the long-term assessment of ChEI treatment in a routine clinical setting. In total, 1,258 outpatients with a clinical diagnosis of probable or possible AD were included. At the start of ChEI therapy (shortly after diagnosis), 1,021 of the patients had mild-to-moderate AD (Mini-Mental State Examination (MMSE) score, 10–26). Among these, 791 individuals (77%) had died by December 31, 2012, and were included in the present study. Patients were evaluated regarding cognitive (MMSE and Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog)) and functional (Instrumental Activities of Daily Living scale (IADL) and Physical Self-Maintenance Scale (PSMS)) abilities, as well as concomitant medications. The date of death was recorded, and survival was compared individually with that of the sex- and age-matched general population.

In Table 1, a t-test was performed to analyze two independent groups, and a χ^2 test was used to analyze categorical variables. One-way analysis of variance (ANOVA) with Bonferroni correction (Figure 1) and a t-test (Figures 2–4) were used to compare the differences between the means. A general linear model was used to determine the participants' characteristics at the start of ChEI treatment that affected independently the time from AD diagnosis to death (Table 2). The following potential predictors were investigated: sex, age, cognitive ability, instrumental and basic ADL, number of medications, and specific concomitant medications (antihypertensive/cardiac therapy, antidiabetic medications, antipsychotic medications, lipid-lowering agents, nonsteroidal anti-inflammatory drugs (NSAIDs)/acetylsalicylic acid, antidepressants, and anxiolytics/sedatives/hypnotics).

Results

Table 1. Baseline characteristics (n = 791)

| | |
|---|------------|
| Female sex | 490 (62%) |
| Antihypertensive/Cardiac therapy | 331 (42%) |
| Antidiabetic therapy | 40 (5%) |
| Antipsychotic therapy | 38 (5%) |
| Lipid-lowering agents | 77 (10%) |
| NSAIDs/acetylsalicylic acid | 246 (31%) |
| Antidepressants | 197 (25%) |
| Anxiolytics/sedatives/hypnotics | 113 (14%) |
| Estimated age at onset, years ^a | 73.0 ± 6.8 |
| Estimated duration of AD, years ^a | 3.1 ± 2.0 |
| Age at the start of ChEI treatment (baseline), years ^a | 76.1 ± 6.4 |
| Education, years ^a | 9.4 ± 2.5 |
| MMSE score, range 30–0 ^a | 21.0 ± 3.8 |
| ADAS-cog score, range 0–70 ^a | 22.0 ± 9.1 |
| IADL score, range 8–31 ^a | 16.7 ± 5.4 |
| PSMS score, range 6–30 ^a | 7.7 ± 2.4 |
| Time from AD diagnosis to death, years ^a | 5.7 ± 2.8 |
| Age at death, years ^a | 81.8 ± 6.5 |
| Lost years compared with the sex- and age-matched general population ^a | 5.3 ± 4.8 |

^aMean ± standard deviation (SD)

AD, Alzheimer's disease; ADAS-cog, Alzheimer's Disease Assessment Scale-cognitive subscale; IADL, Instrumental Activities of Daily Living scale; MMSE, Mini-Mental State Examination; NSAIDs, nonsteroidal anti-inflammatory drugs; PSMS, Physical Self-Maintenance Scale

Table 2. General linear model with time from AD diagnosis to death as the dependent variable and significantly associated predictors

| Independent variables | β | β , 95% CI | p-value |
|--|---------|------------------|---------|
| Intercept | 9.425 | 6.784, 12.066 | <0.001 |
| Sex (male = 0, female = 1) | 0.954 | 0.569, 1.339 | <0.001 |
| Antihypertensive/Cardiac therapy (no = 0, yes = 1) | -0.666 | -1.048, -0.285 | 0.001 |
| Antidiabetics (no = 0, yes = 1) | -1.351 | -2.217, -0.486 | 0.002 |
| Antipsychotics (no = 0, yes = 1) | -0.976 | -1.864, -0.088 | 0.031 |
| Age at first assessment (years) | -0.056 | -0.086, -0.026 | <0.001 |
| ADAS-cog score at baseline | -0.025 | -0.048, -0.002 | 0.032 |
| IADL score at baseline | -0.065 | -0.105, -0.026 | 0.001 |

β values were unstandardized and are expressed per 1 unit increase for continuous variables and for the condition present in dichotomous variables.

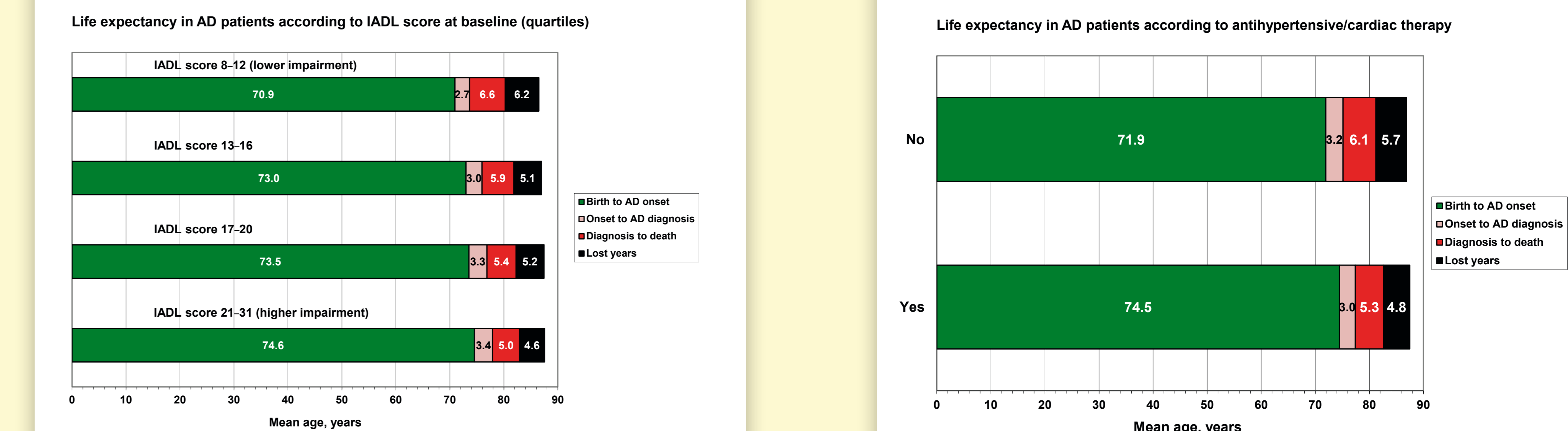
AD, Alzheimer's disease; ADAS-cog, Alzheimer's Disease Assessment Scale-cognitive subscale; CI, confidence interval; IADL, Instrumental Activities of Daily Living scale

IADL score at baseline and antihypertensive/cardiac therapy, antidiabetic medications, and antipsychotic medications were independent predictors of life expectancy after AD diagnosis, after controlling for sex, age, and cognitive ability. Basic ADL ability, number of medications, and specific concomitant medications (lipid-lowering agents, NSAIDs/acetylsalicylic acid, antidepressants, and anxiolytics/sedatives/hypnotics) at baseline were not significant predictors of life expectancy.

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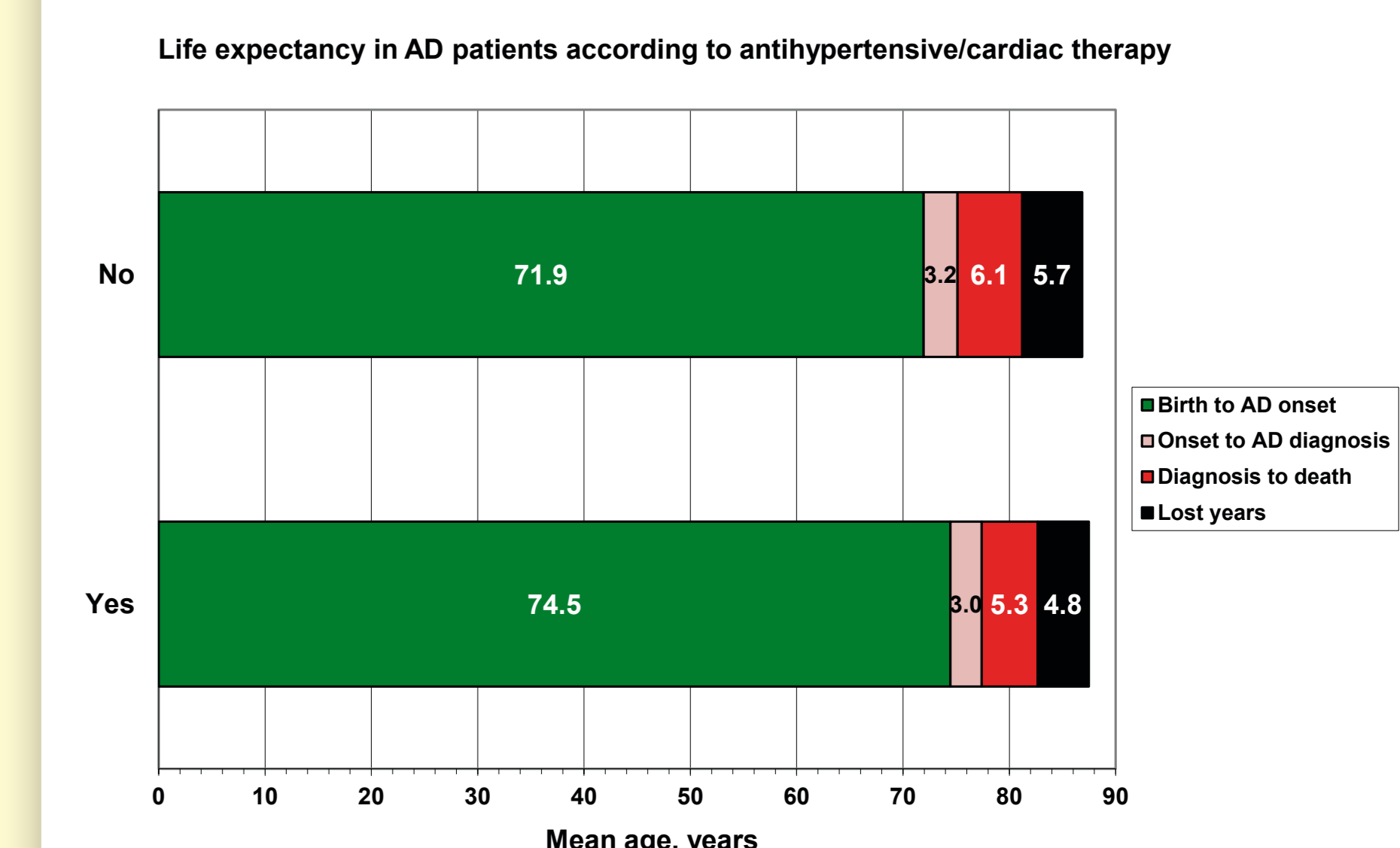
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Figure 1.



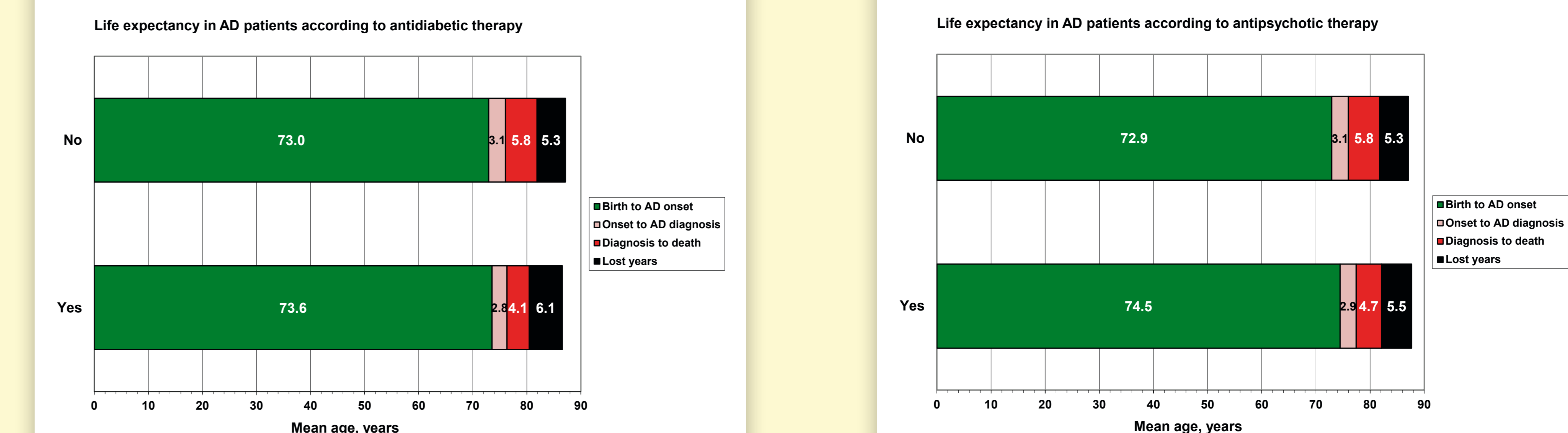
The mean ± SD time from AD diagnosis to death differed among patients with different levels of IADL impairment at baseline divided into quartiles: score of 8–12 (6.6 ± 2.8 years), score of 13–16 (5.9 ± 2.7 years), score of 17–20 (5.4 ± 2.8 years), and score of 21–31 (5.0 ± 2.5 years; $p < 0.001$). The group with the best preserved IADL capacity was younger at the onset of AD and at the time of diagnosis than were the other groups ($p < 0.001$) and had a larger reduction in life expectancy compared with the most impaired group ($p = 0.006$).

Figure 2.



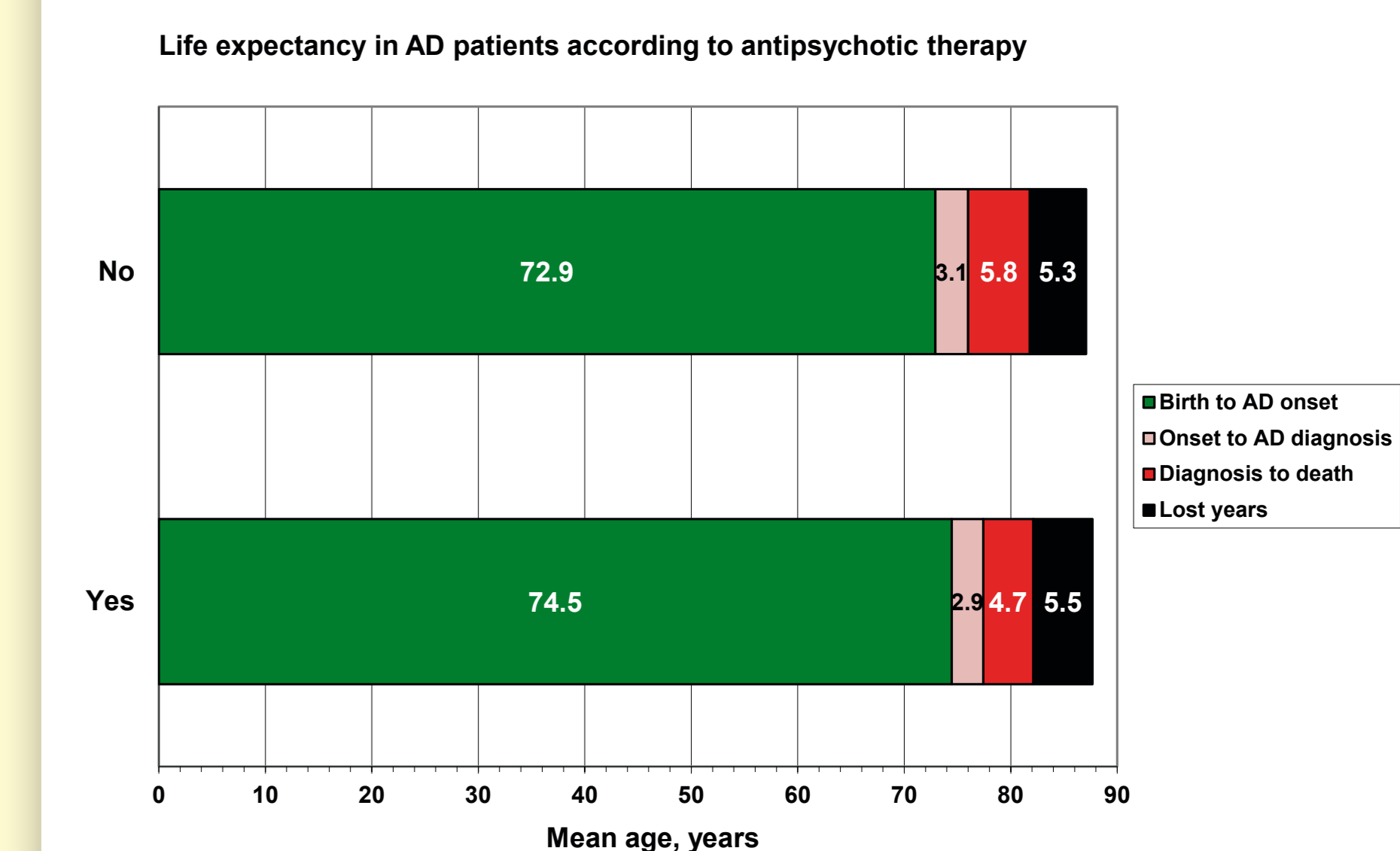
The patients without antihypertensive/cardiac therapy were younger at the onset of AD (mean ± SD; 71.9 ± 7.3 vs 74.5 ± 5.9 years, $p < 0.001$) and at the time of diagnosis (75.1 ± 6.8 vs 77.4 ± 5.6 years, $p < 0.001$) compared with the individuals who received these medications. The time from AD diagnosis to death was longer in patients with no antihypertensive/cardiac therapy (6.1 ± 2.7 vs 5.3 ± 2.8 years, $p < 0.001$).

Figure 3.



The time from AD diagnosis to death was longer in patients with no antidiabetic therapy (mean ± SD; 5.8 ± 2.8 vs 4.1 ± 2.4 years, $p < 0.001$) compared with the individuals who received these medications. The non-users of antidiabetics died at an older age (81.9 ± 6.6 vs 80.3 ± 4.8 years, $p = 0.041$) and had less reduction in life expectancy (41% vs 58%, $p < 0.001$) than did those who received this type of medication. No significant difference in age at onset or age at diagnosis of AD was detected between the groups.

Figure 4.



The time from AD diagnosis to death was longer in patients with no antipsychotic therapy (mean ± SD; 5.8 ± 2.8 vs 4.7 ± 2.5 years, $p = 0.020$). No significant difference in age at onset or age at diagnosis of AD was detected between the groups.