Apathy in UK care home residents with dementia:

longitudinal course and determinants

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Running title

Apathy in dementia

Abstract

Background

Apathy in dementia is common and associated with worse disease outcomes.

Objectives

To describe the longitudinal course of apathy in dementia, and identify associated sociodemographic and disease-related factors.

Methods

Prospective cohort study of UK care home residents with dementia. At baseline, 4, 8, 12, and 16 months, care home staff rated apathy using the Neuropsychiatric Inventory (clinically-significant apathy if ≥4), dementia severity, and provided other sociodemographic information about each participant. We examined the prevalence and persistence of apathy and, in mixed linear models, its association with time, age, sex, dementia severity, antipsychotic use, and baseline apathy and other neuropsychiatric symptoms.

Results

Of 1419 included participants (mean age 85 years (SD 8.5)), 30% had mild dementia, 33% moderate, and 37% severe. The point prevalence of clinically-significant apathy was 21.4% (n=304) and the 16-month period prevalence was 47.3% (n=671). Of participants with follow-up data, 45 (3.8%) were always clinically-significantly apathetic, 3 (0.3%) were always sub-clinically apathetic, and 420 (36.2%) were never apathetic until death or end of follow-up. In adjusted models, apathy increased over time and was associated with having more severe dementia, worse baseline apathy and other neuropsychiatric symptoms.

Conclusion

It is important for clinicians to know that most people with dementia are not apathetic, though it is common. Most of those with significant symptoms of apathy improve without specific treatments, although some also relapse, meaning that intervention may not be needed. Future research should seek to target those people with persistent severe apathy and test treatments in this group.

Keywords

Dementia, apathy, care homes, neuropsychiatric symptoms, neuropsychiatric inventory, cohort study

Key Points

- In 1419 care home-dwelling people with dementia followed over 16 months, we found that apathy was common but not universal.
- The point prevalence of clinically-significant apathy was 21% and its period prevalence over 16 months was 47%.
- More than two-thirds of those without symptoms of apathy at baseline remained apathy free.
- Fewer than half of people with baseline clinically-significant apathy at experienced this as a persistent symptom.
- Apathy worsened over time and was associated with severe dementia, more severe apathy and other neuropsychiatric symptoms.

Introduction

Apathy is a syndrome of diminished motivation which persists over time, with reduced emotions, goal-directed behaviour or cognitive activity [1]. It is the most frequent neuropsychiatric symptom in dementia with a pooled prevalence of 49%, ranging from 19% to 88% [2]. Apathy in dementia is important as it is not only associated with deterioration in functional ability [3, 4], but also linked to higher mortality [4, 5] other neuropsychiatric symptoms [6], and associated with adverse caregiver outcomes [7, 8]. Apathy may indicate a worse disease course with the presence of apathy in mild cognitive impairment (MCI) and community-dwelling older adults associated in longitudinal studies with an increased risk of developing dementia [6, 9, 10].

The longitudinal course of apathy is unclear. One Dutch study of 199 people with dementia (mean mini-mental state examination (MMSE) 18) found apathy to be the most persistent of the neuropsychiatric symptoms studied, with 12% having persistent apathy during five assessments over 2 years, although only half of the sample had complete 2-year follow-up data [11]. Another Dutch study followed 290 nursing homes residents with moderate to severe dementia (mean MMSE 7) of whom 40% completed 2 years' follow-up and found apathy symptom severity did not change over time, but prevalence of apathy increased from 19% to 33% [12]. Over half of participants developed apathy (53%) but between 37% and 58% resolved at each follow-up. Apathy may be more common in behavioural variant frontotemporal dementia than in Alzheimer's disease (AD) [13], in AD compared to vascular dementia [12], and in early-onset AD than late-onset AD [14] .

There are no interventions for apathy with proven effectiveness [15-17], though a recent randomized controlled trial of methylphenidate showed a promising result but the results require replication [18]. This may be partly because of its heterogeneous phenotype and variable course making it difficult to isolate treatment effects. Examining the longitudinal course of apathy in people with dementia in a large longitudinal study, would clarify the nature of apathy and inform those affected

and professionals. Understanding the determinants of apathy may also inform development of future interventions to manage apathy and identify whom these should target.

Therefore, in this study we aimed to 1) describe the prevalence and persistence of clinically-significant apathy in UK care home residents with dementia, 2) investigate the association of other neuropsychiatric symptoms in people with clinically-significant apathy, and 3) identify sociodemographic and disease related factors associated with worse apathy trajectory.

Materials and methods

Data for this study came from the Managing Agitation and Raising Quality of life (MARQUE) longitudinal care home study, which has previously been described in detail [19-21]. MARQUE was approved by the National Research Ethics Committee London Harrow 14/LO/0034 (06/03/14).

Participants and setting

We recruited residents from 86 care homes between January 2014 and November 2015 if they had a clinical diagnosis of dementia or scored more than two on the Noticeable Problems Checklist (NPC), which is a six-item proxy-rated questionnaire assessing cognition and function, validated against clinical criteria [22]. A range of different care homes were included, comprising voluntary, state and private, recruited through third sector partners, NHS trusts and clinicians, a Department of Health newsletter and a NIHR clinical research network.

After care home managers agreed for their home to participate in the study, care home staff then completed the NPC for all residents without known dementia diagnosis to identify those who may have undiagnosed dementia. All those with known dementia or who screened positive for dementia were eligible. Staff asked residents who they judged as having mental capacity using the principles of the UK 2019 Mental Capacity Act if researchers could approach them. These residents were then asked for written informed consent to participate in the study. For all other residents, the staff tried

to contact next-of-kin consultees to ask if the researchers could contact them and proxy consent was obtained in line with the Mental Capacity Act 2005.

Measures and procedures

In a private room at the care home, a trained researcher interviewed a staff member who worked closely with each resident with dementia to complete proxy-rated measures about the resident. Data were collected on five occasions, at baseline, 4 months, 8 months, 12 months and 16 months.

Apathy

We assessed apathy and other neuropsychiatric symptoms using the Neuropsychiatric Inventory (NPI) [23] which is an informant-rated scale assessing the presence and severity of 12 neuropsychiatric symptoms. For each symptom, the informant is asked whether the symptom has been present during the past month. If not, the score for that symptom is 0, but if so, the symptom is rated on severity (1-3) and frequency (1-4) and the score for each symptom is then derived by multiplying the severity and frequency scores, resulting in a score from 0-12. Consistent with previous studies [24], we divided participants into those with 'no apathy' (scoring 0 on NPI apathy subscale), 'sub-clinical apathy' (scoring 1-3) and 'clinically-significant apathy' (scoring 4-12).

Other neuropsychiatric symptoms

Other neuropsychiatric symptoms (delusions, hallucinations, agitation, depression, anxiety, irritability, euphoria, disinhibition, aberrant motor behaviour, night-time behaviour disturbances, and appetite and eating abnormalities) were also assessed using the NPI with the same scoring scale as for apathy, with a score of ≥ 4 considered clinically-significant severity. Total score of the NPI was calculated by summing scores of the 11 items (excluding apathy).

Other variables

We collected demographic information including the resident's age, sex, and marital status

(married/common law partner, single/divorced or separated, and widowed). We asked whether residents had taken antipsychotics, antidepressant, hypnotics/anxiolytics, analgesia, acetylcholinesterase inhibitors, or memantine grouped according to chapters of the British National Formulary [25] either prescribed regularly or as required during the preceding two weeks before baseline [26]. All participants had dementia. Dementia severity was assessed using the Clinical Dementia Rating (CDR) scale [27], where CDR 0.5 or 1 = mild dementia, 2 = moderate dementia, and 3 = severe dementia.

Statistical methods

Statistical analysis was performed with Stata/MP16. First, baseline demographics and presence of other neuropsychiatric symptoms were described for people with no apathy, sub-clinical apathy, and clinically-significant apathy, and characteristics were compared between the three groups using ANOVA for continuous variables and chi-square test for categorical variables.

We then described the longitudinal course of apathy by describing, for each of the three apathy groups, the proportion of participants who had no, sub-clinical, or clinically-significant apathy, or had died at each subsequent time-point 4, 8, 12, and 16 months after baseline. Since deaths of participants may lead to attrition bias, we included the number of dead people cumulatively over time.

We examined the association of apathy with socio-demographic and clinical characteristics using apathy data at all study time points. We used linear mixed models with a random effect for intercept because data were clustered by individuals. We first examined the association of apathy NPI subscale score with study time-point in unadjusted models and then included in our model age (continuous), sex, dementia severity (mild, moderate or severe), use of antipsychotics, apathy at baseline (no apathy, sub-clinical apathy, clinically-significant apathy), and baseline total score of the NPI (excluding the apathy subscale).

Results

We included 1,419 residents with dementia whose sociodemographic and clinical characteristics are summarized in table 1. The mean age of participants was 85 years (standard deviation (SD) 8.5) and 975 (68.7%) were women. The majority (55.7%) were widowed and 333 (24.1%) were married with the remainder single, divorced or separated. There was a range of dementia severity with 418 (29.5%) having mild dementia, 468 (33.1%) moderate, and 530 (37.4%) severe. The most commonly used medications were antidepressant (568, 40.0%). The number of participants at each study phase is shown in Figure 1.

Longitudinal course of apathy

At baseline, 946 participants (66.7%) had no apathy, 169 participants (11.9%) had sub-clinical apathy and 304 (21.4%) had clinically-significant apathy. By the 16-month study time-point, 492 (34.7%) residents had died, comprising 320 (33.8%) of people who had no apathy at baseline, 52 (30.8%) of people with sub-clinical apathy and 120 (39.5%) of those with clinically-significant apathy at baseline. The period prevalence of any apathy during the 16 months of study follow-up was 85.1% (1207 participants) and the period prevalence of clinically-significant apathy during this time was 47.3% (671 participants). Full information about apathy scores at each time-point is in Supplementary Table 1.

The longitudinal progression of apathy is shown in Figure 2. Of the people who had clinically-significant apathy at baseline, 52 (18.2%) had died four months later, 89 (32.5%) at 8 months, 109 (40.7%) at 12 months and 120 (45.8%) at 16 months' follow-up. 100 (35.1%), 80 (29.2%), 70 (26.1%) and 65 (24.8%) of the baseline clinically-significantly apathetic participants had clinically-significant apathy at the 4, 8, 12, and 16-month time-points respectively. The proportions of surviving participants with clinically-significant apathy at baseline who had clinically-significant apathy at 4, 8, 12, and 16 months were 42.9%, 43.2%, 44.0%, and 45.8% respectively.

Of the people who had no apathy at baseline, 89 (10.1%) had died at 4 months, 188 (22.1%) at 8 months, 261 (31.7%) at 12 months, and 320 (39.7%) at 16 months. 606 (69.0%), 491 (57.6%), 411 (49.9%), and 346 (42.9%) of participants who had no apathy at baseline continued to not be apathetic at 4, 8, 12, and 16 months' follow-up respectively. The proportions for surviving participants only who had persistent absence of apathy at these time-points were 76.8%, 73.9%, 73.1%, and 71.3% at 4, 8, 12, and 16 months. Sub-clinical apathy rarely persisted, with only 12.2%, 9.4%, 7.9% and 4.5% of the 169 participants with sub-clinical apathy at baseline remaining in this group at study follow-up.

Of the 1196 people who had at least two assessments, 45 (3.8%) were always clinically-significantly apathetic, 3 (0.3%) were always sub-clinically apathetic, and 420 (36.2%) were never apathetic until death or end of follow-up.

Association of socio-demographic and clinical characteristics with baseline apathy

There were no differences in age, sex, marital status, and use of medications, including antidepressant, antipsychotics, hypnotics, analgesics, acetylcholinesterase inhibitors, or memantine, between the three baseline apathy groups. There was a higher rate of more severe dementia in those with clinically-significant apathy (p <0.001).

Several other neuropsychiatric symptoms were significantly more common in those with apathy (Table 2). Clinically-significant hallucinations (present in 11.1% of those with clinically-significant apathy vs 4.9% of those without apathy), agitation/aggression (52.6% vs 26.7%), depression/dysphoria (25.3% vs 7.4%), anxiety (21.5% vs 10.4%), disinhibition (15.0% vs 6.3%), irritability (31.7% vs 15.8%), sleep disturbance (24.4% vs 11.4%), and appetite disturbance/eating disorder (37.7% vs 10.4%) were more common in those with clinically-significant apathy compared to those without apathy. Only the presence of delusions, elation/euphoria, and aberrant motor behaviour was not associated with apathy. The mean NPI score (excluding the apathy subscale) was

substantially higher for those with clinically-significant apathy (20.2, SD 16.8) than those without apathy (10.3, SD 12.3) or those with sub-clinical apathy (11.3, SD 9.5).

Determinants of apathy over time

Apathy overall increased over follow-up: NPI apathy subscale scores were 0.36 (95% confidence interval (CI) 0.10, 0.62) points higher at 8 months, 0.56 (0.29, 0.84) points higher at 12 months, and 0.71 (0.42, 1.00) at 16 months compared to 4 months (Table 3). In adjusted models, this increase in apathy over time persisted. Having more severe dementia was associated with worse apathy: (1.18 (0.78, 1.58) NPI apathy points higher for those with severe v mild dementia). Having worse baseline apathy was associated with worse apathy (1.73 (1.31, 2.16) points higher apathy score for those who had clinically-significant v no apathy). Worse baseline neuropsychiatric symptoms were also associated with worse apathy (0.03 (0.02, 0.04) points higher apathy score for each one point higher NPI scale score). Older age, sex or taking antipsychotic medication were not associated with apathy.

Discussion

In, to our knowledge, the largest study of apathy in people with dementia including 1419 people with dementia living in UK care homes over 16 months, we found that apathy was a common but not universal symptom, and that it frequently fluctuated over months with most people who had clinically-significant apathy at one time period no longer scoring in the clinically-significant range four months later. In addition, three-quarters of those with no apathy symptoms at baseline never developed clinically-significant apathy. However nearly half of residents were reported as having clinically-significant apathy at least once, indicating that even those who had no apathy at baseline often later had apathy at some point in follow-up. Apathy scores in the whole population worsened over time and this increase was more pronounced in those with more severe dementia, more severe apathy and other neuropsychiatric symptoms at baseline. One third of participants had some level of apathy at baseline and a fifth had clinically-significant levels. Over time, many people in the study

developed apathy, with the large majority of participants (85%) having sub-clinical or clinically-significant apathy at least once during study 16 months' follow-up. However, the longitudinal course of apathy was variable. More than two-thirds (71-77%) of those without symptoms of apathy remained apathy free. In contrast, fewer than half (40-46%) of people had persistent clinically-significant apathy at 4 monthly time points, and only 5-12% had persisting sub-clinical apathy. Only 4% of participants with at least two assessments had persistent clinically-significant apathy until the end of follow-up.

The prevalence of apathy in our large care-home dwelling sample is slightly lower than that found in other smaller studies. We found a third of people had any apathy at baseline, whereas three studies of people with moderate dementia found that point-prevalence of apathy on the NPI ranged from 40-51.3% [11, 28, 29]. Our lower prevalence is surprising as our sample had people with more severe dementia than these studies and were recruited from care homes, rather than community clinic settings as for the other studies. We might expect the nursing home population to have higher rates of apathy but this was not the case. Our finding of baseline point prevalence of 21% for clinically-significant apathy was however consistent with a study of 290 nursing home residents with severe dementia (prevalence 18.8%) [12].

The disparities in apathy prevalence between these studies may reflect differences in the perspective of the rater. Both ours and the care home study [12] used care home staff ratings which may be less influenced by the personality of the person with dementia before the illness. Although not explicitly described, it is likely that the other studies of community-dwelling people with dementia used family-informants [11, 28, 29]. Family members are more likely to compare their relative to the way they were when well and to find apathy distressing, linked with feelings of guilt and difficulties in decision-making [30], so apathy may be more salient in family-raters than professional caregivers, for whom apathy is rarely considered distressing [31].

We expected that apathy would be associated with depression and anxiety, which are commonly grouped as affective neuropsychiatric symptoms [32]. We were surprised that apathy was associated with symptoms of hyperactivity – agitation and irritability – as these may be considered to be antithetical [33], although as expected apathy was not associated with elation and increased motor activity. Our findings are consistent with previous studies which have found associations of apathy with most other neuropsychiatric symptoms, for example uncooperative agitation 2.6x, physical agitation 2.7x, and impulsive or euphoric behaviour 3.9x more common in people with dementia who have apathy than in those who do not [34]. Apathy therefore, when present, is likely to co-exist with other neuropsychiatric symptoms.

We found that more severe dementia, more severe apathy and other neuropsychiatric symptoms at baseline were associated with a worse course of apathy; demographic features and psychotropic prescription were not. This finding is in line with a small longitudinal study of people with newly diagnosed dementia [28] and a large population based survey [4] showing the association between more severe dementia or worse cognitive function and incident apathy. An autopsy study found that apathy was associated with higher neurofibrillary tangle concentration in the anterior cingulate cortex [35] and imaging studies indicate that apathy is linked with prefrontal-subcortical circuit disruption [36, 37] suggesting that apathy reflects neurodegeneration.

Strengths of this study include the large number of participants and the five assessments over 16 months with systematic assessment of neuropsychiatric symptoms. It extends previous research by examining associations longitudinally, has a low attrition, with 85% of participants followed until their death or the end of our study period. However, there are limitations which affect the interpretation of our findings. Firstly, though we aimed to speak to care staff who knew the residents well, they may have been looking after many residents and so there may be measurement error which accounts for variability in apathy scores across time. While the NPI is the most used instrument for assessing apathy in dementia, it lacks detail on specific symptoms which limits our

conclusions. Previous studies have suggested a Hawthorne effect whereby repeated visits to a care home influence neuropsychiatric symptoms in a positive way so this may have affected our longitudinal ratings [38]. We did not collect comorbidities or pain which could have affected apathy and we did not have information about dementia subtype meaning we could not consider whether apathy trajectory varied by dementia type. We did not include data on staffing of, or activities in, included care homes but previous studies have suggested that there are not associated with other neuropsychiatric symptoms [19]. Finally, our observational study did not deliver any intervention to participants, but some may have received treatments aiming to improve apathy as part of their usual clinical care and we do not have information about this. However, as no interventions have proven efficacy [15, 17], these treatments are unlikely to have altered our findings on apathy's longitudinal course.

In conclusion, our results indicate that most people with dementia are not apathetic at any one time but it is common, and fluctuates in its course. It is important for clinicians to know that most people with dementia do not develop apathy and it is not an inevitable symptom. In people with less severe dementia and less severe apathy or other neuropsychiatric symptoms, it is more likely to improve. Clinicians and researchers may suggest social stimulation (as is good practice in care homes) and watchful waiting as appropriate responses since most cases will resolve. Previous reviews suggest that individualized treatments incorporating patients' past preferences and environmental factors are potential treatment approaches [15] but some of the failures of drug treatment to show efficacy may be related to recruiting people who will, in the main, remit spontaneously. There are no treatment options which have consistently proven clinical effectiveness, and researchers should consider targeting those whose symptoms are less likely to remit spontaneously, such as those with more severe dementia, worse apathy and other neuropsychiatric symptoms. These groups may be suitable targets for future trials of promising treatments such as methylphenidate [18]. Future

studies may also identify neurobiological markers of apathy and elucidate those with persistent apathy allowing targeted treatment.

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Conflict of interest

The authors have no conflict of interest to report.

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Table 1. Clinical characteristics according to severity of apathy

Characteristics		All participants (N=1419)		No apathy (N=946)		Sub-clinical apathy (N=169)		Clinically-significant apathy (N=304)		p-value
		n	%	n	%	n	%	n	%	
Age	**(mean ± SD)**	85.0 ± 8.5		85.1 ± 8.3		83.7 ± 9.9		85.2 ± 8.5		0.149
Sex	**Female**	985	69.4	665	70.3	112	66.3	208	68.4	0.529
Marital status	**Married/common law partner**	333	24.1	208	22.6	49	29.9	76	25.6	0.273
	Single, divorced or separated	279	20.2	185	20.1	31	18.9	63	21.2	
	Widowed	771	55.8	529	57.4	84	51.2	158	53.2	
	Missing	36		24		5		7		
Dementia severity	**Mild**	418	29.5	325	34.4	53	31.4	40	13.2	<0.001
	Moderate	468	33.1	319	33.8	63	37.3	86	28.4	
	Severe	530	37.4	300	31.8	53	31.4	177	58.4	
	Missing	3		2		0		1		
Medications	**Antipsychotics**	238	16.8	145	15.3	32	18.9	61	20.1	0.114
	Antidepressant	568	40.0	370	39.1	79	46.8	119	39.1	0.165
	Hypnotic or anxiolytics	273	19.2	181	19.1	32	18.9	60	19.7	0.968
	Analgesia	933	65.8	616	65.1	115	68.1	202	66.5	0.730
	Acetylcholinesterase inhibitor	139	9.8	89	9.4	17	10.1	33	10.9	0.756
	Memantine	84	5.9	50	5.3	13	7.7	21	5.9	0.338

Table 2. Neuropsychiatric symptoms according to severity of apathy

Neuropsychiatric inventory		All subjects (N=1,419)		No apathy (N=946)		Sub-clinical apathy (N=169)		Clinically-significant apathy (N=304)		P value
		n/N	%	n/N	%	n/N	%	n/N	%	
Delusion	Frequency	141/1,398	10.1	93/940	9.9	14/164	8.5	34/294	11.6	0.554
	score	6.9 ± 2.6 (N=139)		6.9 ± 2.7 (N=91)		6.6 ± 2.7 (N=14)		6.9 ± 2.3 (N=34)		
Hallucinations	Frequency	89/1,407	6.3	47/944	4.9	9/166	5.4	33/297	11.1	0.001
	score	5.9 ± 2.2 (N=89)		5.8 ± 2.2 (N=47)		6.0 ± 1.7 (N=9)		6.3 ± 2.3 (N=33)		
Agitation/Aggression	Frequency	459/1,419	32.4	253/946	26.7	46/169	27.2	160/304	52.6	<0.001
	score	6.8 ± 2.6 (N=458)		6.6 ± 2.5 (N=252)		6.1 ± 2.3 (N=46)		7.2 ± 2.8 (N=160)		
Depression/Dysphoria	Frequency	163/1,414	11.5	70/942	7.4	16/168	9.5	77/304	25.3	<0.001
	score	6.2 ± 2.5 (N=159)		5.9 ± 2.4 (N=66)		5.1 ± 2.1 (N=16)		6.6 ± 2.5 (N=77)		
Anxiety	Frequency	183/1,417	12.9	98/945	10.4	20/169	11.8	65/303	21.5	<0.001
	score	6.4 ± 2.6 (N=182)		6.4 ± 2.5 (N=97)		4.9 ± 1.5 (N=20)		6.7 ± 2.8 (N=65)		
Elation/Euphoria	Frequency	41/1,416	2.9	25/945	2.7	4/168	2.4	12/303	3.9	0.464
	score	6.0 ± 2.1 (N=39)		5.9 ± 2.1 (N=23)		5.0 ± 2.0 (N=4)		6.4 ± 2.3 (N=12)		
Disinhibition	Frequency	111/1,413	7.9	60/946	6.3	6/167	3.6	45/300	15.0	<0.001
	score	6.7 ± 2.5 (N=111)		6.8 ± 2.5 (N=60)		7.0 ± 3.0 (N=6)		6.5 ± 2.6 (N=45)		
Irritability/Lability	Frequency	273/1,417	19.3	149/946	15.8	28/168	16.7	96/303	31.7	<0.001
	score	6.9 ± 2.7 (N=272)		6.6 ± 2.5 (N=148)		3.1 ± 2.4 (N=92)		7.7 ± 2.9 (N=96)		
Aberrant motor behaviour	Frequency	259/1,405	19.3	164/940	17.5	27/169	15.9	67/296	22.6	0.092
	score	6.6 ± 2.8 (N=232)		6.3 ± 2.7 (N=147)		6.2 ± 2.6 (N=26)		7.3 ± 3.1 (N=59)		
Sleep	Frequency	198/1,407	14.1	107/940	11.4	18/168	10.7	73/299	24.4	<0.001
	score	6.2 ± 2.3 (N=194)		5.9 ± 2.0 (N=105)		6.2 ± 2.3 (N=17)		6.6 ± 2.6 (N=72)		
Appetite / eating disorder	Frequency	228/1,378	16.6	96/924	10.4	23/165	13.9	109/289	37.7	<0.001
	score	7.3 ± 2.8 (N=220)		7.3 ± 2.8 (N=92)		6.5 ± 2.7 (N=22)		7.6 ± 2.9 (N=106)		
Neuropsychiatric Inventory	**total score**	12.5 ± 13.7 (N=1,419)		10.3 ± 12.3 (N=946)		11.3 ± 9.5 (N=169)		20.2 ± 16.8 (N=304)		<0.001

Table 3. Longitudinal scores on NPI apathy score and relationship to clinical and socio-demographic features

		Unadjusted N=1,230		**Fully adjusted N=1,175**	
		Coefficient	95% CI	Coefficient	95% CI
Characteristic					
Study time-point	**4 months**	Reference		Reference	
	8 months	0.36	(0.10, 0.62)	0.36	(0.10, 0.63)
	12 months	0.56	(0.29, 0.84)	0.55	(0.27, 0.83)
	16 months	0.71	(0.42, 1.00)	0.68	(0.38, 0.97)
Age	**(per year older age)**			-0.01	(-0.03, 0.01)
Sex	**Female**			Reference	
	Male			0.10	(-0.26, 0.45)
Dementia severity	**Mild**			Reference	
	Moderate			0.64	(0.25, 1.03)
	Severe			1.18	(0.78, 1.58)
	Antipsychotic			-0.18	(-0.60, 0.25)
Baseline apathy	**Baseline no apathy**			Reference	
	Baseline sub-clinical apathy			0.85	(0.37, 1.34)
	Baseline clinically-significant apathy			1.73	(1.31, 2.16)
Other baseline neuropsychiatric symptoms	**(per one point higher NPI (minus apathy) score)**			0.03	(0.02, 0.04)

Notes: Outcome is NPI apathy score (range 0-12). The fully adjusted model includes all the characteristics described in the table as covariates.

Figure 1. Participation at each study phase and reasons for non-participation

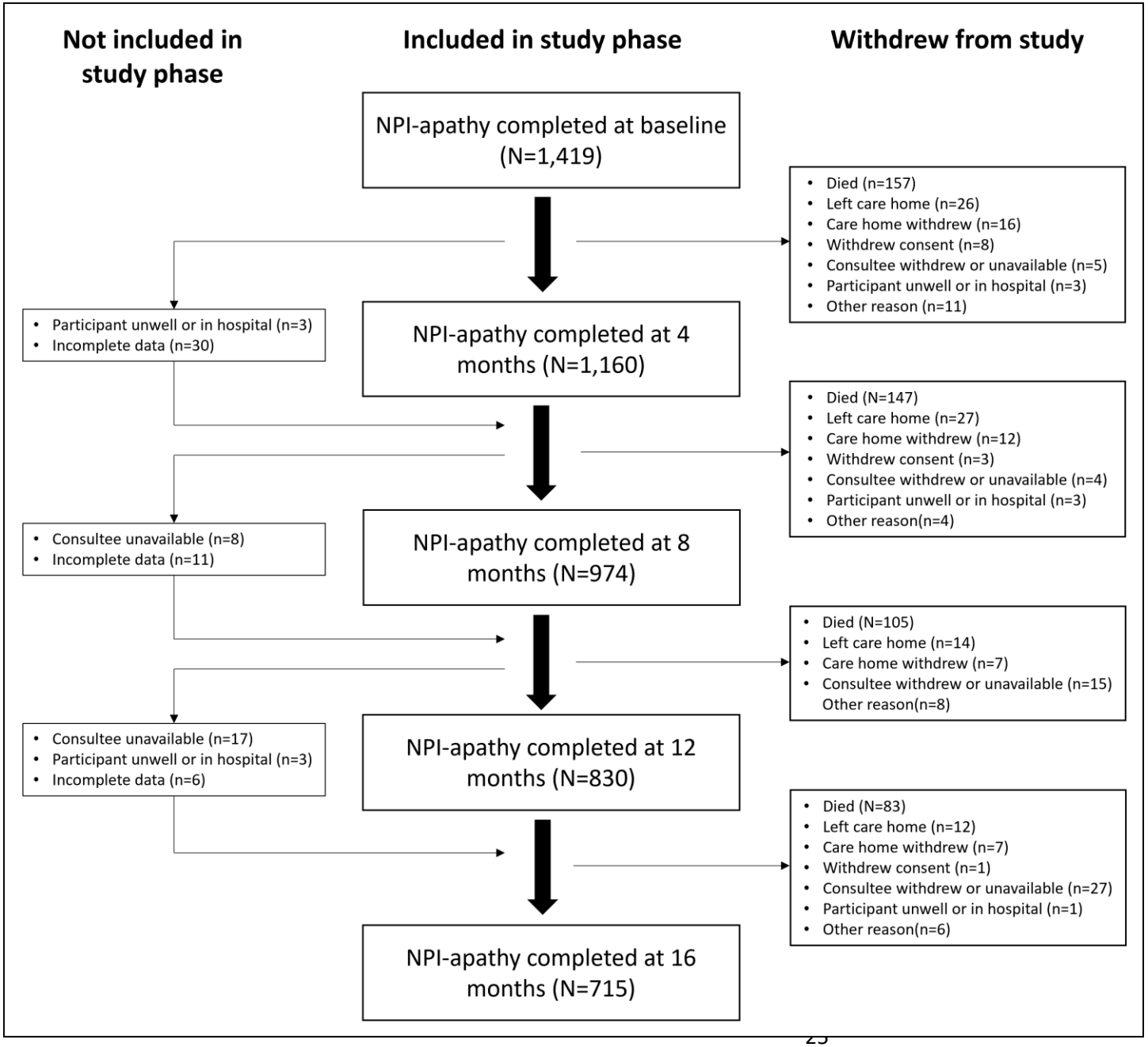
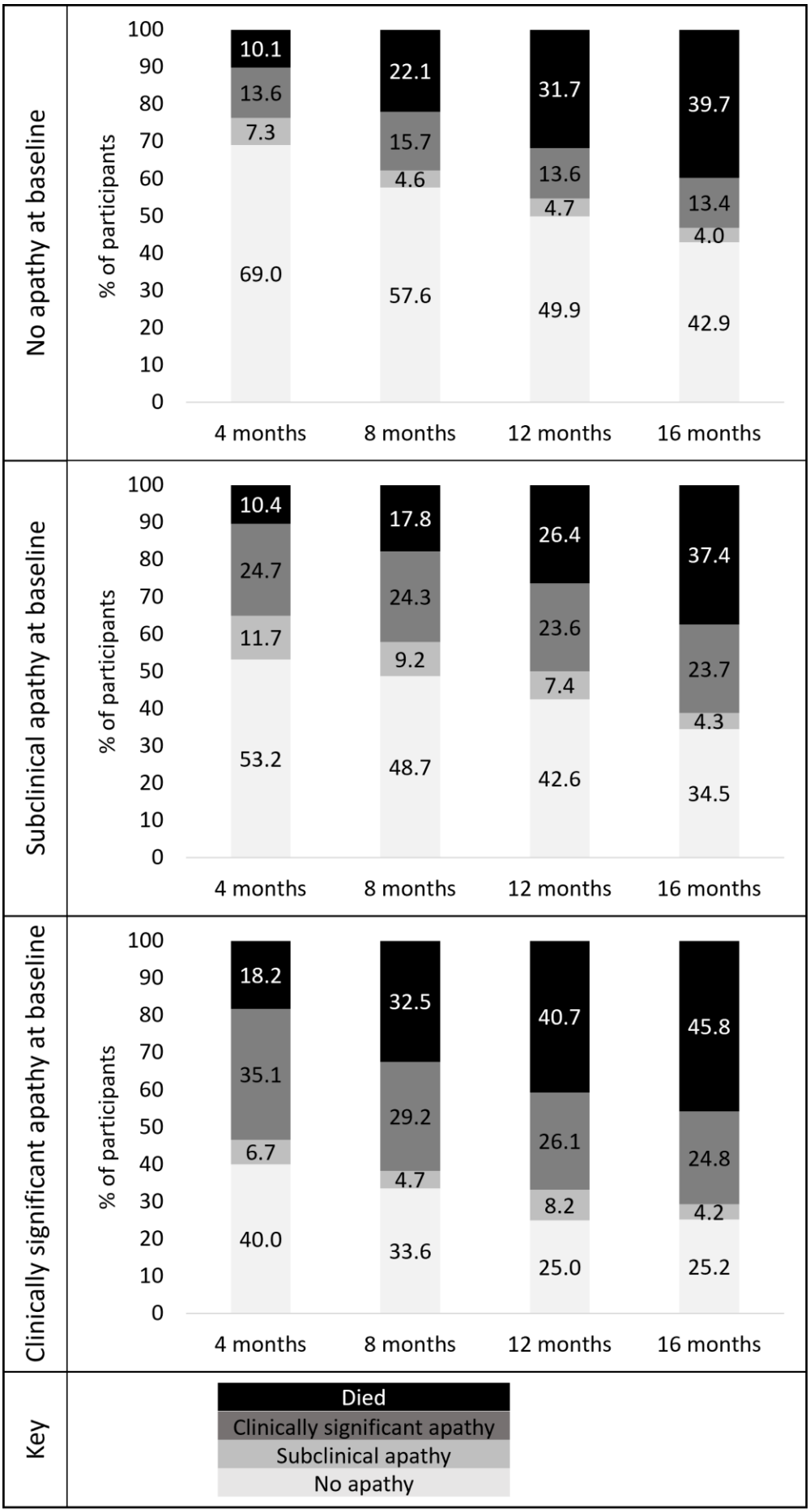

Not included in study phase
Included in study phase
Withdrew from study
NPI-apathy completed at baseline (N=1,419)
Died (n=157)
Left care home (n=26)
Care home withdrew (n=16)
Withdrew consent (n=8)
Consultee withdrew or unavailable (n=5)
Participant unwell or in hospital (n=3)
Other reason (n=11)
Participant unwell or in hospital (n=3)
Incomplete data (n=30)
NPI-apathy completed at 4 months (N=1,160)
Died (N=147)
Left care home (n=27)
Care home withdrew (n=12)
Withdrew consent (n=3)
Consultee withdrew or unavailable (n=4)
Participant unwell or in hospital (n=3)
Other reason(n=4)
Consultee unavailable (n=8)
Incomplete data (n=11)
NPI-apathy completed at 8 months (N=974)
Died (N=105)
Left care home (n=14)
Care home withdrew (n=7)
Consultee withdrew or unavailable (n=15)
Other reason(n=8)
Consultee unavailable (n=17)
Participant unwell or in hospital (n=3)
Incomplete data (n=6)
NPI-apathy completed at 12 months (N=830)
Died (N=83)
Left care home (n=12)
Care home withdrew (n=7)
Withdrew consent (n=1)
Consultee withdrew or unavailable (n=27)
Participant unwell or in hospital (n=1)
Other reason(n=6)
NPI-apathy completed at 16 months (N=715)

Figure 2. Apathy's longitudinal course according to the baseline presence of apathy



Supplementary table 1. Apathy scores at each time-point

		Baseline (N=1419)		4 months (N=1160)		8 months (N=974)		12 months (N=830)		16 months (N=715)	
		n	%	N	%	n	%	n	%	n	%
NPI scores	0	946	66.7	804	69.3	657	67.5	541	65.2	460	64.3
	1	65	4.6	41	3.5	22	2.3	24	2.9	16	2.2
	2	57	4.0	23	2.0	21	2.2	19	2.3	18	2.5
	3	47	3.3	37	3.2	23	2.4	29	3.5	15	2.1
	4	90	6.3	64	5.5	58	6.0	41	4.9	38	5.3
	6	50	3.5	33	2.8	36	3.7	28	3.4	28	4.0
	8	87	6.1	84	7.2	75	7.7	65	7.8	63	8.8
	9	9	0.6	8	0.7	3	0.3	5	0.6	5	0.7
	12	68	4.8	66	5.7	79	8.1	78	9.4	72	10.1
Mean (SD)[a]		5.4	(3.6)	6.1	(3.7)	6.8	(3.7)	6.9	(3.8)	7.2	(3.7)
No apathy[b]		946	66.7	804	69.3	657	67.5	541	65.2	460	64.3
Sub-clinical apathy[b]		169	11.9	100	8.6	66	6.8	72	8.7	49	6.9
Clinically-significant apathy[b]		304	21.4	256	22.1	251	25.8	217	26.1	206	28.8

Notes: NPI = Neuropsychiatric inventory; [a] Mean and standard deviation in those who scored >0; [b] No apathy = 0 on NPI apathy subscale, Sub-clinical apathy = 1-3, Clinically-significant apathy = 4-12