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## The effects of counseling spouse caregivers of people with Alzheimer's disease taking donepezil and of country of residence on rates of admission to nursing homes and mortality

Henry Brodaty, MD, DSc, FRACP, FRANZCP<sup>1,2</sup>, Mary Mittelman, DrPH<sup>3</sup>, Louisa Gibson, BSc (Arch), Grad. Dip Psych., BSc(Psych)Hons<sup>2</sup>, Katrin Seeher, Dipl-Psych<sup>2</sup>, and Alistair Burns, FRCP, FRCPsych, MD<sup>4</sup>

<sup>1</sup> Primary Dementia Collaborative Research Centre, School of Psychiatry, University of New South Wales, Sydney, Australia

<sup>2</sup> Academic Department for Old Age Psychiatry, Prince of Wales Hospital, Randwick, Australia

<sup>3</sup> Department of Psychiatry, New York University School of Medicine, NY

<sup>4</sup> Psychiatry Research Group, University of Manchester, University Place, 3rd Floor East, Oxford Road, Manchester, M13 9PL

### Abstract

**Objective**—Does psychosocial intervention for caregivers whose spouses with Alzheimer's disease (AD) are taking donepezil delay nursing home (NH) placement or death of patients?

**Design**—Randomized controlled trial with 2 years of active treatment and up to 8.5 years of follow-up (M = 5.4 years, SD = 2.4) was conducted.

**Setting**—Outpatients of research clinics in Australia, United Kingdom (UK) and the United States (US).

**Participants**—155 persons with AD and their spouses.

**Intervention**—5 sessions of individual and family counseling (+ prn *ad hoc* counseling) or usual care.

**Measurements**—Time to institutionalization and death using Cox proportional hazards methods.

**Results**—Over a mean of 5.4 years (SD = 2.4), there were no differences in NH placement or mortality by intervention group but there were by country, with Australian patients admitted to NHs earlier than US and UK patients.

**Conclusion**—Earlier NH admission of Australian than UK and US subjects may be due to differences in health care, NH systems, availability and affordability.

### Keywords

caregiver; Alzheimer's disease; dementia; nursing home placement; mortality; intervention

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Corresponding author: Professor Henry Brodaty, Director of Aged Care Psychiatry, Prince of Wales Hospital, Euroa Centre, Avoca Street, Randwick, NSW 2031, Australia; Tel (+61-2) 9382 3759; Fax (+61-2) 9382 3762, e-mail address: h.brodaty@unsw.edu.au.

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## Objective

Family caregivers of people with dementia experience physical, psychological, financial and/or social burden (1) and are crucial in maintaining a person with dementia in the community. Negative factors associated with caregiving have been identified as the main predictors of nursing home (NH) placement (2).

Caregiver interventions can improve caregiver outcomes such as subjective well-being, psychological morbidity, and ability/knowledge and can reduce the impact on caregivers of behavioral symptoms of care recipients and their risk of institutionalization(3–6). A structured, intensive 10-day training program conducted in Sydney, Australia decreased caregiver distress, delayed institutionalization and increased patient survival(7,8). A family intervention conducted in Manchester, UK reduced distress and depression in caregivers of persons with dementia, (9). The New York University Caregiver Intervention (NYUCI) (10), which included individual and family counseling, support group participation, and ad hoc (on demand) counseling, generally by telephone, reduced the rate of NH placement (11,12) and improved caregiver depression (10,13) and management of problem behaviors (14). Delay in NH admission can benefit caregivers and patients and result in significant economic savings (15).

Cholinesterase inhibitors such as donepezil may delay NH admission (16,17) and reduce both caregiver burden (18–20) and time spent caring (19,20) and possibly reduce mortality in people with dementia residing both in nursing homes (21,22) and in the community (23,24). The present study aimed to investigate whether the addition of a psychosocial caregiver intervention to cholinesterase inhibitor treatment for patients provided further benefit to patients and spouse caregivers with respect to delay of institutionalization.

Previous studies have identified older age, greater severity of cognitive and functional decline, behavioral and psychological symptoms of dementia (BPSD) and poorer general physical health as predictors of greater mortality in persons with dementia (2,25–33). As well as these variables, caregiver burden has been shown to be a risk factor for nursing home admission (2,12).

The Three Country Study (3CS), conducted in Australia, the United Kingdom (UK) and the United States (US) substantially replicated the NYU intervention (10) and added donepezil treatment for patients. We previously confirmed our primary hypothesis that five counseling sessions would reduce depression two years after enrollment (34). This paper examines our secondary hypothesis, that the 3CS intervention would delay NH placement and improve patient survival after controlling for factors known to influence these outcomes. In addition we were interested in whether there were differences in these effects across the three sites.

## Methods

### Subjects

Subjects were a volunteer sample of 158 patient/caregiver dyads (Australia: 52; UK: 54; US: 52) recruited at one of three sites: Australia, the University of New South Wales, Academic Department for Old Age Psychiatry, Prince of Wales Hospital in Sydney; UK, the University of Manchester, Division of Psychiatry; and US, the Silberstein Aging & Dementia Research Center at the New York University School of Medicine (NYU-ADRC). All patients were required to have stable physical health for the previous year and meet the National Institute of Neurological and Communicative Diseases and Stroke - Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) (35) and the Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> Edition (DSM-IV) (36) criteria for probable Alzheimer's disease (AD), have a Global Deterioration Scale (GDS) (37) score of 4 to 5 at the time of enrollment, have

no contra-indication to taking donepezil, be stable with other medications, be able to give informed consent (or not object to participating) and be community dwelling with their spouse.

Participants were required to be the spouse and primary caregiver of the patient, and give informed consent. Caregivers were excluded if they had previously received formal caregiver counseling. In addition, at least one family member other than the caregiver had to be potentially available to participate in the family counseling sessions, although on a few occasions at the UK site, family members declined to, or could not take part in the counseling sessions.

### Study Design

Dyads were randomly assigned by lottery to the control (donepezil and standard services) or treatment group (donepezil, standard services and psychosocial caregiver intervention). Standard services included resource information, help in an emergency and the routine services normally provided to patients and family members at each site, but not formal structured counseling sessions.

All patients received donepezil for up to 24 months free of charge. Patients, who started taking donepezil at enrollment, began with a dose of 5 mg per day which was increased to 10 mg at first follow up. Others were maintained on the dose they were taking upon study entry. This dose was maintained throughout the duration of the study unless contraindicated by patient reaction.

Caregivers and patients were assessed by independent raters, using structured questionnaires, every three months for the first year and every six months for the second year except that there was no 9-month follow-up in the UK. Strenuous efforts were made to keep raters blind to group assignment. All follow-up assessments included the baseline measures. Caregivers were periodically contacted for up to 8.5 years ( $M = 5.4$  years,  $SD: 2.4$  years, range: 5 months–8.5 years) after enrollment, and patient NH placement and/or death dates were recorded if applicable.

### Psychosocial Intervention

Caregivers in the treatment group received five counseling sessions within three months of enrollment. These comprised one individual session with the spouse followed by three family counseling sessions, which included the family members who were invited by the caregiver to participate, and then another individual session with the spouse. Ad hoc counseling on demand by telephone (and/or face-to-face in Australia) was available to caregivers and their family members for up to two years (whereas in the original NY study it continued indefinitely). Additional in-person counseling, as distinct from telephone counseling, was only provided at the Australian site. No consistent records were kept of the number of telephone contacts subsequent to formal counseling, but family members in the treatment group knew the counselors and could call them, while those in the control group had generally never met the counselors and were therefore unlikely to call them.

The intervention strategy was manualized and based on the NYU intervention (10). While there were four family counseling sessions in the original intervention, taking place within four months of enrollment, there were three sessions in the 3CS replication, taking place within three months of enrollment. This change was made to accommodate the need for a 3-month follow-up of patients beginning donepezil at enrollment. Previous experience in the NYUCI suggested that it was not possible to schedule four family sessions plus two individual sessions within three months. As in the original intervention, the content of the sessions was individualized and could include education about AD, information about available resources

in the community family issues about helping the caregiver or care of the person with dementia and help in understanding how to manage difficult patient behavior. The importance of emotional support and assistance for the spouse caregiver was a general theme. Changes in patient status, new symptoms, other family problems and emergencies and requests for resource information often resulted in ad hoc calls from caregivers and family members. Principal investigators had regular telephone conferences during the study period, and counselors also had telephone conference discussions about specific cases. Principal investigators at each site were involved in regular meetings with counselors as well.

## Measures

The assessment of the caregiver included demographic characteristics such as gender, age, race, education, and income. Caregiver depression was measured with the revised Beck Depression Inventory (BDI-II) (38), and social support with items from the Stokes Social Network List (39).

Patient assessment included the Mini-Mental State Examination (MMSE) (40), Global Deterioration Scale (GDS) (37), Alzheimer's Disease Assessment Scale – cognitive subscale (ADAS-cog) (41), Alzheimer's Disease Cooperative Study – Activities of Daily Living (ADCS-ADL) (42) and Revised Memory and Behavior Problems Checklist (RMBPCL) (43). Donepezil dosage, concurrent medications, including psychotropic medication; (previous and) current alcohol intake and adverse events were recorded at each visit. Caregivers rated patient physical health assessed at each visit on three items from the OARS (potential sum of scores ranges between 3–10) (44)..

## Analyses

Data were analyzed using SPSS version 14. Cox Proportional Hazards models were used to assess the effect of treatment group on time to NH admission or death separately. Time in days (from first entering the study) to NH admission or death was the dependent variable. NH placement was right censored using date of death, when appropriate. Treatment group and country of residence were entered as covariates. Factors that were found to correlate with the time to NH admission or death in univariate analyses or were reported in other research were entered into the models, namely: patient age and gender, baseline ADAS-cog and ADCS-ADL scores. In addition, NH placement, which might affect survival time (26), was included as a covariate when assessing mortality. Behavioral and psychological symptoms in dementia as measured with the Revised Memory and Behavior Problem Checklist were not associated with time until NH admission or death in univariate analyses. Unlike the steady decline of cognition and function in AD, BPSD fluctuate (45,46) and so baseline levels were not included as a covariate in our regression models. To obtain pair wise comparisons for all three countries each model was run twice changing the reference.

In the UK sample, baseline ADCS-ADL scores were missing for two patients. A sensitivity analysis excluding those two patients did not change the results of the Cox Proportional Hazards models. Their three months scores were therefore used as substitutes for the missing baseline ADCS-ADL scores. Three UK patients (2%) who withdrew prior to three months and were not included in the analysis, had all been assigned to the control group and did significantly better on the MMSE, GDS and ADAS-Cog at baseline than the remaining patients (Mann-Whitney Test,  $Z = -2.323$ ,  $p = 0.020$ ,  $Z = -2.046$ ,  $p = 0.041$ , and  $Z = -2.747$ ,  $p = 0.006$ , respectively). The results presented are for the remaining 155 patient-caregiver dyads.

## Results

### Baseline variables

Baseline characteristics of patients and caregivers are summarized in table 1. Briefly, the mean ages of patients and caregivers were 73.8 yrs (SD = 7.48, 52–91 yrs) and 71.3 yrs (SD = 8.20, 47–88 yrs) respectively, with patients having a mean MMSE score of 20.3 (SD = 5.61). Eighty-eight patients were rated as GDS4 on the GDS, 62 as GDS5. Five patients were inadvertently included with GDS ratings of 3 or 6 which was only discovered after randomization, so they permitted to remain in the study.

Treatment and control group subjects did not differ significantly at enrollment with respect to caregiver depression (BDI), gender or age; or patient gender, age, GDS, MMSE, RMBPCL, ADCS-ADL, ADAS-Cog or physical health (see table 1). However, comparisons by country revealed some differences as regards ADAS-Cog and ADCS-ADL scores (table 1). Post-hoc pairwise Mann-Whitney U comparisons with Bonferroni corrections revealed that there were significant differences in ADAS-Cog scores between the UK and both the US ( $Z = -2.55$ ,  $p = 0.011$ ) and Australia ( $Z = -3.45$ ,  $p = 0.001$ ), suggesting that UK patients were less cognitively impaired at baseline. Post-hoc pairwise comparisons of ADCS-ADL differences by country indicated that UK patients were also less impaired in ADLs than US patients (Mann-Whitney,  $Z = -2.52$ ,  $p = 0.012$ ). No differences were found between Australian and either UK or US patients. Regarding the remaining baseline parameters no differences by country were found.

### Survival at home (Table 2)

The results of the first Cox Proportional Hazards model assessing the effect of treatment and country of residence on time to NH admission are displayed in table 2. Older age and higher baseline ADCS-ADL scores (i.e. more functional independence) were found to predict increased time at home. Australians were at higher risk for NH placement than UK or US patients (table 2 & figure 1). Caregiver counseling, patient gender, baseline cognitive functioning, physical health as well as caregiver depression at baseline did not predict NH placement.

On post-hoc analyses, when data for all three countries were combined, no difference was found in times to NH placement between treatment (M = 4.1 years, SD = 2.4 years) and control (M = 4.3 years, SD = 2.4 years) patients (Log-Rank test,  $\chi^2 = 0.000$ ,  $df = 1$ ,  $p = 0.998$ ). When individual country data were examined, half of the Australian patients whose spouses had had counseling (the treatment group) were still at home at date of death or censoring date compared to only 23% of control patients (Pearson  $\chi^2$ ,  $df = 1$ ,  $p = 0.044$ ). This treatment group effect was not found for UK or US patients (Pearson  $\chi^2$ ,  $df = 1$ ,  $p = 0.322$  and  $p = 0.749$ , respectively) (see table 3).

### Mortality

According to the second Cox Proportional Hazards model, time to death was similar for treatment (M = 5.5 years, SD = 2.4) and control (M = 5.3 years, SD = 2.4) patients (Log-rank test not significant,  $\chi^2 = 0.258$ ,  $df = 1$ ,  $p = 0.612$ ) and across the three countries (Log-rank test not significant,  $\chi^2 = 1.004$ ,  $df = 1$ ,  $p = 0.316$ ). Increased survival was predicted by lower baseline ADAS-cog scores, higher baseline ADL scores and placement in a NH (not admitted to a NH: M = 4.9 years, SD = 2.5; admitted to NH: M = 5.9 years, SD = 2.2) as well as caregiver depression at baseline (Table 4). Patients' gender, age and physical health did not predict time to death.

A post-hoc analysis of deceased patients revealed that there were no national differences in mean survival times. Moreover, there was no significant interaction effect for country\*NH admission on survival (MANOVA,  $F = 1.844$ ,  $df = 2$ ,  $p = 0.165$ ).

Finally we examined whether extra sessions of in-person counseling at the Australian site influenced outcomes ( $M = 10.0$ ,  $SD = 4.17$ ). The total number of counseling sessions did not influence mortality outcomes ( $HR = 0.074$ , (95% CI: 0.817–1.160),  $p = 0.764$ ) but was associated with slightly but significantly increased rates of NH admissions ( $HR = 1.188$  (95% CI: 1.001–1.409),  $p = 0.048$ ).

## Conclusion

In this first international study of psychosocial intervention performed across three countries, counseling did not alter rates of NH admission or death though there were significant inter-country differences in rates of institutionalization. Contrary to our previous findings that comprehensive caregiver training (7,8) and counseling and support (10,11) significantly delayed NH placement, by more than 1.5 years in the NY study (11), no difference in time to NH admission was observed between the treatment and control groups. Although in a previous study we reported that CG training increased survival until death at five years (but not at eight) (2), we did not find an effect here.

However, in our post-hoc analysis a significant difference in NH placement was observed between countries, with Australian patients being admitted to NHs significantly earlier than both UK and US patients. In particular, very few patients entered NHs in the US (25%) compared with Australia (64%), even though absolute observation times differed only slightly from one country to another (Australia 8.7 years, UK 8.4 years and USA 8.1 years). It seems likely that differences between countries outweighed the effects of CG counseling. There were several important differences between this and the original NY study: (i) participants here were much less impaired than those in the NY study and thus less likely to enter a nursing home in the US; (ii) ad hoc counseling here was available only for up to two years but continued indefinitely in the NYU study; (iii) all patients were taking donepezil; and (iv) awareness, expectations and mainstream treatment were almost certainly different in the decade since Mittelman's intervention..

Why in Australia, but not in USA or UK, was the rate of NH admission so much lower in the counseling group? The higher rate of NH admission in Australia generally allowed more scope to demonstrate effects on institutionalization. Also, differences between countries in the health care, NH systems and in community care may mitigate admission rates. In Australia there are no long-term care insurance schemes but NHs are affordable for anyone assessed as having need, NH fees are income based and, in circumstances of hardship, can be waived altogether through government subsidies (47). The UK has a publicly funded health and social care system financed through general taxation although for long term care, persons are expected to contribute to their care costs if their income and savings is above a certain level. Means tested local authority (nursing) homes exist but most NHs are private and non-income tested. Government subsidies are available, but may not cover the fees charged by these homes (48). In the US, Medicaid will pay most NH costs for eligible low income earners, providing a Medicaid place is available. The majority of residents must initially pay privately, and some may have invested in specialized private long-term care insurance to help meet the high costs (49,50). However, at the New York site a large proportion of patients were eligible for Medicaid, so the decision to place an ill spouse in a NH was not primarily financial, although those with means may have opted for care at home. While there may be little difference between the three countries in terms of the total number of NH places available (51), in the UK, only a

small number may be government subsidized making NH placement unattainable for lower income earners in some regions.

Availability and affordability of community care, which may maintain patients at home longer, also differ across countries. In Australia, community services are well developed although they have waiting lists and some costs to pay. The UK has a publicly funded health and social care system financed through general taxation. For long term care, in England, people are expected to contribute to their care costs if their income and savings are above a certain level but the local authority will pay in full for people with low incomes. In the US, long term care insurance pays for home as well as NH care, which may be a disincentive for NH admission. Medicaid will cover custodial care at home for eligible older adults (with demonstrably low incomes); this is a disincentive to place people in nursing homes.

“Usual care” might also differ by country. In Australia, aged care is funded and administered nationally thereby minimizing regional differences in delivery of services. The system of care is similar to that in the UK with the majority of community care available at minimal cost and domiciliary assessment and consultations with dementia nurses the norm. In the UK usual care consists of outpatient clinic appointments and follow-up, usually in the person’s own home to monitor the effects of medication and solve problems with care that may emerge. GP advice is also freely available and attendance at local day centres is offered. At the US site usual care includes a family conference with a social worker after each diagnostic evaluation and availability of a social worker to answer questions, give advice or resource information when requested. Moreover, one or more caregiver support groups are available, and more recently also support groups for people in both the early and middle stages of AD. It is also suggested that all families contact the Alzheimer’s Association for additional information and resources.

We note that counselors and counseling techniques possibly differed both qualitatively and quantitatively despite each counselor providing the prescribed five sessions, using the manual developed by Mittelman et al. (52) and offering subsequent ad hoc counseling. While further support was offered by telephone in all three countries, the Australian counselor also made herself available for extra individual and/or family in-person sessions. A sensitivity analysis performed for the Australian sample found a slight but significant association between more counseling sessions and *greater* risk of NH placement for patients, probably indicating that those in greatest need were requesting more help. Finally, when the study was initiated, donepezil was expensive and neither subsidized in Australia nor in the UK. Consequently, some patient/caregiver dyads may have enrolled only to receive donepezil without being receptive to counseling. In contrast, many participants in the U.S. were able to obtain donepezil through health insurance and were more likely to have enrolled in order to get the benefit of the counseling.

Unexpectedly, NH placement was found to predict increased survival in Australia and the UK. Literature investigating the effect of NH placement on patients’ mortality is contradictory (53–56). Among those patients who died during the study period UK and Australian participants lived longer when they were admitted to a NH whereas the opposite occurred in the US perhaps providing more evidence suggesting that reasons for NH placement may have differed. Another possibility is that NHs may differ in their level of care.

Behavioral and psychological symptoms of dementia have been found in previous research to predict NH admission (57,58) and death (54,59,60). However, in this study as BPSD at baseline were not associated with time to NH admission or death in univariate analyses and there is longitudinal variability in their levels (45,46), BPSD were not included as a covariate in our regression models. BPSD scores more proximal to NH admission or death might be better predictors for those events.

Further research is necessary to ascertain the reasons why caregiver counseling is effective in delaying NH admission in some environments but not others. Better matching of intervention to needs is likely to result in better outcomes; for example, we did not restrict counseling to depressed caregivers. The impact of the comparative affordability and availability of resources to assist with care at home versus care in institutions on the timing of placement decisions should be examined.

We conclude that among study participants across all three countries, caregiver counseling did not delay NH admission or increase survival until death. However, there were differences between countries in time to NH placement, with Australian patients being admitted to NHs earlier than UK or US patients, possibly due to differences in national health care and NH systems, availability and affordability. Future multinational research could reveal the effects of these and other possible national differences, and thereby elucidate the reasons for nursing home placement, and perhaps lead to better interventions to assure that they occur when they are in the best interests of caregivers and persons with dementia.

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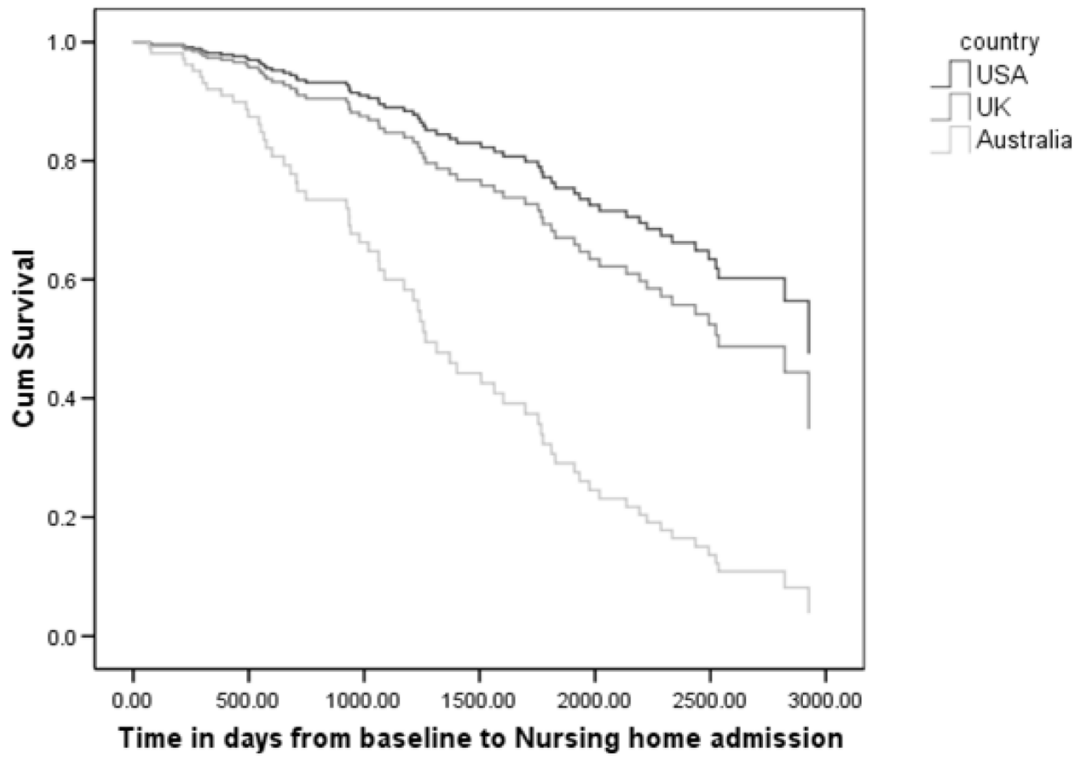
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**Figure 1.** Nursing home survival between Australia, the UK and the US at up to 8.5 years.

Table 1

## Baseline characteristics of patients and caregivers

	Total (N=155)	Treatment (n=79)	controls (n=76)	Mann-Whitney		country			Kruskal-Wallis (df=2)	
				Z	p	AUS (n=52)	UK (n=51)	USA (n=52)	chi2	p
Patients										
age: M(SD)	73.8 (7.48)	73.9 (7.74)	73.7 (7.28)	-0.858	0.391	75.0 (7.23)	72.9 (6.37)	73.0 (8.55)	2.463	0.292
gender: M:F	87:68	47:32	40:36			31:21	22:29	34:18		
MMSE: M(SD)	20.3 (5.61)	20.9 (5.16)	19.8 (5.99)	-0.581	0.561	20.0 (5.46)	20.3 (6.22)	20.7 (5.27)	0.453	0.797
ADCS-ADL: M(SD)	55.3 (13.32)	56.7 (11.41)	54.0 (14.85)	-0.045	0.964	54.4 (12.91)	53.5 (14.0)	58.1 (13.03)	6.559	<b>0.038</b>
ADAS-Cog: M(SD)	25.8 (11.40)	25.7 (11.11)	25.9 (11.73)	-0.206	0.837	28.8 (10.45)	21.1 (12.29)	26.8 (10.79)	12.876	<b>0.002</b>
GDS: M(SD)	4.4 (0.53)	4.4 (0.49)	4.4 (0.58)	-0.406	0.685	4.4 (0.50)	4.2 (0.54)	4.5 (0.55)	3.207	0.201
RMBPCL: M (SD)	9.84 (8.43)	10.04 (8.91)	9.63 (7.96)	-0.062	0.951	9.23 (9.27)	9.31 (8.05)	10.98 (7.94)	3.437	0.179
Phys. health	5.7 (1.51)	5.5 (1.52)	5.8 (1.50)	-1.61	0.107	5.5 (1.38)	5.8 (1.70)	5.8 (1.54)	0.314	0.855
Caregivers										
age: M (SD)	71.3 (8.2)	71.5 (7.98)	71.1 (8.41)	-0.641	0.521	71.8 (8.20)	72.6 (5.63)	69.6 (9.46)	1.133	0.567
gender M:F	69:86	33:46	36:40			21:31	29:22	19:33		
BDI: M(SD)	8.7 (6.53)	9.2 (7.02)	8.3 (6.05)	-0.508	0.611	9.1 (5.48)	7.1 (6.68)	9.8 (7.30)	3.001	0.223

M: mean, SD: Standard deviation, USA: United States of America, UK: United Kingdom, AUS: Australia; Significant results are printed bold

Table 2

Predictors for NH placement at up to 8.5 years.

	Wald	df	Sig.	HR	Lower	Upper
Treatment group	.044	1	.835	1.057	.627	1.781
Patient age	6.330	1	.012	<b>.956</b>	.923	.990
Patient gender	1.358	1	.244	1.376	.804	2.355
ADCS-ADL at baseline	13.976	1	<.001	<b>.948</b>	.922	.975
ADAS-Cog at baseline	.705	1	.401	1.013	.983	1.043
UK vs Australia *	9.302	1	.002	<b>.344</b>	.173	.683
USA vs Australia *	17.408	1	<.001	<b>.228</b>	.114	.456
UK vs USA */	.905	1	.342	1.509	.646	3.525
Patient physical health at baseline	.951	1	.329	.908	.747	1.103
Caregiver depression at baseline	.034	1	.853	1.004	.967	1.042

Significant HR are printed bold,

\* indicates reference group,

/ in order to get pair wise comparisons for all three countries, Cox regression was run twice changing the reference group

**Table 3**  
Nursing home status and mortality between countries and treatment groups at up to 8.5 years (M = 5.4 years).

	Treatment				Control				TOTAL
	Australia	UK	US	Australia	UK	US	UK	US	
<b>N</b>	26	27	26	26	24	26	24	26	84
<b>Not admitted to NH</b>	<b>13 (50%)<sup>f</sup></b>	12 (44%)	19 (73%)	<b>6 (23%)<sup>f</sup></b>	14 (58%)	20 (77%)	14 (58%)	20 (77%)	84
<b>Admitted to NH</b>	13 (50%)	15 (56%)	7 (27%)	20 (77%)	10 (42%)	6 (23%)	10 (42%)	6 (23%)	71
<b>Alive</b>	11 (42%)	13 (48%)	14 (54%)	11 (42%)	11 (46%)	12 (46%)	11 (46%)	12 (46%)	73
<b>Deceased</b>	15 (58%)	14 (52%)	12 (46%)	15 (58%)	13 (54%)	14 (54%)	13 (54%)	14 (54%)	85

<sup>f</sup> Pearson  $\chi^2$  significant, (df = 1, p = 0.044)

Table 4

Predictors for mortality at up to 8.5 years.

	Wald	df	Sig.	HR	Lower	Upper
Treatment group	.005	1	.946	.984	.612	1.581
Patient age	1.102	1	.294	1.019	.984	1.056
Patient gender	.072	1	.789	.932	.558	1.558
ADCS-ADL at baseline	5.005	1	.025	<b>.971</b>	.947	.996
ADAS-Cog at baseline	10.040	1	.002	<b>1.041</b>	1.016	1.068
NH placement	8.253	1	.004	<b>.449</b>	.260	.775
UK vs Australia*	.045	1	.833	.936	.508	1.727
USA vs Australia*	3.028	1	.082	.574	.307	1.073
UK vs USA*/	1.963	1	.161	1.630	0.823	3.230
Patient physical health at baseline	.691	1	.406	.931	.787	1.102
Caregiver depression at baseline	3.866	1	.049	<b>.959</b>	.920	1.000

Significant HR are printed bold.

\* indicates reference group

/ in order to get pair wise comparisons for all three countries, Cox regression was run twice changing the reference group