

# **Weight loss in Alzheimer's disease, vascular dementia and dementia with Lewy bodies: Impact on mortality and hospitalization by dementia subtype**

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The contribution of each author: Design study: PS, CM; practical performance: SGT, MR, SJ, DT, KT; data analysis: CM, KT; preparation manuscript: PS, CM, LS, NV; critical review manuscript: RS. All authors contributed to the draft and revision of the manuscript and approved the version to be published.

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Informed consent to participate was granted by individuals before starting the assessment.

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## **Weight loss in Alzheimer's disease, vascular dementia and dementia with Lewy bodies: Impact on mortality and hospitalization by dementia subtype**

### **Abstract**

**Objectives:** Loss of weight is associated with cognitive decline as well as several adverse outcomes in dementia. The aim of this study was to assess whether weight loss is associated with mortality and hospitalization in dementia subtypes.

**Methods:** A cohort of 11,607 patients with dementia in Alzheimer's disease (AD), vascular dementia (VD), or dementia with Lewy bodies (DLB) was assembled from a large dementia care health records database in Southeast London. A natural language processing algorithm was developed to establish whether loss of weight was recorded around the time of dementia diagnosis. Cox proportional hazard models were applied to examine the associations of reported weight loss with mortality and emergency hospitalization.

**Results:** Weight loss around the time of dementia was recorded in 25.5% of the whole sample and was most common in patients with DLB. A weight loss-related increased risk for mortality was detected after adjustment for confounders (Hazard ratio (HR):1.07; 95% confidence interval (CI):1.02-1.15) and in patients with AD (HR: 1.11;95% CI:1.04-1.20), but not in DLB and VD. Weight loss was associated with a significantly increased emergency hospitalization risk (HR: 1.14; 95% CI: 1.08-1.20) and in all three subtypes.

**Conclusions:** While there were associations with increased hospitalization risk for all three subtype diagnoses, weight loss was only associated with increased mortality in AD. Weight loss should be considered as an accompanying symptom in dementia and interventions should be considered to ameliorate risk of adverse outcomes.

**Keywords:** dementia, Alzheimer's disease, weight loss, Lewy bodies, mortality, hospitalization

### **Key-points**

Weight loss is associated with increased hospitalization risk for dementia.

Weight loss was only associated with increased mortality in Alzheimer's Disease.

Weight loss should be considered as an accompanying symptom in dementia.

## Introduction

Weight loss (WL) is common in late life and affects nearly 30% of older adults<sup>1</sup>. It is associated with increased risk for cognitive decline and the development of mild cognitive impairment and dementia<sup>2,3</sup>. In general populations of older people, WL is associated with higher rates of mortality, institutionalization, decline in functional status, worse quality of life, and frailty<sup>4-7</sup>. Although age is a risk factor for both cognitive impairment and WL, there is growing evidence that cognitive decline and nutritional deficiency are closely interrelated, regardless of aging<sup>8</sup>. However, the relationship between dementia and WL is complex and people with dementia might be more prone to losing weight for several reasons. These include, for example, difficulties in activities of daily living, such as shopping and cooking, which may limit food consumption<sup>9</sup>. Further, WL can be affected by behavioral and psychological symptoms of dementia by both reducing food intake and increasing physical activity<sup>3</sup>. Patients may have reduced food intake due to progression of cholinergic deficits and dementia causing dysphagia and alteration of taste and smell which, in consequence, reduces patients' interest in food<sup>10-12</sup>. Lastly, acetylcholinesterase inhibitors, commonly prescribed in Alzheimer's disease (AD), are associated with WL<sup>13</sup>. Subsequently WL is common in people with dementia<sup>14</sup> and is similarly to the general population associated with hospitalization and mortality<sup>15,16</sup> as well as a more frequent occurrence of neuropsychiatric symptoms and more rapid cognitive decline<sup>17,18</sup>.

Although most of the research on outcomes of WL in patients with dementia has been conducted in those with AD, a recent study has shown that patients with dementia with Lewy bodies (DLB) and vascular dementia (VD) more frequently presented with malnutrition at the time of dementia diagnosis than patients with AD<sup>8</sup>. However, it is not known if outcomes related to WL, which is one of the most important signs of malnutrition<sup>9</sup>, differ between dementia subtypes. Dementia in AD, VD and DLB differ in underlying pathology, clinical features, and prognosis, and we hypothesized that WL would affect adverse outcomes differently in these three dementia subtypes. We investigated this in a large naturalistic sample of people diagnosed with dementia in relation to mortality and emergency hospitalization.

## Methods:

### **Data source**

Data source for this study was the South London and Maudsley NHS Foundation Trust (SLaM) Clinical Record Interactive Search (CRIS) system, which provides research access to more than 500,000 anonymized health records from SLaM within a robust governance framework<sup>19,20</sup>. SLaM is one of Europe's largest providers of dementia and mental health care serving more than 1.4 million people in Southeast London. CRIS has received ethical approval as an anonymized data resource (Oxford Research Ethics Committee C, reference 18/SC/0372) and is linked to national data on hospitalization within England (Hospital Episode Statistics HES))<sup>21</sup> and mortality data from the Office of National Statistics (ONS).

Data were extracted both from structured fields routinely completed in the source record and from clinical documentation. Identification of relevant information from free-text entries was conducted through natural language (NLP) processing algorithms supported by General Architecture for Text Engineering (GATE) software<sup>22,23</sup>.

### **Patient sample**

We identified patients who received a diagnosis of dementia in SLaM services between 1st January 2007 and 31st December 2015. *These patients reside in the SLaM catchment area covering the ethnically and socio-economically diverse South London boroughs of Croydon, Lambeth, Southwark, and Lewisham, whereby SLaM is the near-monopoly provider of services establishing dementia diagnoses in this area.* Dementia subtype diagnoses included were Alzheimer's disease (AD; according to World Health Organization 10th revision of the International Statistical Classification of Diseases and Related Health Problems (WHO ICD-10)<sup>24</sup>: F00), vascular dementia (VD; ICD-10: F01) and dementia with Lewy bodies (DLB). As there is no specific ICD-10 code, which is consistently used in UK dementia services to categorize DLB, this was identified through natural language processing from diagnostic statements in clinic letters and events as previously described<sup>25</sup>. Patients were excluded if they had no specific dementia subtype diagnosis or if another subtype than the aforementioned three was recorded. While we identified subtype diagnoses across the whole patient record, the date of first mention of any dementia diagnosis served as the index date. If several dementia subtypes were recorded in the electronic health record we prioritized DLB > AD > VD as mutually exclusive groups. The sample was stratified according to dementia subtype diagnosis.

### ***Exposure***

A GATE-supported natural language processing algorithm was used to identify any statements regarding WL in a 1-year window (6 months before to 6 months after index date). The machine-learning based NLP algorithm identifies the terms 'loss' and 'weight' with no more than 2 words between those terms' and examples of positive annotations include 'significant weight loss' and 'pleased with his weight loss', while negative annotations include 'no weight loss' or 'denies weight loss'. Negative annotations include 'no weight loss' or 'denies weight loss' and unknown annotations include 'to maintain adequate diet and avoid weight loss' or 'the latter reduced in line with weight loss'. Only patients with a positive annotation were considered to experience weight loss, while those with a negative or unknown annotation were considered as not exposed. Examination of a random sample of 100 unannotated documents extracted from keyword searches yielded a precision of 90% and recall of 88%.

### ***Outcomes***

In the full cohort and the subtype strata, patients with recorded WL were compared to those with no recorded WL in relation to all-cause mortality and any emergency hospitalization to acute care (non-psychiatric) hospitals<sup>21</sup>. Mortality data (via ONS linkage) was available to a census point on 10<sup>th</sup> December 2016 and hospitalization data (via HES linkage) until a census point 31<sup>st</sup> March 2016.

### ***Covariates***

From both structured fields and natural language processing applications, we extracted socio-demographic factors (age, gender, marital status, ethnicity, and a neighborhood-level index of multiple deprivation<sup>26</sup>) and cognition (identified via MMSE score closest to the date of diagnosis<sup>27</sup>). We used the Health of the Nation Outcome Scales (HoNOS65+) to ascertain mental and physical health problems, as well as functional impairment (Burns and others 1999). The HoNOS65+ is a validated measure of patient welfare in the UK and encompasses 12 clinician-rated subscales. Each subscale is rated on a scale ranging from 0 (no problem) to 4 (severe or very severe problem). To facilitate interpretation, we dichotomized the scores to 'minor or no problems' (scores 0 or 1) and 'mild to severe problems' (scores 2 to 4). We created a more fine-grained ordinal scale for physical illness or disability (no or minor problem, mild problems, moderate problem and severe to very severe problem) and further ascertained whether the patients had been hospitalized in the year before dementia diagnosis (ascertained from HES<sup>21</sup>).

Lastly, we used an NLP algorithm to ascertain pharmacotherapy from a comprehensive gazetteer of all past and current generic medication names (as well as most trade names). We identified whether

patients were prescribed an antidepressant or antipsychotic in a one-year window (from 6 months before to 6 months after) around index date and/or an acetylcholinesterase inhibitor (AChEI) within 6 months after diagnosis. We further established whether patients were considered to be subject to polypharmacy around index date, defined as the concurrent prescription of four or more medications<sup>28</sup>.

### ***Statistical analyses***

STATA 15<sup>29</sup> software was used for all analyses. Descriptive statistics according whether WL was recorded were generated and presented accordingly. We constructed three Cox regression models to examine whether recording of WL at the time of dementia diagnosis was related to mortality and emergency hospitalization: Model 1 was adjusted for age and gender. Model 2 included age, gender, marital status, ethnicity, index of deprivation, MMSE score and dementia subtype. In Model 3 the items from Model 2 were included and we added HoNOS subscales, previous hospitalization, and pharmacotherapy. We first examined hazards related to recorded WL and then separately in the three subtype diagnosis strata. We also tested the interaction of WL and VD/DLB compared to AD in relation to mortality and emergency hospitalization.

Of patients included, 23% had missing data on at least one of the other covariates and therefore we imputed missing values using chained equations to maximize statistical power<sup>30</sup>. We used the *mi* package in STATA to create 23 imputed datasets by replacing missing values through simulated values assembled from potential covariates and outcome values. Coefficients were combined in final analysis according to Rubin's rules<sup>31</sup>.

## Results

We identified 14,093 patients with a first diagnosis of dementia in the follow-up period, from whom we excluded 2,486 (17.6%) as they had no diagnosis of AD, VD or DLB. The final sample consisted of 11,607 patients of whom 61.8% were female. Mean (SD) age at diagnosis was 80.5 (9.4) years and mean (SD) MMSE score 18.6 (6.4). In terms of dementia subtypes 8,238 (71.0%) were diagnosed with AD, 2,821 (24.3%) with VD and 548 (4.7%) with DLB. Reported WL around the time of dementia diagnosis was recorded in 25.5% (n= 2,957) of the total sample and was most common in DLB (31.4%, n=172), followed by AD (25.8%, n=2,129) and VD (23.3%, n=656) ( $p<0.001$ ).

Patient characteristics according to recorded WL are presented in Table 1. Patients with WL were more likely to be female, from a non-White ethnic background, living in a more deprived area, and less likely to be married or cohabiting; however, no significant difference was present in age or MMSE score at dementia diagnosis. A diagnosis of AD and DLB were more common in the group with WL and VD less frequent. Neuropsychiatric symptoms and functional problems were more prevalent at the time of dementia diagnosis in those with WL, with the greatest difference in depressed mood (22.3% vs. 13.0%). This was also reflected in pharmacotherapy, whereby those with WL were more frequently recorded as receiving antidepressant, antipsychotic and acetylcholinesterase inhibitor medications. Patients with WL were also more likely to have polypharmacy as defined for this project (concurrent prescription of four or more medications). Relationships with physical illness were less clear. Although there was a significant difference across groups, this varied across illness severities and no difference was detected in relation to previous hospitalization.

### ***Weight loss and mortality***

In total 6,241 patients (53.7%) died in follow-up period and median survival time was 4.3 years (interquartile range (IQR): 1.9-7.6 years). WL at dementia diagnosis was associated with a 7% increased mortality risk after adjusting for age and gender (Model 1, see Table 2). After adjusting for other demographics and dementia subtype (Model 2) this effect remained significant, which was also the case after further adjustments for mental and physical health symptoms and pharmacotherapy (Model 3). When the association of WL with mortality was examined in the three subtype diagnosis strata, this was strongest in patients with AD in all models, and was much closer to the null in VD and DLB groups (see Table 2). A significant WL x subtype interaction was detected when comparing VD to AD in Model 1 (see Supplementary Table 1), with a lower WL related mortality risk in those with VD (Hazard ratio (HR): 0.87, 95% Confidence interval (CI): 0.76-0.99,  $p$ -value=0.031).



***Weight loss and emergency hospitalization***

Over the follow-up period 7,770 patients (66.9%) had an emergency hospitalization and the median time to first emergency hospitalization was 1.4 (IQR: 0.4-3.7) years. WL was associated with a 14% increased hospitalization risk in the age and gender adjusted model (see Table 2) which remained significant after further adjustments in Model 2 and Model 3. The association of WL with increased hospitalization risk was also significant in all three subtype strata. In Model 3, adjusted for 21 potential confounders, the WL-related hospitalization risk increase was stronger in DLB (38% increase) compared to AD (12%) and VD (15%); but no statistically significant interactions were detected (see Supplementary Table 1).

## Discussion

In more than 11,000 patients diagnosed with AD, VD or DLB, recorded WL around the time of dementia diagnosis was associated with a 9% increased mortality and a 14% increased emergency hospitalization risk. While the increased hospitalization risk was present across all three subtype diagnoses, strongest in those with DLB, the association between WL and mortality appeared to be only increased in those with AD.

WL is an important clinical feature of dementia, often preceding the clinical onset of dementia and already accelerating around the time of diagnosis<sup>9,12</sup>. Some studies have highlighted the role of neurodegenerative processes in specific brain regions, genetic factors and inflammatory processes for nutritional and weight changes in AD<sup>9-32-34</sup>. Another important point is that AChEIs prescribed for treatment of certain dementia subtypes can cause WL, which makes it more difficult to control WL in patients with dementia<sup>13</sup>. In our study, WL was more common in DLB than in AD or VD, partly consistent with a previous finding that malnutrition was more likely in DLB and VD compared to AD<sup>8</sup>; this used a wider assessment of malnutrition via the Mini-Nutritional Assessment-Short Form (MNA-SF) tool<sup>35</sup>, which in addition to WL also assesses food intake (including swallowing difficulties), mobility, neuropsychological problems and Body Mass Index. As swallowing and mobility difficulties might be more common in VD than in AD<sup>36,37</sup> this could explain the difference between the two studies. In our analysis, 31.4% of patients with DLB had WL, which is supported by DLB yielding a higher cholinergic deficit than other forms of dementia<sup>38</sup>. That both HoNOS psychiatric symptoms/disorders and the use of antidepressants and antipsychotics (which were potentially used to treat them) were more prevalent in those with WL than in those without also supports this hypothesis and could potentially explain the increased incidence of WL in patients with DLB.

WL in people with dementia is associated with a number of adverse outcomes, including hospitalization and mortality<sup>15,16</sup>. In line with our analysis, the relationship between WL and increased mortality in AD has been demonstrated in several studies. White and colleagues followed 666 AD patients for 6 years and found that  $\geq 5\%$  WL was a significant predictor of death and that mortality was reduced in those who gained weight<sup>16</sup>. Another study demonstrated a 3.8-fold increased risk of mortality in AD patients with WL compared to those without during 60 months of follow-up<sup>39</sup>. While the impact of WL in dementia in general and AD has been investigated in several studies, to the best of our knowledge our study is the first to assess differences between dementia subtypes. Patients with non-AD such as VD or DLB are known to have an adverse prognosis and shorter survival than

those with AD<sup>40-42</sup> and this might attenuate the effect WL has on mortality. In addition to general risk factors for mortality, survival in VD is specifically related to vascular risk factors including diabetes mellitus, smoking, coronary heart disease, congestive heart failure, short or long daily sleep duration and hypnotic use<sup>43,44</sup>, while depression and VD might have synergistic effects on mortality<sup>45</sup>. In patients with DLB factors associated with an increased mortality risk are co-morbid AD pathology, number and severity of DLB core symptoms, extrapyramidal signs, and orthostatic hypotension<sup>41</sup>. In both VD and DLB these factors might act independently or synergistically, but ultimately play a stronger role in predicting mortality than WL. Another possible explanation might be that WL is more closely related to underlying neuropathology in AD and thus is a stronger marker of severity and progression<sup>12</sup>.

Our study found that recorded WL was associated with increased hospitalization risk regardless of dementia subtype. Emergency hospitalization is two times higher in people with dementia patients than those without<sup>46</sup> and predictors of hospital admission in people with dementia include multimorbidity, polypharmacy, lower functioning<sup>47</sup>, falling, caregiver burden, but also WL<sup>48</sup>. Comparing reasons for admission by dementia subtype, hospitalization due to stroke and cardiovascular causes are unsurprisingly common in VD, while falls-related hospitalizations and infections are more common in DLB<sup>25,49</sup>. We did not detect a significant interaction between a diagnosis of DLB and hospitalization. However, the power of a test for interaction is lower compared to a test for direct effects and the DLB group was comparatively small. Hence this 38% increased hospitalization risk warrants further consideration. Malnutrition, for which WL is one of the most important indicators, is known to be implicated in several reasons for hospitalization in patients with DLB as falls, orthostatic hypotension or neuropsychiatric symptoms<sup>50</sup>.

Although the present study is the first to investigate outcomes of WL in the most common dementia subtypes and included a large sample size, there are some limitations. First, our data were collected from routine clinical records and documentation of any finding is dependent on the judgement of the individual clinician. Second, the natural language processing algorithm used depends on the quality of data entry, which can vary by both clinician and patient<sup>20</sup>. In relation to the main exposure WL, we were not able to ascertain whether the WL was voluntary or unexpected and recorded instances will have mainly relied on self- or caregiver report. Third, we only assessed recording of WL around the time of dementia diagnosis, rather than weight trajectories over time<sup>9</sup>. In longitudinal analyses for mortality this would consider patients developing WL in the more advanced stages of dementia as unexposed, which in turn might bias Cox regression hazard ratios towards the null in mortality

analyses on the smaller cohorts of patients with DLB and VD. Fourth, although we found seemingly lower WL related mortality risks in VD and DLB compared to AD, the interaction term was only statistically significant in the age- and gender adjusted model for VD. This is not surprising as power of the test for interaction is lower compared to the test of direct effects, and it is recommended to increase the type one error rate to increase power for such tests. Although we cannot make firm conclusions, this gives an indication that differences between subtypes in relation to WL related mortality risk could exist. Lastly, we were only able to assess WL and other aspects related to frailty and malnutrition, as loss of appetite, digestive problems, swallowing difficulties or reduced mobility require further evaluation.

### **Conclusion and Implications**

WL is recorded relatively commonly in around 25% in patients with dementia at the time of diagnosis and is associated with an increased risk of mortality and emergency hospitalization. While an increased emergency hospitalization risk was detected in all three subtypes of dementia, a WL related mortality risk was only detected in those with AD. Therefore, clinicians who review people with all three subtypes of dementia in their daily clinical practice should at least consider monitoring their patients' weight (and/or collate already-recorded levels from routine records) and might consider eliminating factors that may cause WL and/or ameliorating the potential nutritional and functional consequences of WL. Dietary restrictions should be avoided in all three subtypes of dementia, particularly in those with AD. In addition, to prevent emergency hospitalization and mortality in these patients, oral nutritional supplements should be initiated as soon as WL occurs. However, larger scale prospective studies are needed to examine the consequences of WL in dementia subtypes and the efficacy of nutritional interventions to ameliorate WL and associated adverse outcomes.

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# **Weight loss in Alzheimer's disease, vascular dementia and dementia with Lewy bodies: Impact on mortality and hospitalization by dementia subtype**

**Table 1: Sample characteristics by the presence of weight loss**

Risk factors	Weight loss present (n=2,957)	No weight loss (n=8,650)	P value <sup>1</sup>
<b>Socio-demographic status and cognitive function<sup>2</sup></b>			
Mean age at dementia diagnosis (SD)	80.5 (8.8)	80.5 (9.6)	0.784
Female gender (%)	65.8%	60.4%	<0.001
Non-White ethnicity (%)	26.1%	24.1%	0.031
Married or cohabiting status (%)	31.3%	35.3%	<0.001
Mean index of deprivation (SD)	27.7 (10.9)	26.9 (11.1)	<0.001
Mean MMSE score at diagnosis (SD)	18.5 (6.2)	18.7 (6.5)	0.156
<b>Dementia subtype (%)</b>			
Alzheimer's disease (AD)	72.0%	70.6%	<0.001
Vascular dementia (VD)	22.2%	25.0%	
Dementia with Lewy bodies (DLB)	5.8%	4.4%	
<b>HoNOS symptoms/disorders (%)<sup>2</sup></b>			
Agitated behaviour	22.8%	18.5%	<0.001
Non-accidental self-injury	2.9%	1.1%	<0.001
Problem-drinking or drug taking	3.7%	2.6%	0.003
Hallucinations and/or delusions	18.4%	12.1%	<0.001
Depressed mood	22.3%	13.0%	<0.001
<b>HoNOS Physical illness or disability scale (%)<sup>2</sup></b>			
No or minor problem	47.0%	45.9%	
Mild problem	25.8%	27.1%	
Moderate problem	22.5%	20.4%	
Severe to very severe problem	4.7%	6.6%	
<b>Hospitalization prior to dementia diagnosis<sup>3</sup></b>	50.9%	52.0%	0.315
<b>HoNOS functional problems (%)<sup>2</sup></b>			
Activities of daily living	61.9%	58.6%	0.002
Living conditions	14.0%	11.3%	<0.001
Occupational / recreational activities	34.6%	31.4%	0.001
Social relationships	20.7%	15.7%	<0.001
<b>Pharmacotherapy<sup>4</sup></b>			
Polypharmacy ( $\geq 4$ medications)	56.0%	43.4%	<0.001
Acetylcholinesterase inhibitor (AChEI)	29.7%	25.5%	<0.001
Antidepressant	35.2%	24.1%	<0.001
Antipsychotic	20.0%	12.8%	<0.001

1 - ANOVA or Chi<sup>2</sup> test; 2 - at the time of dementia diagnosis; 3 – in the year prior to dementia diagnosis; 4 – in a 6 months' window around dementia diagnosis (AChEI only after)

\* significantly different to group Ag-P- (p<0.05); # significantly different to group Ag-P+ (p<0.05)

**Table 2: Risks for adverse outcomes in association with weight loss according to dementia subtype diagnosis groups using Cox proportionate hazard models (Hazard ratios (95% CI))**

	Mortality			Emergency Hospitalisation		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Full sample (n=11,607)	<b>1.07</b> <b>(1.01-1.13)</b>	<b>1.09</b> <b>(1.03-1.16)*</b>	<b>1.09</b> <b>(1.02-1.15)*</b>	<b>1.15</b> <b>(1.09-1.21)</b>	<b>1.16</b> <b>(1.10-1.22)*</b>	<b>1.14</b> <b>(1.08-1.20)*</b>
Alzheimer's disease (n=8,238)	<b>1.12</b> <b>(1.05-1.20)</b>	<b>1.14</b> <b>(1.07-1.22)</b>	<b>1.11</b> <b>(1.04-1.20)</b>	<b>1.15</b> <b>(1.08-1.22)</b>	<b>1.15</b> <b>(1.08-1.22)</b>	<b>1.12</b> <b>(1.06-1.19)</b>
Vascular dementia (n=2,821)	0.99 (0.89-1.10)	1.02 (0.91-1.13)	1.04 (0.93-1.16)	<b>1.14</b> <b>(1.03-1.26)</b>	<b>1.15</b> <b>(1.04-1.28)</b>	<b>1.15</b> <b>(1.04-1.28)</b>
Dementia with Lewy bodies (n=548)	0.94 (0.74-1.18)	0.98 (0.77-1.23)	0.99 (0.77-1.28)	<b>1.29</b> <b>(1.04-1.59)</b>	<b>1.29</b> <b>(1.04-1.60)</b>	<b>1.38</b> <b>(1.09-1.75)</b>

**Model 1:** Adjusted for age and gender

**Model 2:** Adjusted for age, gender, marital status, ethnicity, index of deprivation, and MMSE score

**Model 3:** Adjusted for the above, HoNOS scores (agitation, psychosis, non-accidental self-injury, problem-drinking or drug taking, depressed mood, physical illness or disability, activities of daily living, living conditions, occupational / recreational activities, social relationships), pharmacotherapy, and hospitalisation in the year prior to dementia diagnosis

\* additionally adjusted for dementia subtype

**Bold** p<0.05

**Italics** 0.05<p<0.10



**Supplementary Table 1: Weight loss x subtype interactions comparing vascular dementia and dementia with Lewy bodies to Alzheimer's disease in Cox regression models**

	Mortality					
	Model 1		Model 2		Model 3	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Alzheimer's disease (n=8,238)	Reference		Reference		Reference	
Vascular dementia (n=2,821)	0.87 (0.76-0.99)	0.031	0.88 (0.78-1.00)	0.057	0.92 (0.81-1.05)	0.217
Dementia with Lewy bodies (n=548)	0.82 (0.64-1.04)	0.106	0.83 (0.66-1.06)	0.138	0.87 (0.68-1.11)	0.261
	Emergency Hospitalisation					
	Model 1		Model 2		Model 3	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Alzheimer's disease (n=8,238)	Reference		Reference		Reference	
Vascular dementia (n=2,821)	0.99 (0.88-1.11)	0.812	0.99 (0.88-1.12)	0.883	1.02 (0.90-1.15)	0.768
Dementia with Lewy bodies (n=548)	1.11 (0.89-1.38)	0.338	1.13 (0.90-1.40)	0.290	1.13 (0.91-1.41)	0.272

**Model 1:** Adjusted for age and gender

**Model 2:** Adjusted for age, gender, marital status, ethnicity, index of deprivation, and MMSE score

**Model 3:** Adjusted for the above, HoNOS scores (agitation, psychosis, non-accidental self-injury, problem-drinking or drug taking, depressed mood, physical illness or disability, activities of daily living, living conditions, occupational / recreational activities, social relationships), pharmacotherapy, and hospitalisation in the year prior to dementia diagnosis

HR=hazard ratio; 95% CI = 95% Confidence interval