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Utility, Costs and Cost-Utility of Amyloid-PET in the Diagnostic Process of Memory Clinic Patients: A Trial-Based Economic Evaluation From AMYPAD-DPMS

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ABSTRACT

Background: Amyloid positron emission tomography (PET) is instrumental in achieving an accurate diagnosis and may help to limit health-seeking behavior. Currently, amyloid-PET is not routinely used in clinical practice due to lack of evidence on cost-utility. We assessed the cost-utility of early versus no amyloid-PET in the diagnostic work-up of memory clinic patients after 6 months.

Methods: We assessed cost-utility of patients enrolled in AMYPAD-DPMS (EudraCT Number: 2017-002527-21) from six European memory clinics and randomized in ARM1; early amyloid-PET, ARM2; no amyloid-PET or ARM3; (amyloid-PET at request of the managing physician). ARM3 was not part of the cost-utility analysis. The EuroQol classification system (EQ-5D-5L), visual analogue scale (VAS), and ICEpop Capability measure for older people (ICECAP-O) were collected at baseline and 6 months. Costs were calculated from cost diaries at baseline, 3 and 6 months. The incremental cost-effectiveness ratio (ICER) was calculated using EQ-5D-5L and a societal perspective.

Results: From April 2018, to October 2020, 844 participants were screened and 840 were randomized (290 ARM1; 270 ARM2 and 280 ARM3). $N = 514$ (250 ARM1; 264 ARM2) were included in the economic evaluation. Amyloid-PET resulted in higher costs at 6 months (ARM1 vs. ARM2 Δ€1384, bootstrapped 95% CI [7, 2761]). No significant difference in EQ-5D-5L, VAS or ICECAP-O was found. The incremental cost-effectiveness ratio (ICER) was €461,333 per QALY.

Conclusion: Although patients receive an early etiological diagnosis, the cost-utility after 6 months is not favorable for amyloid-PET. The cost-utility will need to be reassessed when considering amyloid-PET to select patients for anti-amyloid biologics.

For affiliations refer to page 8.

1 | Background

Over the past decade, the Alzheimer's disease (AD) field has moved toward better and earlier diagnosis, even in stages where patients do not fulfill the criteria of a dementia syndrome. A major contributor to this shift is the introduction of biomarker tests, such as amyloid-PET, which allows the assessment of amyloid-β in the brain.

Amyloid-PET has two main applications. First, it can be used to select patients for disease-modifying therapies. This is important as the success of such treatments relies on targeting the right individuals, ensuring effective resource allocation, and avoiding unnecessary treatment in those unlikely to benefit. Second, amyloid-PET is instrumental in achieving an accurate diagnosis. Studies have shown that adding amyloid-PET to the diagnostic process improves diagnostic confidence and helps to optimize patient management [1–3]. An early diagnosis of AD provides patients and their care partners with an explanation for the symptoms that they experience. Such an early and accurate diagnosis is the gatekeeper for access to the right services and support for these patients. On the other hand, ruling out AD can reassure patients and their care partners. Altogether this can help to maintain quality of life in the earliest stages of the disease [4]. Moreover, it has the potential to reduce unnecessary future healthcare appointments and investigations. This accurate diagnosis also helps to limit health-seeking behavior, including avoiding redundant appointments, diagnostics, and treatments that may stem from diagnostic uncertainty. In our study, we specifically focus on the second application of amyloid-PET.

Two earlier studies evaluated the effect of additional amyloid-PET testing in the diagnostic routine for AD and showed that this resulted in fewer emergency room (ER) visits and hospitalizations and a lower rate of institutionalization [5, 6]. However, to date, there is no evidence from prospective randomized controlled trials or from studies that specifically focus on the use of amyloid-PET and related costs in the diagnostic process.

The current study reports a secondary analysis of the AMYPAD-DMPS project—a randomized clinical study examining the clinical effect in terms of diagnostic confidence of amyloid PET in memory clinic patients [7, 8]. With the rationale that amyloid-PET provides a more accurate diagnosis and that physicians will promptly act upon this, we anticipate an effect on healthcare utilizations in the short term. In the current study we aim to determine, by means of a randomized controlled trial, the effect of an early amyloid-PET in the diagnostic work-up of memory clinic patients on the utility, healthcare and non-healthcare costs after 6 months.

2 | Methods

Participants were memory clinic patients who had been enrolled in the AMYPAD Diagnostic and Patient Management Study (DPMS). AMYPAD-DPMS is a European, prospective, multicenter, randomized controlled trial examining the effect of amyloid-PET on diagnostic confidence. Participants were randomized into three study arms. The design and rationale of the AMYPAD-DPMS project is described elsewhere [8]. Shortly, the characterization of the three arms were: ARM1, amyloid-PET was performed early in the diagnostic workup (within 1 month from baseline); ARM2, no amyloid-PET; and ARM3, amyloid-PET was performed at request of the managing physician. The study design was closely aligned with routine clinical practice. Following the initial clinical consultation—during which an MRI or CT scan was either already available or newly prescribed—patients underwent screening, including assessment of inclusion and exclusion criteria. Notably, individuals who had previously undergone amyloid PET, FDG-PET, or CSF biomarker testing were excluded from participation. However, after enrollment, treating physicians in all study arms were free to request additional diagnostic procedures such as CSF analysis, FDG-PET, or structural imaging, based on clinical judgment and standard local practices. Patients with dementia were required to have a study partner available for the duration of the study. For a detailed description please see Frisoni et al. (2019) [8].

In line with health technology assessment (HTA) practices, we here compare the intervention (ARM1) with no intervention (ARM2) group to get a clear and interpretable estimate of incremental cost-effectiveness. Therefore, ARM3 was not part of the current cost-utility analysis (CUA). In AMYPAD-DPMS, participants underwent follow-up visits up to 13 months. The last follow-up visit in the current study was at 6 months because ARM 2 had an exit amyloid-PET test at 8 months. Baseline characteristics of the whole cohort (thus including ARM3 patients) have been described previously [7, 8].

3 | Study Population

Participants had variable baseline cognitive stages, ranging from subjective cognitive decline plus (SCD+) to mild cognitive impairment (MCI) and dementia. Participants included in the present study were enrolled from seven European memory clinics in six countries: (i) University and University Hospital of Geneva (UNIGE; Geneva, Switzerland), (ii) Amsterdam University Medical Center, location VUmc (Amsterdam UMC; Amsterdam, The Netherlands), (iii) Centre Hospitalier Universitaire de Toulouse (CHUT; Toulouse, France), (iv) Barcelona βeta Brain Research Center (BBRC; Barcelona, Spain), (v) University of Cologne and Deutsches Zentrum für Neurodegenerative Erkrankungen (DZNE; Cologne, Germany), (vi) Essex Memory Clinic (St. Margaret's Hospital, Essex, UK), and (vii) Centre Hospitalier Universitaire Vaudois (CHUV; Lausanne, Switzerland). Ethics approval was obtained in all centers. All participants gave written informed consent (EudraCT Number: 2017–002527-21).

4 | Utilities and QALYs

Quality of life was assessed at baseline and after 6 months using the five-level version of the EuroQol classification system (EQ-5D-5L) and the visual analog scale (VAS), the most common health-related quality of life instruments used in cost-utility analyses, and the ICEpop Capability measure for older people (ICECAP-O), a broader measure of wellbeing [9]. Utilities were calculated based on country specific valuation sets for EQ-5D-5L [10–14]. A country specific valuation set for Switzerland

is lacking in the literature, therefore we used the France valuation set for the site UNIGE and CHUV [15].

5 | Measurement and Valuation of Resources and Costs

We estimated the costs from a societal and healthcare perspective at baseline and after 3 and 6 months using cost diaries (Appendix 1). Because of the time horizon of 6 months, costs were not discounted.

Cost diaries were used to assess self-reported healthcare resource use and societal costs; that is hospital admissions, outpatient visits, emergency room (ER) visits, emergency transportations, diagnostic tests, visits to health care providers outside the hospital (general practitioner (GP), practice nurse, physiotherapist, psychiatrist, occupational therapist, social worker, psychologist), service use (district nurse, home aid, transportation), prescribed dementia medications, institutionalizations, productivity losses, caregiver productivity losses, and informal care. Cost diaries were translated into seven languages and are very similar to the iMTA questionnaire with additional dementia specific items [16]. Cost diaries could be completed by participants themselves, their study partner or completed together (details summarized in Table S1).

Costs were calculated on a country-by-country basis and country-specific unit prices were retrieved from (1) standard reference costs, (2) costs reimbursed by health insurers, (3) costs charged to uninsured patients, (4) EU HCSCD database, (5) costs reported in literature, and (6) expert opinion. In case none of these sources provided a unit price, costs were calculated from other countries and interpolated between countries using purchasing power parities. All unit prices were translated to the reference year 2019 using consumer price indices. Local currencies were converted (British pound, Swiss franc) to Euros. Table S2 provides an overview of the unit costs per country. To handle missing cost items and diary data, multiple imputation by chained equations (MICE) was applied.

6 | Analysis

Differences in utilities at 6 months and costs at three and 6 months were assessed using regression analyses to control for baseline utility and cost values, respectively. Confidence intervals for costs were obtained by bootstrapping. As per protocol, the base case CUA weighed societal costs at 6 months against UK EQ-5D-5L –based QALYs at 6 months. We also performed a CUA from a healthcare perspective (excluding non-healthcare costs) and with two different utility measures (VAS and ICECAP-O). We carried out subgroup analyses where we stratified for (1) baseline syndrome diagnosis (SCD+, MCI, and dementia) and (2) amyloid-PET result in ARM1 (negative or positive). Results are presented in cost-effectiveness planes based on 5000 bootstraps and cost-effectiveness acceptability curves. All analyses followed the intention to treat principle. Results from per-protocol analyses can be found in Table S3. This economic evaluation was conducted and reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 statement [17].

7 | Results

In the present study, we included 250 ARM1 (amyloid-PET) and 264 ARM2 participants (no amyloid-PET) form whom the baseline and six-month follow-up visits as well as information on quality of life and costs were available. The baseline characteristics of the sample are shown in Table 1. The two randomization arms were similar with regard to age, sex, education, cognitive status and stage. Baseline quality of life and costs were also comparable between ARM1 and ARM2.

7.1 | Utilities

After 6 months from baseline, the valuation of quality of life was similar in ARM1 and ARM2 according to all utility measures: EQ-5D-5L (difference = −0.003, 95% CI [−0.02, 0.02]), VAS (difference: 0.01, 95% CI [−0.02, 0.03]), and ICECAP-O (difference: −0.01, 95% CI [−0.03, 0.01]) (Table 2).

7.2 | Costs

Total costs were higher in ARM1 compared to ARM2 three months after randomization (total cost difference €1458, bootstrapped 95% CI [851, 2067]). There was no difference in healthcare and non-healthcare costs 3 months after baseline (healthcare cost difference €-159 [−552, 223]) and non-healthcare cost difference €-54 bootstrapped 95% CI [−543, 434] (Table 2).

TABLE 1 | Baseline characteristics.

	ARM1: Early amyloid-PET	ARM2: no-PET
	***n* = 264**	***n* = 250**
Age (years)	71 ± 8	71 ± 8
Gender, Female	120 (45%)	121 (48%)
Education, years	13 ± 4	13 ± 4
MMSE	25 ± 4	25 ± 4
Syndrome diagnosis		
SCD+	77 (29%)	72 (29%)
MCI	108 (41%)	99 (40%)
AD dementia	79 (30%)	79 (32%)
Baseline utilities (T0)		
EQ-5D-5L	0.82 ± 0.19	0.84 ± 0.17
VAS	0.75 ± 0.16	0.75 ± 0.18
ICECAP-O	0.85 ± 0.12	0.85 ± 0.12
Baseline costs	€830 ± 194	€830 ± 122

Note: Values are mean ± SD. Table S4 provides an overview of costs per cost type. Analyses were corrected for baseline values.
Abbreviations: EQ-5D-5L, five level version of the EuroQol classification system; ICECAP-O, ICEpop capability measure for older people; MMSE, Mini-mental state examination; MCI, mild cognitive impairment; SCD+, subjective cognitive decline +; VAS, visual analogue scale.

TABLE 2 | Utilities and costs 3 and 6 months after randomization.

	Arm 1: Early amyloid-PET	Arm 2: no-PET	Difference Arm 1- Arm2
	n = 264	*n* = 250	[bootstrapped 95% CI]
Utilities			
EQ-5D-5L	0.87 ± 0.19	0.87 ± 0.18	−0.003 [−0.02, 0.02]
VAS	0.75 ± 0.18	0.74 ± 0.20	0.01 [−0.02, 0.03]
ICECAP-O	0.82 ± 0.18	0.82 ± 0.18	−0.01 [−0.03, 0.01]
Costs (€)			
T03			
Amyloid-PET	1790 ± 802	0	NA
Healthcare costs	332 ± 793	475 ± 2825	−159 [−552, 233]
non-healthcare (without amyloid-PET) costs	688 ± 2862	727 ± 2701	−54 [−543, 434]
Total costs T03	2683 ± 3080	1193 ± 3816	1458 [851, 2067]
T06			
Healthcare costs	397 ± 840	606 ± 3779	−230 [−733, 273]
non-healthcare costs	1303 ± 4410	1098 ± 3663	191 [−516, 897]
Total costs T06	1673 ± 4591	1712 ± 5564	−75 [−982, 833]
T06 Cumulative			
Healthcare costs	**2396 ± 1621**	**1110 ± 6244**	**1250 [412, 2088]**
Non-healthcare costs	**1991 ± 6569**	**1826 ± 5621**	**136 [−932, 1204]**
Total costs	**4355 ± 6825**	**2905 ± 8584**	**1384 [7, 2761]**

Note: Values are mean ± SD. Table S4 provides an overview of costs per cost type. Analyses were corrected for baseline values.
Abbreviations: EQ-5D-5L, five level version of the EuroQol classification system; VAS, visual analogue scale; ICECAP-O, ICEpop capability measure for older people.

Six months after baseline, there was no difference in costs between ARM1 and ARM2 (total cost difference €-75, bootstrapped 95% CI [−982, 833], healthcare cost difference €-230, bootstrapped 95% CI [−733 to 273] and non-healthcare costs difference €191, bootstrapped 95% CI [−516, 897], Table 2).

Cumulative total costs 6 months after randomization remained significantly higher for participants who received early amyloid-PET compared to no-PET (€1384, bootstrapped 95% CI [7, 2761]). With regard to informal care costs and caregiver productivity loss costs, no differences were found between ARM1 and ARM2 on 3 and 6 months after baseline (Table S4). Costs per cost type at 3 and 6 months after randomization, including volumes, are summarized in Table S3. Correcting for site did not change the results (Table S5).

7.3 | Cost-Utility Analysis

From a societal perspective, the incremental cost effectiveness ratio (ICER) was €461,333 per QALY. Whether an intervention is deemed cost-effective depends on the cost-effectiveness threshold, however the probability of amyloid-PET being cost-effective even at a high cost-effectiveness threshold of €100,000 remains low (6%, Figure 1A). If a healthcare instead of a societal perspective is taken, the ICER is €416,666 per QALY and the probability of being cost-effective at a cost-effectiveness threshold of €100,000 is 6% (Figure 1B).

8 | Subgroup Analyses

The utility (measured with EQ-5D-5L) decreased and costs increased with increasing cognitive stage severity in both ARM1 and ARM2 (Table 3). There were no differences in EQ-5D-5L at 6 months between ARM1 and ARM2 in the SCD, MCI or dementia stage.

We observed a cost difference (healthcare and total costs) between ARM1 and ARM2 in the MCI stage, in the SCD stage for healthcare costs only, but no differences in the dementia stage (Table 3).

Secondly, we stratified by amyloid-PET results (Table 4). Only participants in ARM1 received an amyloid-PET and stratification by amyloid-PET result was therefore only done in ARM1 and compared with all participants in ARM2. We found no significant differences in EQ-5D-5L between strata.

Total costs were significantly higher in ARM1 participants with a positive amyloid-PET compared to ARM2, where the largest cost difference is attributable to healthcare costs. Difference in total costs were smaller for ARM1 participants with a negative

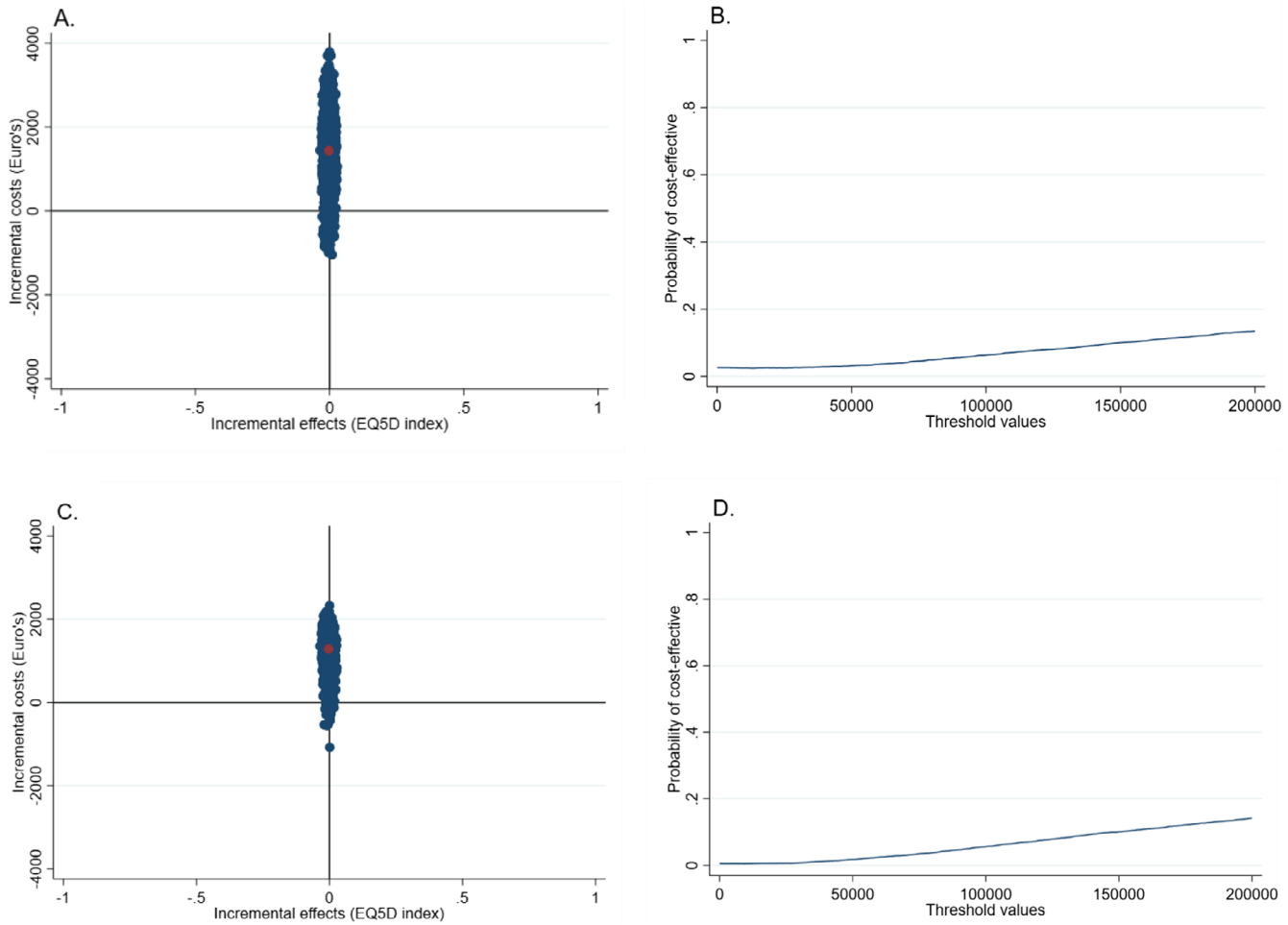

FIGURE 1 | Cost-effectiveness plane and acceptability curve for total costs (A and B) and healthcare only costs (C and D). Red dot indicates ICER. Utilities were based on EQ5D-5 L index. A.CE plane for total costs, B. CE acceptability curve for total costs, C. CE plane for healthcare costs and D. CE acceptability curve for healthcare costs.

amyloid-PET result versus ARM2 participants, because ARM1 participants with a positive amyloid-PET had higher non-healthcare costs, although not significantly, than those with a negative amyloid-PET.

9 | Discussion

Six months after baseline, we found no differences in quality of life between participants who had received an amyloid-PET compared to participants who had not yet received an amyloid-PET. The difference in costs was estimated at €1384 and mostly consisted of costs of the amyloid-PET scan. As a result, the ICER was not favorable for amyloid-PET 6 months after baseline from both a societal and a healthcare perspective.

The current study is a secondary analysis of the AMYPAD-PDMS study [7, 8]. The primary outcome of the AMYPAD-DPMS study was diagnostic confidence and we showed that the proportion of participants with very high diagnostic confidence was significantly higher in ARM1 compared to ARM2. The study also compared diagnostic confidence with ARM3, where amyloid-PET was performed at request of the managing physician. ARM3 was very comparable with ARM1, as 87% of patients received an amyloid-PET within 1.5 months after baseline. In the current study, ARM1 was compared to ARM2 because this comparison provides the clearest contrast in terms of costs and effects, allowing us to evaluate whether routine use of amyloid PET is cost-effective. While ARM 3 may resemble certain real-world practices if amyloid-PET is considered standard care, it is conceptually closer to ARM 1 than ARM 2, and we expect that the results from the current analyses could be translated to ARM3. Whether an intervention is deemed cost-effective depends on the willingness to pay threshold. In this European, prospective, randomized controlled study, the willingness to pay differs among countries. For example, the ICER threshold in the UK is £20,000–£30,000 [9] (about €22,500-33,800), in the Netherlands €20,000–80,000 [9] and in Switzerland CHF 100,000/QALY [18] (about €100,000). We examined the probability of being cost-effective for different cost-effectiveness thresholds using cost-effectiveness acceptability curves and found that for varying willingness to pay thresholds the probability remained low.

The difference in self-rated quality of life, measured by EQ-5D-5L, between participants who had received amyloid-PET and those who had not yet received amyloid-PET was small. However, EQ5D is known to be insensitive to capturing disease-specific and more subtle health effects of an intervention. We

TABLE 3 | Utility and Costs 6 months after randomization stratified for cognitive stage.

	ARM1: Early amyloid-PET	ARM2: no-PET	
	n = 264	*n* = 250	B [bootstrapped 95% CI]
EQ-5D-5L			
SCD+	0.90 ± 0.12	0.90 ± 0.12	0.0004 [−0.03–0.03]
MCI	0.86 ± 0.21	0.89 ± 0.14	−0.01 [−0.04—0.01]
Dementia	0.85 ± 0.21	0.83 ± 0.25	0.01 [−0.02–0.05]
Cumulative costs			
Healthcare costs			
SCD+	2110 ± 1218	646 ± 2312	1444 [834–2053]
MCI	2537 ± 1907	657 ± 1705	1893 [1400–2385]
Dementia	2483 ± 1520	2102 ± 10,700	287 [−2131–2706]
Non-healthcare costs			
SCD+	168 ± 543	604 ± 3340	−436 [−1240—366]
MCI	712 ± 1477	757 ± 2013	−55 [−542–432]
Dementia	5519 ± 11,139	4278 ± 8758	1148 [−2053–4349]
Total costs			
SCD+	2171 ± 1237	1114 ± 5277	1032 [−252–2317]
MCI	3246 ± 1477	1421 ± 2581	1828 [1136–2521]
Dementia	8001 ± 11,281	6396 ± 13,544	1418 [−2404–5241]

Note: Analyses were corrected for baseline values.
Abbreviations: AD, Alzheimer's diseasel; EQ-5D-5L, five level version of the EuroQol classification system; MCI, mild cognitive impairment; SCD, subjective cognitive decline.

therefore also used ICECAP-O as an alternative measure. ICECAP-O takes a broader perspective and defines well-being in terms of the capability approach (i.e., being able to do and be what is important in life) [19, 20]. However, we did not find any differences using ICECAP-O either.

In the European context of a disease for which to date no curative treatment options have been approved and are therefore not available, demonstrating cost-effectiveness of an early diagnosis is challenging. Amyloid-PET has been repeatedly shown to impact clinical decision-making and clinical management [1–3, 7, 21–23]. Given that physicians have greater confidence in the diagnosis and that physicians promptly act on this information, one would expect to see a difference in healthcare utilization, at least in a hospital setting, in the months immediately following diagnosis. Also from a patients' perspective, being better informed about the underlying disease could result in fewer visits to for example, a GP. Along this line of reasoning, a 6 months' time frame would be realistic. There are other studies that assess resource utilization after an early or more accurate diagnosis. Although these studies were not randomized and did not evaluate utilities alongside costs, the timeline of these studies was longer. The IDEAS study found a reduction of ER visits and hospitalization over 12 months in patients with amyloid-PET compared to patients without.5 And another study observed in a cohort of memory clinic patients that over the course of 5 years, costs related to health-seeking behavior, costs of institutionalization and related costs were lower in patients with amyloid-PET in their diagnostic routine. Six Other studies that examined the effect of an early diagnosis with subsequent intervention on (healthcare) costs showed a positive effect on institutionalization and (proxy) costs [24–27]. In these studies, as in ours, the subsequent interventions were treatment options that are currently available; that is symptomatic treatment with acetylcholine inhibitors for the patient or caregiver support. As new therapies are gaining regulatory approval, amyloid PET may also be considered to select patients for anti-amyloid biologicals. However, assessing the cost-utility of amyloid PET to select patients is challenging at this stage because only moderate short-term effects on measures of cognition and function have been demonstrated for anti-amyloid biologicals. The translation of these effects to long-term outcomes is still uncertain and requires modeling. In addition, the EMA has only approved one anti-amyloid biologic so far, and only for a restricted subgroup, excluding people with two copies of the ApoE4 gene and/or those on anticoagulant therapy.

In two subgroup analyses, we examined whether the results differed by cognitive stage or amyloid-PET positivity. We did not find a difference for the SCD, MCI, and dementia subgroups. The highest costs were observed in the dementia stage, but interestingly these costs did not differ between participants who had undergone amyloid-PET and participants who had not. It was anticipated that in the dementia stage high costs would be observed anyway in both arms and that the extra costs of the

TABLE 4 | Utility and costs at 6 months stratified for amyloid-PET result.

	ARM1 A+	ARM1 A-	ARM2: no-PET	ARM1 A+ vs. ARM2	ARM1 A- vs. ARM2	ARM1 A+ vs. ARM1 A-
	$n = 124$	$n = 118$	$n = 250$	B [95% CI]	B [95% CI]	B [95% CI]
Utility						
EQ-5D-5L	0.90 ± 0.12	0.85 ± 0.22	0.87 ± 0.18	0.01 [−0.01–0.04]	0.01 [−0.01–0.04]	0.02 [0.01–0051]
Cumulative costs						
Healthcare costs	2441 ± 1742	2385 ± 1518	1110 ± 6244	1330 [343–2318]	1274 [270–2318]	56 [−1106–1219]
Non-healthcare costs	2290 ± 7205	1533 ± 6192	1826 ± 5621	464 [−864–1793]	−292 [−1643—1059]	757 [−808–2321]
Total costs	4723 ± 7459	3852 ± 6300	2905 ± 8584	1818 [142–3495]	947 [−758—2651]	872 [−1102–2846]

Note: Analyses were corrected for baseline values.
Abbreviation: EQ-5D-5L, five level version of the EuroQol classification system.

amyloid-PET would not be compensated for. However, costs in patients in the dementia stage were driven by a few participants with very high costs so the amyloid-PET costs were only moderate. Furthermore, we found that a positive amyloid-PET scan resulted in higher healthcare costs, mainly because of the costs of the amyloid-PET itself. Nevertheless, this increase in costs was less pronounced for the participants with a negative amyloid-PET result. It is possible that extra care at home was arranged after a positive amyloid-PET or participants and/or their care partners decided to (partly) stop working, with corresponding costs. The cost difference between amyloid positive and negative patients was not significant, but the mean difference was substantial. It should be noted that the AMYPAD-DPMS study was powered to detect a clinical outcome 'diagnostic confidence', although the sample size was sufficiently large to show a clinically relevant effect on the EQ-5D-5L with high power [7, 8]. Based on the group sizes ($n = 264$ and $n = 250$), a two-sided test with $\alpha = 0.05$ would have 80% power to detect a difference of 0.045 in EQ-5D utility scores, assuming a standard deviation of 0.2.

One of the strengths of our study is its randomized design which increases our confidence in the validity of the results. Besides, this study was performed in an international setting. Although this poses the challenge of different healthcare systems, we were able to perform a cost-utility analysis that is not limited to a single country only. Another strength is that, by design, there was no crossover of amyloid-PET in ARM2 in the first 6 months. Finally, participants had a baseline diagnosis that covered the whole continuum of disease severity in memory clinic patients. To summarize, because our study was a multi-country study, had a randomized design, and participants had a variable baseline diagnosis, our results are likely to be representative of clinical practice in memory clinics in different settings.

Yet, as thoroughly discussed above, an important limitation of this study was its short duration. In addition, part of the recruitment of the AMYPAD-DPMS participants took place during the COVID-19 pandemic. As a result, recruitment was temporarily halted. When recruitment resumed, the healthcare systems often did not allow the diagnostic system to function as it did before COVID-19 (e.g., clinicians were unable to order additional diagnostic tests to the extent as they did prior to COVID-19) [28, 29]. Although the COVID-19 pandemic coincided with part of the study period and temporarily affected clinical operations, its overall impact on the study outcomes appears to have been limited. Most participants were included before the onset of the pandemic, and patient enrollment was paused during the initial lockdown to minimize disruptions. Due to the randomized design, any influence of the pandemic was evenly distributed across study arms. While clinicians may have faced temporary restrictions in ordering certain diagnostic tests, post hoc analyses (data not shown) suggest that these factors did not materially affect diagnostic pathways, healthcare utilization, or overall cost patterns. We therefore consider the potential impact of COVID-19 on the cost-effectiveness results to be negligible.

10 | Conclusion

After 6 months, we found no differences in quality of life between patients who underwent amyloid-PET and patients who

had not undergone amyloid-PET, while costs were higher in those who underwent amyloid-PET. This indicates in the first 6 months after diagnosis the trial-based cost-effectiveness profile is not favorable for amyloid-PET. The current analyses were performed to assess the cost-utility of an accurate diagnosis in a setting where no treatment options are available. The cost-effectiveness of amyloid-PET needs to be reassessed when disease-modifying therapies are widely available and amyloid-PET is considered to select patients for anti-amyloid biologicals.

Author Contributions

Ingrid S. van Maurik: methodology, investigation, formal analysis, writing – original draft. **Daniele Altomare:** data curation, writing – review and editing, project administration, resources. **Lyduine E. Collij:** project administration, writing – review and editing. **Camilia Caprioglio:** data curation, project administration, writing – review and editing, resources. **Christian Moro:** data curation, project administration, writing – review and editing, resources. **Valentina Garibotto:** writing – review and editing. **Jean-François Demonet:** writing – review and editing. **Philip Scheltens:** writing – original draft. **Gill Farrer:** writing – review and editing. **Rosella Gismondi:** writing – review and editing. **Andrew W. Stephens:** writing – review and editing. **Jean Domingo Gispert:** writing – review and editing. **José Luis Molinuevo:** writing – review and editing. **Oriol Grau-Rivera:** writing – review and editing. **Paul Edison:** writing – review and editing. **Zuzana Walker:** writing – review and editing. **Frank Jessen:** writing – review and editing. **Alexander Dzrezga:** writing – review and editing. **Philip Zeyen:** writing – review and editing. **Pierre Payoux:** writing – review and editing. **Laure Saint-Aubert:** writing – review and editing. **Julien Delrieu:** writing – review and editing. **Agneta Nordberg:** writing – review and editing. **Frederik Barkhof:** conceptualization, supervision, writing – review and editing, funding acquisition. **Giovanni B. Frisoni:** conceptualization, supervision, writing – review and editing, funding acquisition. **Johannes Berkhof:** methodology, conceptualization, writing – original draft, supervision, writing – review and editing.

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Conflicts of Interest

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Data Availability Statement

The corresponding author (ISvM) is the custodian of the data and will provide deidentified participant data on reasonable request (i.vanmaurik@amsterdamumc.nl), with the completion of a data access agreement.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Appendix 1

The Resource Utilization Questionnaire

About the questionnaire

1. The questionnaire has two versions, a baseline and a follow-up questionnaire.
2. The participant will be asked to fill in the questionnaire at the following study visits: Baseline, 3 months, 6 months and 13 months.
3. The baseline questionnaire focusses on the last 30 days. The follow-up questionnaires focus on the resource utilization during the previous 3 months.
4. Resource utilization from the questionnaires will be entered on to the eCRF afterwards by the researchers.
5. The questionnaire needs to be filled in by the participant and his/her study partner if the participant has one.

Site ID: _____

Participant ID (6 digits): _____

BASELINE QUESTIONNAIRE (T0)

- Who filled in this form?

☐ Participant
☐ Study partner
☐ Both participant and study partner

A1. | Questions About the Participant

A1.1 | Description of Participant

1. Age:
   _____years
2. Sex:
   ☐ Male
   ☐ Female
3. Who do you live with?
   ☐ Alone
   ☐Spouse
   ☐ Sibling
   ☐ Child
   ☐ Other, *please specify:* _____
4. Please specify your current living accommodation:
   ☐ Own home
   ☐ Intermediate forms of accommodation (not dementia-specific)
   ☐ Dementia-specific residential accommodation
   ☐ Long-term institutional care
   ☐ Other, *please specify:* _____

A1.2 | Participant Health Care Resource Utilization

1. During the last 30 days, have you been admitted to a hospital for one or more nights?
   ☐ Yes
   ☐ No, *go to question 4*
2. How many times were you admitted to a hospital (for one or more nights)?
   _____times, during the last 30 days
3. Please specify the total number of nights spent in each type of ward:

Ward	Number of nights during the last 30 days
Intensive care unit	
Geriatric	
Mental health	
Internal medicine	
Surgery	
Neurology	
General ward	
Other (*please specify*):	

4. During the last 30 days, did you visit the hospital for an outpatient visit?
   ☐ Yes
   ☐ No, *go to question 6*
5. How many times did you visit the hospital for an outpatient visit?
   _____Number of times

6. During the last 30 days, did you receive care during day treatment?

   ☐ Yes

   ☐ No, *go to question 8*

7. How many times did you visit the hospital for a day treatment?

   _____number of times

8. Did you receive care in a hospital emergency room?

   ☐ Yes

   ☐ No, *go to question 10*

9. How many times did you receive care in an emergency room?

   _____number of times

10. Did you have to use an ambulance?

    ☐ Yes

    ☐ No, *go to question 12*

11. How many times did you use an ambulance?

    _____number of times

12. Did you receive diagnostic tests during the last 30 days:

    ☐ Yes

    ☐ No, *go to question 14*

13. Please specify the diagnostic tests you had during the last 30 days:

Diagnostic test	Date
Amyloid PET	
CSF/Lumbar puncture	
MRI scan	
CT scan	
SPECT scan	
Blood test	
Urine test	
x-ray	
Ultrasound	
Neuropsychological test	
Other *(please specify):*	

14. During the last 30 days, did you have to stay for the night in an institution other than a hospital (e.g., a rehabilitation center or mental hospital)?

    ☐ Yes

    ☐ No, *go to question 16*

15. Please specify the type of institution where you stayed and the number of nights:

Type of institution	Number of nights during the last 30 days
Rehabilitation center	
Mental hospital	
Residential care	
Other *(please specify):*	

16. During the last 30 days, how many times did you receive care from a health care provider **outside a hospital?** Please specify the number of visits for each type of care received:

Type of care	Number of visits during last 30 days
General practitioner	
Geriatrician	
Practice nurse	
Psychiatrist	
Physiotherapist	
Occupational therapist	
Social worker	
Psychologist	
Other *(please specify):*	

17. For each service listed below, please specify the number of times the service was received during the last 30 days and the average number of hours per visit:

Service	Number of times during last 30 days	Number of hours per time
District nurse		
Home aid (paid assistance in daily activities)		
Day care at an institution		
Transportation (care related but not by ambulance)		
Other *(please specify):*		

18. Are you currently taking any prescription medications?

    ☐ Yes, *please complete below*

    ☐ No, *go to part A1.3*

19. Please specify the medications you are using:

Name of medication	Strength	Frequency	Number of days taken over last 30 days
Example: *Aspirin*	*500 mg*	*2 times a day*	*10 days*

Name of medication	Strength	Frequency	Number of days taken over last 30 days

A1.3 | Participant Employment Status

1. Do you currently have a paid job?
   ☐ Yes
   ☐ No, *go to question 3*
2. How many hours do you work for pay per week?

_____hours distributed over _____ days

3. During the last 30 days, did you decide to permanently reduce the number of hours?
   ☐ Yes
   ☐ No, *go to question 5*
4. By how many hours have you reduced the number of hours that you usually work each week?

_____hours

5. Are you currently on long-term sickness leave (at least 2 weeks) for part or all of your working hours?
   ☐ Yes
   ☐ No, *go to question 7*
6. For how many hours (total) have you currently been on long term sickness leave?

_____hours

7. Why did you have to stop or reduce your working hours?
   ☐ Reached retirement age
   ☐ Early retirement
   ☐ Laid off
   ☐ Cognitive health problems
   ☐ Other health related problems
   ☐ Other, *please specify:* _____

A2. | Questions for Study Partner

The following questions are about the impact of assisting the participant in his/her daily activities.

1. Do you support the participant in his/her daily activities?
   ☐ Yes, *then please continue below*
   ☐ No, *then this is the end of the questionnaire*

A2.1 | Information About Study Partner

1. Age:
   _____years
2. Sex:
   ☐ Male
   ☐ Female
3. Relationship to the participant:
   ☐ Spouse
   ☐ Sibling
   ☐ Child
   ☐ Friend
   ☐ Other, *please specify:* _____
4. Do you live with the participant?
   ☐ Yes
   ☐ No

A2.2 | Help Given to Participant

1. During the last 30 days, how many days did you assist the participant with daily activities?
   _____days
2. On a typical day during the last 30 days, how much time per day did you assist the participant with daily activities?

   _____hours per day

A2.3 | Study Partner Employment Status

1. Do you currently work for pay?
   ☐ Yes
   ☐ No, *go to question 3*
2. How many hours do you work for pay per week?

_____hours distributed over _____ days

3. During the last 30 days, did you decide to permanently reduce the number of hours?
   ☐ Yes
   ☐ No, *go to question 5*
4. By how many hours have you reduced the number of hours that you usually work each week?

_____hours

5. Why did you stop/reduce the hours that you work?
   ☐ Reached retirement age
   ☐ Early retirement
   ☐ Laid off
   ☐ Own health problems
   ☐ To care for the participant
   ☐ Other, *please specify*: _____

Thank you—this is the end of the questionnaire.

Site ID: _____

Participant ID (6 digits): _____

FOLLOW-UP QUESTIONNAIRE, 3 m After Baseline (T1)

- Who filled in this form?

☐ Participant
☐ Study partner.
☐ Both participant and study partner

B1 | Trial Participant

B1.1 | Description of Participant

1. Age:
   _____years
2. Sex:
   ☐ Male
   ☐ Female
3. Who do you live with?
   ☐ Alone
   ☐ Spouse
   ☐ Sibling
   ☐ Child
   ☐ Other, *please specify:* _____

B1.2 | Participant Living Accommodation

1. During the last three months, did you **permanently** change your living accommodation?
   ☐ Yes
   ☐ No, *go to B1.3*
2. Please specify your current living accommodation:
   ☐ Own home
   ☐ Intermediate forms of accommodation (not dementia-specific)
   ☐ Dementia-specific residential accommodation
   ☐ Long-term institutional care
   ☐ Other, *please specify:* _____
3. Please specify the date on which the change occurred:
   _____/_____/_____
   dd/mm/yy
4. Please specify the principal reason for this change in living accommodation:
   ☐ Worsening of participant's cognitive function
   ☐ Worsening of participant's ability to perform daily tasks (e.g., eating, dressing, housework)
   ☐ Poor study partner health
   ☐ Improvement of participant's cognitive function
   ☐ Improvement of participant's ability to perform daily tasks (e.g., eating, dressing, housework)
   ☐ Improved study partner health
   ☐ Other *(please specify):* _____

B1.3 | Participant Health Care Resource Utilization

1. During the last 30 days, have you been admitted to a hospital for one or more nights?
   ☐ Yes
   ☐ No, *go to question 4*
2. How many times were you admitted in a hospital (for one or more nights)?
   _____times, during the last 30 days
3. Please specify the total number of nights spent in each type of ward:

Ward	Number of nights during the last 30 days
Intensive Care Unit	
Geriatric	
Mental health	
Internal medicine	
Surgery	
Neurology	
General ward	
Other *(please specify):*	

4. During the last 30 days, did you visit the hospital for an outpatient visit?
   ☐ Yes
   ☐ No, *go to question 6*
5. How many times did you visit the hospital for an outpatient visit?
   _____number of times
6. During the last 30 days, did you receive any kind of day treatment in a hospital?
   ☐ Yes
   ☐ No, *go to question 8*
7. How many times did you visit the hospital for a day treatment?
   _____number of times
8. Did you receive care in a hospital emergency room?
   ☐ Yes
   ☐ No, *go to question 10*
9. How many times did you receive care in an emergency room?
   _____number of times
10. Did you have to use an ambulance?
    ☐ Yes
    ☐ No, *go to question 12*
11. How many times did you use an ambulance?
    _____number of times
12. Did you receive diagnostic tests during the last 30 days:
    ☐ Yes
    ☐ No, *go to question 14*
13. Please specify the diagnostic tests you had during the last 30 days:

Diagnostic test	Date
Amyloid PET	
CSF/Lumbar puncture	
MRI scan	
CT scan	
SPECT scan	
Blood test	
Urine test	

Diagnostic test	Date
x-ray	
Ultrasound	
Neuropsychological test	
Other *(please specify):*	

14. During the last 30 days, did you have to stay for the night in an institution other than a hospital (e.g., a rehabilitation centre or mental health hospital)?

☐ Yes

☐ No, *go to question 16*

15. Please specify the type of institution where you stayed and the number of nights:

Type of institution	Number of nights during the last 30 days
Rehabilitation center	
Mental health hospital	
Residential care	
Other *(please specify):*	

16. During the last 30 days, how many times did you receive care from a health care provider **outside the hospital?** Please specify the number of visits for each type of care received:

Type of care	Number of visits during last 30 days
General practitioner	
Geriatrician	
Practice nurse	
Psychiatrist	
Physiotherapist	
Occupational therapist	
Social worker	
Psychologist	
Other *(please specify):*	

17. For each service listed below, please specify the number of times the service was received during the last three months and the average number of hours per visit:

Service	Number of times during last 3 months	Number of hours per time
District nurse		
Home aid (paid assistance in daily activities)		
Day care at an institution		
Transportation (care related but not by ambulance)		
Other *(please specify):*		

18. Are you currently taking any prescription medications?

☐ Yes, *please complete below*

☐ No, *go to part A1.3*

19. Please specify the medications you are using:

Name of medication	Strength	Frequency	Number of days taken over last 30 days
Example: *Aspirin*	*500 mg*	*2 times a day*	*10 days*

B1.4 | Participant Employment Status

1. Do you currently work for pay?
   ☐ Yes
   ☐ No, *go to question 3*
2. How many hours do you work for pay per week?

   _____hours
3. During the last three months, did you decide to permanently reduce the number of hours?

   ☐ Yes

   ☐ No, *go to question 5*
4. By how many hours have you reduced the number of hours that you usually work each week?

   _____hours

5. During the last three months, have you been on long-term sickness leave (at least two weeks) for part or all of your working hours?

   ☐ Yes

   ☐ No, *go to question 7*

6. For how many hours (total) have you currently been on long term sickness leave?

   _____hours

7. Why did you have to stop or reduce your working hours?

   ☐ Reached retirement age

   ☐ Early retirement

   ☐ Laid off

   ☐ Cognitive health problems

   ☐ Other health related problems

   ☐ Other, *please specify:* _____

B2 | Study Partner

1. Do you support the participant in his/her daily activities?

   ☐ Yes, *then please continue below*

   ☐ No, *then this is the end of the questionnaire*

B2.1 | Description of Study Partner

1. Age:
   _____years
2. Sex:

   ☐ Male

   ☐ Female

3. Relationship to participant:

   ☐ Spouse

   ☐ Sibling

   ☐ Child

   ☐ Friend

   ☐ Other, *please specify:* _____

4. Do you live with the participant?

   ☐ Yes

   ☐ No

B2.2 | Help Given to Participant

1. During the last three months, how many days did you spend providing help to the participant?
   _____days
2. On a typical care day during the last three months, how much time per day did you assist the participant with daily activities?

   _____hours and minutes per day

B2.3 | Study Partner Employment Status

1. During the last three months, did you work for pay (for part or all of the period)?
   ☐ Yes
   ☐ No, *go to question 3*
2. How many hours do you currently work in total for pay per week?

   _____hours

3. During the last three months, did you decide to permanently reduce the number of hours?

   ☐ Yes

   ☐ No, *go to question 5*

4. By how many hours have you reduced the number of hours that you usually work each week?

   _____hours

5. Why did you stop/reduce working?

   ☐ Reached retirement age

   ☐ Early retirement

   ☐ Laid off

   ☐ Own health problems

   ☐ To care for the participant

   ☐ Other, *please specify:* _____

Thank you—this is the end of the questionnaire.

Site ID: _____

Participant ID (6 digits): _____

FOLLOW-UP QUESTIONNAIRE, 6 m After Baseline (T2)

- Who filled in this form?

☐ Participant
☐ Study partner
☐ Both participant and study partner

C1 | Trial Participant

C1.1 | Description of Participant

1. Age:
   _____years
2. Sex:

   ☐ Male

   ☐ Female

3. Who do you live with?

   ☐ Alone

   ☐ Spouse

   ☐ Sibling

   ☐ Child

   ☐ Other, *please specify:* _____

C1.2 | Participant Living Accommodation

1. During the last three months, did you **permanently** change your living accommodation?
   ☐ Yes
   ☐ No, *go to B1.3*
2. Please specify your current living accommodation:

   ☐ Own home

   ☐ Intermediate forms of accommodation (not dementia-specific)

   ☐ Dementia-specific residential accommodation

   ☐ Long-term institutional care

   ☐ Other, *please specify:* _____

3. Please specify the date on which the change occurred:

_____/_____/_____

dd/mm/yy

4. Please specify the principal reason for this change in living accommodation:

☐ Worsening of participant's cognitive function

☐ Worsening of participant's ability to perform daily tasks (e.g., eating, dressing, housework)

☐ Poor study partner health

☐ Improvement of participant's cognitive function

☐ Improvement of participant's ability to perform daily tasks (e.g., eating, dressing, housework)

☐ Improved study partner health

☐ Other *(please specify):* _____

C1.3 | Participant Health Care Resource Utilization

1. During the last 30 days, have you been admitted to a hospital for one or more nights?
   ☐ Yes
   ☐ No, *go to question 4*
2. How many times were you admitted in a hospital (for one or more nights)?

   _____times, during the last 30 days
3. Please specify the total number of nights spent in each type of ward:

Ward	Number of nights during the last 30 days
Intensive Care Unit	
Geriatric	
Mental health	
Internal medicine	
Surgery	
Neurology	
General ward	
Other *(please specify):*	

4. During the last 30 days, did you visit the hospital for an outpatient visit?

   ☐ Yes

   ☐ No, *go to question 6*
5. How many times did you visit the hospital for an outpatient visit?

   _____number of times
6. During the last 30 days, did you receive any kind of day treatment in a hospital?

   ☐ Yes

   ☐ No, *go to question 8*
7. How many times did you visit the hospital for a day treatment?

   _____number of times
8. Did you receive care in a hospital emergency room?

   ☐ Yes

   ☐ No, *go to question 10*
9. How many times did you receive care in an emergency room?

   _____number of times
10. Did you have to use an ambulance?

    ☐ Yes

    ☐ No, *go to question 12*
11. How many times did you use an ambulance?

    _____number of times
12. Did you receive diagnostic tests during the last 30 days:

    ☐ Yes

    ☐ No, *go to question 14*
13. Please specify the diagnostic tests you had during the last 30 days:

Diagnostic test	Date
Amyloid PET	
CSF/lumbar puncture	
MRI scan	
CT scan	
SPECT scan	
Blood test	
Urin test	
x-ray	
Ultrasound	
Neuropsychological test	
Other *(please specify):*	

14. During the last 30 days, did you have to stay for the night in an institution other than a hospital (e.g., a rehabilitation center or mental health hospital)?

    ☐ Yes

    ☐ No, *go to question 16*
15. Please specify the type of institution where you stayed and the number of nights:

Type of institution	Number of nights during the last 30 days
Rehabilitation center	
Mental health hospital	
Residential care	
Other *(please specify):*	

16. During the last 30 days, how many times did you receive care from a health care provider **outside the hospital?** Please specify the number of visits for each type of care received:

Type of care	Number of visits during last 30 days
General practitioner	
Geriatrician	
Practice nurse	
Psychiatrist	
Physiotherapist	
Occupational therapist	
Social worker	
Psychologist	
Other *(please specify):*	

17. For each service listed below, please specify the number of times the service was received during the last three months and the average number of hours per visit:

Service	Number of times during last 3 months	Number of hours per time
District nurse		
Home aid (paid assistance in daily activities)		
Day care at an institution		
Transportation (care related but not by ambulance)		
Other *(please specify):*		

18. Are you currently taking any prescription medications?

☐ Yes, *please complete below*

☐ No, *go to part A1.3*

19. Please specify the medications you are using:

Name of medication	Strength	Frequency	Number of days taken over last 30 days
Example: *Aspirin*	*500 mg*	*2 times a day*	*10 days*

Name of medication	Strength	Frequency	Number of days taken over last 30 days

C1.4 | Participant Employment Status

1. Do you currently work for pay?
   ☐ Yes
   ☐ No, *go to question 3*
2. How many hours do you work for pay per week?

   _____hours
3. During the last three months, did you decide to permanently reduce the number of hours?

   ☐ Yes

   ☐ No, *go to question 5*
4. By how many hours have you reduced the number of hours that you usually work each week?

   _____hours
5. During the last three months, have you been on long-term sickness leave (at least two weeks) for part or all of your working hours?

   ☐ Yes

   ☐ No, *go to question 7*
6. For how many hours (total) have you currently been on long term sickness leave?

   _____hours
7. Why did you have to stop or reduce your working hours?

   ☐ Reached retirement age

   ☐ Early retirement

   ☐ Laid off

   ☐ Cognitive health problems

   ☐ Other health related problems

   ☐ Other, *please specify:*

C2 | Study Partner

1. Do you support the participant in his/her daily activities?

   ☐ Yes, *then please continue below*

   ☐ No, *then this is the end of the questionnaire*

C2.1 | Description of Study Partner

1. Age:
   _____years
2. Sex:

   ☐ Male

   ☐ Female

3. Relationship to participant:

☐ Spouse

☐ Sibling

☐ Child

☐ Friend

☐ Other, *please specify:* _____

4. Do you live with the participant?

☐ Yes

☐ No

C2.2 | Help Given to Participant

1. During the last three months, how many days did you spend providing help to the participant?
_____days

2. On a typical care day during the last three months, how much time per day did you assist the participant with daily activities?

_____hours and minutes per day

C2.3 | Study Partner Employment Status

1. During the last three months, did you work for pay (for part or all of the period)?
☐ Yes
☐ No, *go to question 3*

2. How many hours do you currently work in total for pay per week?

_____hours

3. During the last three months, did you decide to permanently reduce the number of hours?

☐ Yes

☐ No, *go to question 5*

4. By how many hours have you reduced the number of hours that you usually work each week?

_____hours

5. Why did you stop/reduce working?

☐ Reached retirement age

☐ Early retirement

☐ Laid off

☐ Own health problems

☐ To care for the participant

☐ Other, *please specify:* _____

Thank you—this is the end of the questionnaire.

Site ID: _____

Participant ID (6 digits): _____

FOLLOW-UP QUESTIONNAIRE, 13 m After Baseline (T3)

- Who filled in this form?

☐ Participant
☐ Study partner
☐ Both participant and study partner

D1 | Trial Participant

D1.1 | Description of Participant

1. Age:
_____years

2. Sex:

☐ Male

☐ Female

3. Who do you live with?

☐ Alone

☐ Spouse

☐ Sibling

☐ Child

☐ Other, *please specify:* _____

D1.2 | Participant Living Accommodation

1. During the last three months, did you **permanently** change your living accommodation?
☐ Yes
☐ No, *go to B1.3*

2. Please specify your current living accommodation:

☐ Own home

☐ Intermediate forms of accommodation (not dementia-specific)
☐ Dementia-specific residential accommodation

☐ Long-term institutional care

☐ Other, *please specify:* _____

3. Please specify the date on which the change occurred:

_____/_____/_____

dd/mm/yy

4. Please specify the principal reason for this change in living accommodation:

☐ Worsening of participant's cognitive function

☐ Worsening of participant's ability to perform daily tasks (e.g., eating, dressing, housework)

☐ Poor study partner health

☐ Improvement of participant's cognitive function

☐ Improvement of participant's ability to perform daily tasks (e.g., eating, dressing, housework)

☐ Improved study partner health

☐ Other *(please specify):* _____

D1.3 | Participant Health Care Resource Utilization

1. During the last 30 days, have you been admitted to a hospital for one or more nights?
☐ Yes
☐ No, *go to question 4*

2. How many times were you admitted in a hospital (for one or more nights)?

_____times, during the last 30 days

3. Please specify the total number of nights spent in each type of ward:

Ward	Number of nights during the last 30 days
Intensive Care Unit	
Geriatric	
Mental health	
Internal medicine	
Surgery	
Neurology	
General ward	
Other *(please specify):*	

4. During the last 30 days, did you visit the hospital for an outpatient visit?

☐ Yes

☐ No, *go to question 6*

5. How many times did you visit the hospital for an outpatient visit?

_____number of times

6. During the last 30 days, did you receive any kind of day treatment in a hospital?

☐ Yes

☐ No, *go to question 8*

7. How many times did you visit the hospital for a day treatment?

_____number of times

8. Did you receive care in a hospital emergency room?

☐ Yes

☐ No, *go to question 10*

9. How many times did you receive care in an emergency room?

_____number of times

10. Did you have to use an ambulance?

☐ Yes

☐ No, *go to question 12*

11. How many times did you use an ambulance?

_____number of times

12. Did you receive diagnostic tests during the last 30 days:

☐ Yes

☐ No, *go to question 14*

13. Please specify the diagnostic tests you had during the last 30 days:

Diagnostic test	Date
Amyloid PET	
CSF/Lumbar puncture	
MRI scan	
CT scan	
SPECT scan	
Blood test	
Urin test	
x-ray	
Ultrasound	
Neuropsychological test	
Other *(please specify):*	

14. During the last 30 days, did you have to stay for the night in an institution other than a hospital (e.g., a rehabilitation centre or mental health hospital)?

☐ Yes

☐ No, *go to question 16*

15. Please specify the type of institution where you stayed and the number of nights:

Type of institution	Number of nights during the last 30 days
Rehabilitation center	
Mental health hospital	
Residential care	
Other *(please specify):*	

16. During the last 30 days, how many times did you receive care from a health care provider **outside the hospital?** Please specify the number of visits for each type of care received:

Type of care	Number of visits during last 30 days
General practitioner	
Geriatrician	
Practice nurse	
Psychiatrist	
Physiotherapist	
Occupational therapist	
Social worker	
Psychologist	
Other *(please specify):*	

17. For each service listed below, please specify the number of times the service was received during the last three months and the average number of hours per visit:

Service	Number of times during last three months	Number of hours per time
District nurse		
Home aid (paid assistance in daily activities)		
Day care at an institution		
Transportation (care related but not by ambulance)		
Other *(please specify):*		

18. Are you currently taking any prescription medications?

☐ Yes, *please complete below*

☐ No, *go to part A1.3*

19. Please specify the medications you are using:

Name of medication	Strength	Frequency	Number of days taken over last 30 days
Example: *Aspirin*	*500 mg*	*2 times a day*	*10 days*

D1.4 | Participant Employment Status

1. Do you currently work for pay?
   ☐ Yes
   ☐ No, *go to question 3*
2. How many hours do you work for pay per week?

   _____hours
3. During the last three months, did you decide to permanently reduce the number of hours?

   ☐ Yes

   ☐ No, *go to question 5*
4. By how many hours have you reduced the number of hours that you usually work each week?

   _____hours
5. During the last three months, have you been on long-term sickness leave (at least two weeks) for part or all of your working hours?

   ☐ Yes

   ☐ No, *go to question 7*
6. For how many hours (total) have you currently been on long term sickness leave?

   _____hours
7. Why did you have to stop or reduce your working hours?

   ☐ Reached retirement age

   ☐ Early retirement

   ☐ Laid off

   ☐ Cognitive health problems

   ☐ Other health related problems

   ☐ Other, *please specify:* _____

D2 | Study Partner

1. Do you support the participant in his/her daily activities?

   ☐ Yes, *then please continue below*

   ☐ No, *then this is the end of the questionnaire*

D2.1 | Description of Study Partner

1. Age:
   _____years
2. Sex:

   ☐ Male

   ☐ Female
3. Relationship to participant:

   ☐ Spouse

   ☐ Sibling

   ☐ Child

   ☐ Friend

   ☐ Other, *please specify:* _____
4. Do you live with the participant?

   ☐ Yes

   ☐ No

D2.2 | Help Given to Participant

1. During the last three months, how many days did you spend providing help to the participant?
   _____days
2. On a typical care day during the last three months, how much time per day did you assist the participant with daily activities?

   _____hours and minutes per day

D2.3 | Study Partner Employment Status

1. During the last three months, did you work for pay (for part or all of the period)?
   ☐ Yes
   ☐ No, *go to question 3*
2. How many hours do you currently work in total for pay per week?

   _____hours
3. During the last three months, did you decide to permanently reduce the number of hours?

   ☐ Yes

   ☐ No, *go to question 5*

4. By how many hours have you reduced the number of hours that you usually work each week?

   _____hours

5. Why did you stop/reduce working?

   ☐ Reached retirement age

   ☐ Early retirement

   ☐ Laid off

   ☐ Own health problems

   ☐ To care for the participant

   ☐ Other, *please specify:* _____

Thank you—this is the end of the questionnaire.