

Becoming or remaining agitated: the course of agitation in people with dementia living in care homes: the English longitudinal Managing Agitation and Raising Quality of Life (MARQUE) study

Running title: course of agitation in people with dementia

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ABSTRACT

Care home residents with dementia often have accompanying agitation. We investigated agitation's course at 5 time-points in 1424 people with dementia over 16 months in 86 English care homes.

We categorised baseline agitation symptoms on the Cohen-Mansfield Agitation Inventory (CMAI) into none (CMAI=29; 15%), subclinical (CMAI=30-45; 45%) or clinically-significant (CMAI>45; 40%). 88% of those with no agitation at baseline remained free of clinically-significant agitation at all follow-ups. Seventy percent of those exhibiting clinically-significant agitation at baseline had clinically-significant agitation at some follow-ups.

Over a 16-month observation period, this study finds many care home residents with dementia never develop clinically significant agitation and interventions should be for treatment not prevention.

Keywords: dementia, agitation, nursing homes, neuropsychiatric symptoms

INTRODUCTION

The majority of people living in care homes have dementia. Many exhibit agitated behaviours which often lead to breakdown of care at home by family or paid carers and to the person living with dementia needing to move to a care home [1]. The prevalence of agitation in care home residents with dementia has been estimated at between 24% and 88% in residential facilities in Europe and the United States [2,3]. These symptoms are associated with an annual excess cost per person with dementia in care homes of £1,125.[4]

There have been large longitudinal studies of agitation in nursing home residents with dementia in Norway and the Netherlands [5,6]. Selbæk [6] used a composite measure comprising Neuropsychiatric Inventory (NPI) subscales and found that agitation symptoms increased with time and dementia severity. This assessment of agitation uses the NPI scale differently from the way it was designed. However, the Cohen-Mansfield Agitation Inventory (CMAI) is specifically designed to measure agitation comprehensively [7]. Previously in a small study in a mixed community and care home study, nearly 80% of 224 people with dementia who had no symptoms of agitation at baseline remained free of symptoms at 6 month follow-up suggesting agitation may not be an inevitable consequence of increasing severity as it is often conceptualised [8]. Hendriks [5] reported a stable prevalence of agitation over 3.5 years, with some agitation resolving, but they recorded agitation only as present or absent, limiting interpretation of findings.

In our cross-sectional findings from the MARQUE study, which includes the largest naturalistic study of care home residents with dementia to date, we reported that forty-five percent of those with moderate or severe dementia had clinically significant agitation, with lower rates reported among residents with mild dementia [2]. It is unclear whether these high rates of agitation particularly in those with more severe dementia relate to agitation worsening over time, with dementia progression (and the high proportion of residents with dementia who have a more severe illness); or may reflect high rates of agitation in people transitioning to care homes.

Knowledge about the course of agitation over time and its association with disease severity will help inform family carers, care home staff, managers and professional staff. In the current study, we investigate whether people living with dementia in care homes developed agitation as their dementia deteriorated, remained stable or improved over up to 16 months. We seek to understand the prognosis of people living in care homes with dementia - with no agitation, subclinical and clinically significant agitation at baseline to help inform clinical practice.

METHODS

National Research Ethics Committee London-Harrow 14/LO/0034 (06/03/14) granted ethical approval for the study. Where care home workers judged that residents had capacity to consent, they were approached by researchers who assessed their decisional capacity and asked them for informed consent if appropriate. For those who did not have capacity to consent, care home staff asked the resident's family carer for permission for researchers to contact them. In line with the Mental Capacity Act (2005), the family carer was invited to be a personal consultee and make a decision regarding research participation for the resident. If a personal consultee could not be found, we used a professional consultee.

Data came from the MARQUE cohort study [2]. We recruited residents between January 2014 and November 2015 from 86 care homes in England, comprising 97 clusters. A cluster within a care home was delineated by the staff working independently within that cluster and never working in other parts of the care home. Residents were eligible to participate if they had a clinical diagnosis of dementia or scored more than two on the Noticeable Problems Checklist[9]. We interviewed informants every four months for 16 months after baseline. Sixteen months' follow-up was chosen because, in the UK, people spend an average of two years in a care home and we wanted to follow most residents through their care home trajectory[10]. Further details on recruitment procedures are published elsewhere[2].

Measures

The staff member who knew the resident best completed proxy measures, facilitated by trained researchers. They recorded sociodemographic information at baseline and the following measures at each time point:

The Cohen-Mansfield Agitation Inventory (CMAI)[7] is a 29 item instrument designed to measure agitation symptoms in people with dementia; frequency of different agitated behaviours are rated using a seven-point scale, from never (score 1) to several times per hour (score 7). Possible scores range from 29 to 203. We categorised scores as: no agitation (a score of 29), subclinical agitation (score 30 to 45) or clinically significant agitation (a score of 46 or more) [2].

Clinical Dementia Rating (CDR) [11] rates the severity of symptoms of dementia in six domains to generate an overall severity category.

Statistical methods

We conducted analyses using Stata v14. We describe baseline characteristics by agitation category using appropriate summary statistics and we calculated agitation at each follow-up point according to each resident's initial category of agitation. We visualised the data using stacked bar charts percentage in each agitation category at each time point by baseline agitation category. At each follow-up point, we collected data on all participants. Where the person had died since the last follow-up, we noted this and included them cumulatively over time. We performed a sensitivity analysis to consider the data without the deaths of participants included.

RESULTS

We recruited 1,424 (47%) of 3053 residents with dementia and recorded their baseline CMAI score; 1,198 (84%) had at least one CMAI follow-up assessment (Figure 1). Table 1 describes

sample sociodemographic and illness characteristics. A greater percentage of those with clinically significant agitation were prescribed antipsychotics or hypnotics or anxiolytics or attended a psychiatric outpatient or community psychiatric appointment at baseline compared with those with less severe or no agitation. By 16 months, 489 (34%) of the residents had died; 89 (18%) had no agitation at baseline, 229 (47%) had subclinical agitation at baseline and 171 (35%) had clinically significant agitation. At the 16-month follow-up point, a CMAI score was available for 737 (52%) residents.

[Figure 1 here]

[Table 1 here]

Over time, the median CMAI score remained fairly stable; 41 (IQR 33, 55) at baseline and 39 (IQR 31, 52) at 16 months. Figure 2 and supplementary Figure show that most residents remained in the agitation group (no, sub-clinical or clinically significant agitation) in which they scored at baseline.

[Figure 2 here]

Of the 209 (15%) residents who exhibited no agitation at baseline, 183 (88%) remained free of clinically significant agitation at all follow-ups at which they were rated and 26/209 (12%) developed clinically significant agitation at any time over the 16 months' follow-up. Twenty-one residents had no agitation and were seen at all five time points. At baseline 8 (38%) had mild dementia, 6 (29%) moderate dementia and 7 (33%) severe dementia. By 16 months 14 (67%) had severe dementia, 5 (24%) moderate dementia and 2 (10%) mild dementia.

Of the 646 (45%) residents who had subclinical agitation at baseline, 440/646 (68%) never developed clinically-significant agitation and 206/646 (32%) developed clinically significant agitation at any time over the 16 months' follow-up. Fifty-nine residents had subclinical

agitation at all five time points; just under half (28) had mild dementia at baseline, 18 (31%) moderate dementia and 13 (22%) severe dementia. By 16 months, a fifth (12) had mild dementia, just over a quarter (16) had moderate dementia and 21 (53%) severe.

Of the 569 (40%) participants who had clinically significant agitation at baseline, 94/301 (31%) also had clinically significant agitation at all four subsequent follow-up points. Of these, 21 (22%) had mild dementia at baseline, 31 (33%) moderate dementia and 42 (45%) severe dementia. At 16 months, none of these residents had mild dementia and 76 (81%) had severe dementia. Seventy percent (396/569) had clinically significant agitation at one or more follow-up points.

For those who had no agitation at baseline 93/209 (44%) died over 16 months' follow-up, 233/646 (36%) of those with subclinical agitation and 171/569 (30%) with clinically significant agitation at baseline. The patterns of agitation are not affected by death (Figure 2).

At baseline there were 418 people with mild dementia, of whom 17% experienced no agitation, 55% subclinical agitation and 28% clinically significant agitation. These proportions were very similar 16 months later for the 247 participants from this cohort who remained in the study. Of those with mild dementia at baseline who remained in the study at 16 months, 29% continued to have mild dementia, 43% had progressed to moderate and 28% to severe dementia.

At baseline, there were 467 people with moderate dementia, of whom 10% experienced no agitation, 44% subclinical agitation and 45% clinically significant agitation. Among the 247 people remaining at 16 months, 18% had no agitation, 47% subclinical agitation and 36% clinically significant agitation. Of those with moderate dementia at baseline who remained in the study at 16 months, 28% continued to have moderate dementia at 16 months, and 72% had progressed to severe dementia.

There were 535 people who had severe dementia at baseline, of whom 17% had no agitation, 39% subclinical agitation and 45% had clinically significant agitation. Among the 243 participants from this cohort who remained in the study at 16 months, 23% had no agitation, 38% had subclinical agitation and 38% had clinically significant agitation.

DISCUSSION

Our study shows that although agitation is present in some care home residents with dementia, it is not universal and a significant minority of the residents remained free of clinically significant agitation over 16 months, despite increasing dementia severity. We have previously shown that level of agitation is not associated with time to death, and thus our findings are not explained by those who were more agitated dying earlier.[12] In that paper we postulated that this was because those who were not agitated moved to care homes at a later stage of dementia or when they were older, meaning they died sooner. It is an important finding that agitation is not an inevitable part of dementia as it becomes more severe. Our study also shows that residents may experience different levels of agitation during the course of their dementia and that it cannot be assumed that agitation will worsen with increased dementia severity. Median agitation scores were slightly lower at 16 months relative to baseline in this study.

People with clinically significant agitation are, as expected, more often prescribed antipsychotic, hypnotics or anxiolytics than those without. We do not know when these were prescribed in relation to the onset of clinically significant agitation but it is likely they are being used as treatment, although clearly they are not completely effective. The harms associated with antipsychotic prescribing usually outweigh the benefits and there has been a move away from prescribing antipsychotics to people with dementia over the past decade[13]. There have been non-pharmacological interventions aimed at decreasing the levels of agitation in care homes and preventing it occurring. These have had mixed success. MARQUE [14] did not show a statistically significant difference in CMAI between randomised groups. However,

WHELD [15], using person-centred care, aiming to improve communication with people with dementia; a combination of social, sensory experiences or other activities; education about antipsychotic review and addressing physical problems succeeded. Future interventions aimed at reducing levels of agitation in care homes should focus on those who have moderate to severe agitation because these are the residents likely to benefit, as demonstrated in the TIME trial [16]. It offered a comprehensive assessment of the resident, a structured case conference for the staff and doctor and involved development and implementation of a tailored plan. Reducing resident levels of agitation may also decrease care worker burnout and increase their ability to cope with work [17,18].

Strengths and limitations

This study is the largest longitudinal study of people with dementia in care homes. Data were collected every four months, giving up to four follow-up time points of data. We were able to include residents with more severe dementia, without capacity to consent by allowing family or professional consultees to provide assent. As the measures used in this study were obtained from the member of care home staff that knew the resident best, the CMAI scores are likely to reflect their agitation status. We were also able to collect data about death and they did not account for our findings of stability within agitation categories. In unadjusted analyses, survival was predicted by having clinically significant levels of agitation but in models adjusted for age, sex, dementia severity, number of medications and whether taking antipsychotics (N=1146) survival was not predicted by agitation caseness (HR 0.80, 95% CI 0.64, 1.01) [12],

Some factors that may contribute to the patterns of agitation shown in this paper may not have been recorded. For example, we did not collect information on dementia subtypes. We do not know whether residents had similar levels of agitation earlier in the course of their dementia, nor do we know how long they had dementia before the study started but we can compare severity of dementia, which may be a more accurate measure of illness duration as

it is difficult to date the beginning of dementia. While this study provides one of the longest follow-up periods of a large sample of people living with dementia in care homes, a longer follow-up duration would have provided data that are more complete. As our main finding was of relative stability of levels of agitation in a large sample with diverse levels of dementia severity over five follow-up time points over a sustained period, however, we do not think this would have altered our findings.

Conclusion

Carers and people with dementia would like to know what to expect over the course of dementia. We can now say that most (around 85%) care home residents with dementia who are free of clinically significant agitation will remain so. Among those with clinically significant agitation, most will recover but relapse and around 75% will have clinically significant agitation at any time point. Worryingly, a third of survivors to 16 months, had persistent, clinically significant levels of agitation over the entire study period. Interventions for agitation should focus on treatment not prevention.

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AUTHOR CONTRIBUTIONS

GL and CC gained funding for the study, LM analysed the data and wrote the first draft of the manuscript. All authors provided comment and approved the manuscript before submission.

COMPETING INTERESTS

None declared

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REFERENCES

- [1] Hoe J, Jesnick L, Turner R, Leavey G, Livingston G (2017) Caring for relatives with agitation at home: A qualitative study of positive coping strategies. *BJPsych Open* **3**, 34–40.
- [2] Livingston G, Barber J, Marston L, Rapaport P, Livingston D, Cousins S, Robertson S, La Frenais F, Cooper C (2017) Prevalence of and associations with agitation in residents with dementia living in care homes: MARQUE cross-sectional study. *BJPsych Open* **3**, 171–178.
- [3] Anatchkova M, Brooks A, Swett L, Hartry A, Duffy RA, Baker RA, Hammer-Helmich L, Sanon Aigbogun M (2019) Agitation in patients with dementia: A systematic review of epidemiology and association with severity and course. *Int. Psychogeriatrics*.
- [4] Panca M, Livingston G, Barber J, Cooper C, Frenais F La, Marston L, Cousins S, Hunter RM (2019) Healthcare resource utilisation and costs of agitation in people with dementia living in care homes in England - The Managing Agitation and Raising Quality of Life in Dementia (MARQUE) study. *PLoS One* **14**, 1–11.
- [5] Hendriks SA, Smalbrugge M, Galindo-Garre F, Hertogh CPM, van der Steen JT (2015) From Admission to Death: Prevalence and Course of Pain, Agitation, and

- Shortness of Breath, and Treatment of These Symptoms in Nursing Home Residents With Dementia. *J. Am. Med. Dir. Assoc.* **16**, 475–481.
- [6] Selbæk G, Engedal K, Benth JS, Bergh S (2014) The course of neuropsychiatric symptoms in nursing-home patients with dementia over a 53-month follow-up period. *Int. Psychogeriatrics*.
- [7] Cohen-Mansfield J, Billig N (1986) Agitated Behaviors in the Elderly: I. A Conceptual Review. *J. Am. Geriatr. Soc.* **34**, 711–721.
- [8] Ryu SH, Katona C, Rive B, Livingston G (2005) Persistence of and changes in neuropsychiatric symptoms in Alzheimer disease over 6 months: The LASER-AD study. *Am. J. Geriatr. Psychiatry*.
- [9] Levin E (1989) *Noticeable Problems Checklist*, National Institute for Social Work, London.
- [10] Steventon A, Roberts A (2012) Estimating length of stay in publicly-funded residential and nursing care homes: A retrospective analysis using linked administrative data sets. *BMC Health Serv. Res.*
- [11] Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL (1982) A new clinical scale for the staging of dementia. *Br. J. Psychiatry*.
- [12] Laybourne A, Livingston G, Cousins S, Rapaport P, Lambe K, La Frenais F, Savage H, Manela M, Stringer A, Marston L, Barber J, Cooper C (2019) Carer coping and resident agitation as predictors of quality of life in care home residents living with dementia: Managing Agitation and Raising Quality of Life (MARQUE) English national care home prospective cohort study. *Int. J. Geriatr. Psychiatry* **34**, 106–113.
- [13] Cooper C, Lodwick R, Walters K, Raine R, Manthorpe J, Iliffe S, Petersen I (2017) Inequalities in receipt of mental and physical healthcare in people with dementia in the UK. *Age Ageing*.
- [14] Livingston G, Barber J, Marston L, Stringer A, Panca M, Hunter R, Cooper C, Laybourne A, La Frenais F, Reeves S, Manela M, Lambe K, Banerjee S, Rapaport P (2019) Clinical and cost-effectiveness of the Managing Agitation and Raising Quality of Life (MARQUE)

- intervention for agitation in people with dementia in care homes: a single-blind, cluster-randomised controlled trial. *The Lancet Psychiatry* **6**, 293–304.
- [15] Ballard C, Corbett A, Orrell M, Williams G, Moniz-Cook E, Romeo R, Woods B, Garrod L, Testad I, Woodward-Carlton B, Wenborn J, Knapp M, Fossey J (2018) Impact of person-centred care training and person-centred activities on quality of life, agitation, and antipsychotic use in people with dementia living in nursing homes: A cluster-randomised controlled trial. *PLOS Med.* **15**, e1002500.
- [16] Lichtwarck B, Selbaek G, Kirkevold Ø, Rokstad AMM, Benth JŠ, Lindstrøm JC, Bergh S (2018) Targeted Interdisciplinary Model for Evaluation and Treatment of Neuropsychiatric Symptoms: A Cluster Randomized Controlled Trial. *Am. J. Geriatr. Psychiatry.*
- [17] Costello H, Walsh S, Cooper C, Livingston G (2018) A systematic review and meta-analysis of the prevalence and associations of stress and burnout among staff in long-term care facilities for people with dementia. *Int. Psychogeriatrics.*
- [18] Rapaport P, Livingston G, Hamilton O, Turner R, Stringer A, Robertson S, Cooper C (2018) How do care home staff understand, manage and respond to agitation in people with dementia? A qualitative study. *BMJ Open* **8**, e022260.

Table 1: Baseline characteristics by baseline agitation category

Characteristic	No agitation		Sub clinical agitation		Clinically significant agitation	
	n/N	%	n/N	%	n/N	%
Male	61/209	29	185/646	29	195/569	34
Age mean (SD)	86 (N=209)	(9)	86 (N=646)	(9)	85 (N=569)	(9)
White	199/207	96	615/639	96	524/567	92
Married/ common law partner	42/205	20	139/628	22	161/552	29
Single, divorced or separated	39/205	19	135/628	22	101/552	18
Widowed	124/205	60	354/628	56	290/552	53
Dementia severity						
Mild	70/208	34	231/644	36	117/568	21
Moderate	49/208	24	206/644	32	212/568	37
Severe	89/208	43	207/644	32	239/568	42
Time in the care home (years) median (IQR)	2.2 (N=206)	(0.9, 4.3)	2.0 (N=631)	(0.9, 3.4)	1.8 (N=561)	(0.8, 3.3)
Medication prescription						
Antipsychotics	19/209	9	93/646	14	127/569	22
Antidepressant	78/209	37	260/646	40	228/569	40

Hypnotic or anxiolytic	21/209	10	94/646	15	156/569	27
Any psychotropic	102/209	49	337/646	52	359/569	63
Analgesia	144/209	69	417/646	65	375/569	66
Psychiatric service use						
Psychiatric outpatient or memory clinic	1/209	0.5	20/646	3	19/569	3
Attended community psychiatric appointment	19/209	9	83/646	13	109/569	19

Figure 1: Flow chart of resident inclusions over time

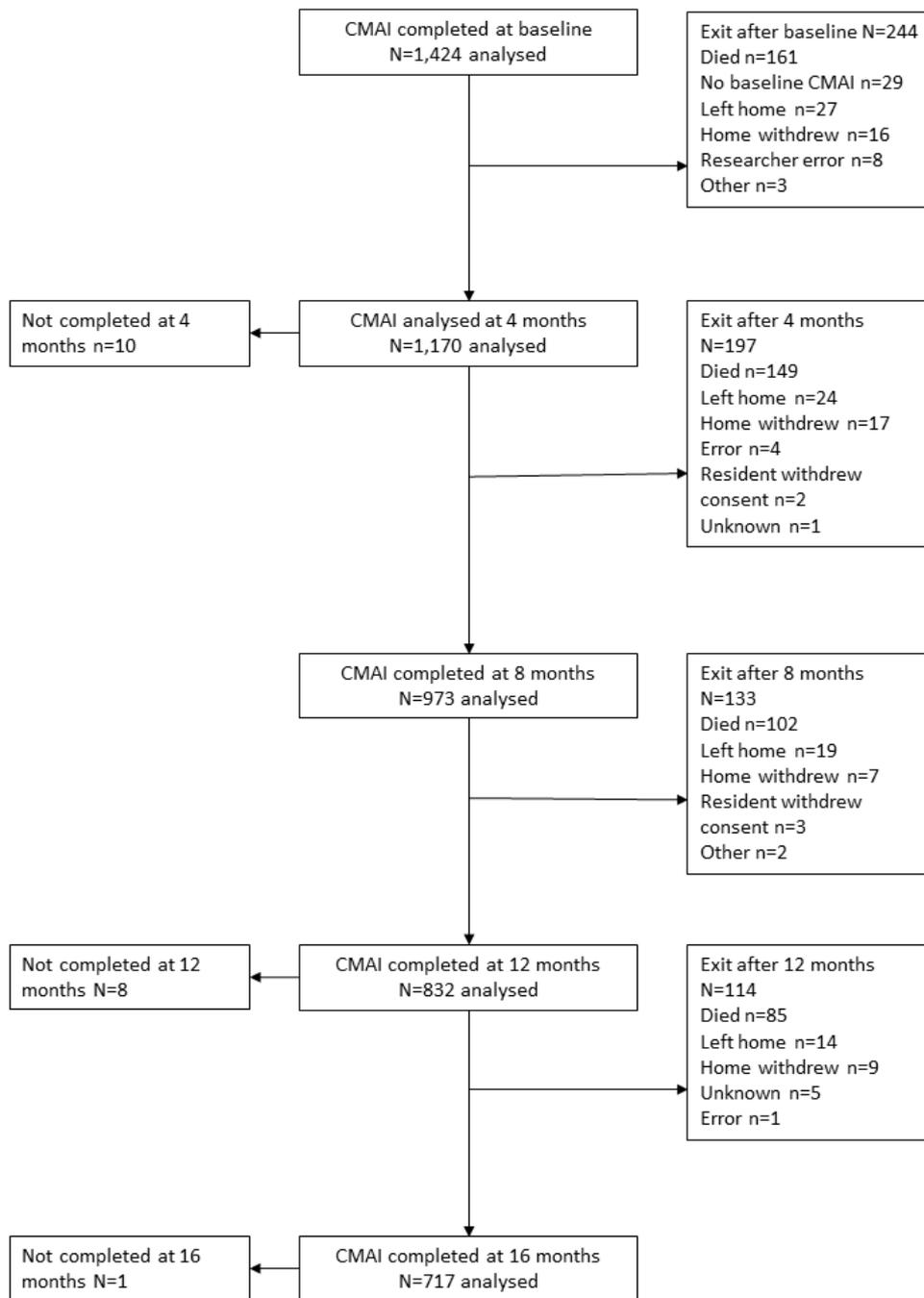
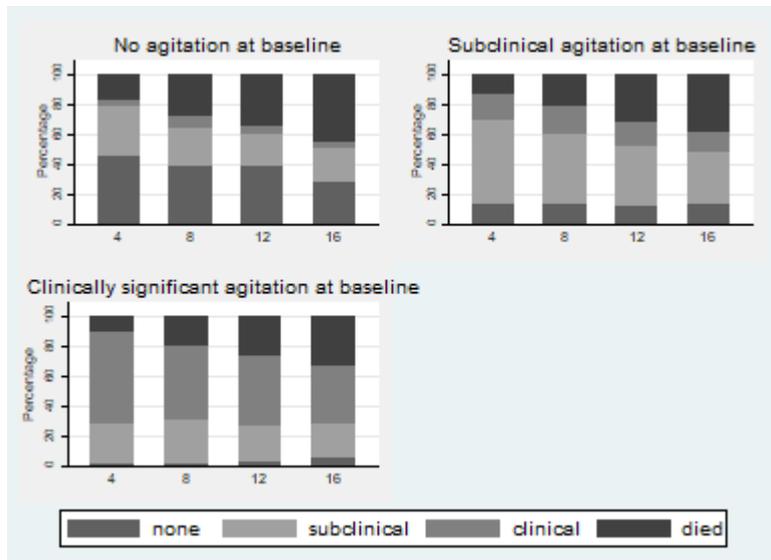


Figure 2: Agitation categories at each follow up time (in months) with cumulative deaths by agitation category at baseline



Supplementary material

Agitation categories at each follow up time (in months) by agitation category at baseline without those who died

