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Nutritional Status is Associated with Severe Dementia and Mortality: The Cache County Dementia Progression Study

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Abstract

Purpose: Studies have reported faster cognitive/functional decline in persons with dementia (PWD) with malnutrition. We investigated whether baseline nutritional status predicted severe dementia and mortality in a population-based sample.

Patients: A maximum of three hundred PWD were assessed annually for up to 8.6 years.

Methods: Nutritional status was assessed using a modified Mini-Nutritional Assessment (mMNA). Severe dementia was defined as: “severe” Clinical Dementia Rating or Mini-Mental State Exam score ≤ 10 . Using Cox proportional hazards models, we examined the association between baseline mMNA score (or its subcomponents) with each outcome. Covariates included demographics; dementia onset age, type, and duration; APOE genotype; and residency with caregiver.

Results: Compared to “well-nourished”, “malnourished” PWD had 3–4 times the hazard of severe dementia (HR = 4.31; $p = .014$) and death (HR = 3.04; $p < .001$). Those “at risk for malnutrition” had twice the hazard of severe dementia (HR = 1.98; $p = .064$) and 1.5 times the hazard of death (HR = 1.46; $p = .015$). MMNA subcomponents of food group intake, weight loss, BMI, mobility, health status, protein consumption, and mid-arm circumference predicted one or both outcomes.

Conclusions: Nutritional status is an important predictor of clinical outcomes in dementia and may provide an avenue for intervention.

Keywords

Malnutrition; Severe Dementia; Alzheimer’s disease; Dementia; Mortality

INTRODUCTION

Dementia is a clinical, usually progressive, syndrome characterized by declines in cognitive and functional abilities resulting in an eventual loss of independence and ultimately, death.¹ Alzheimer's disease (AD) is the most common cause of dementia in late-life.² No available intervention effectively halts or reverses its effects. Identifying modifiable factors that enhance patient functioning and minimize burden on families and caregivers is an important goal.

Recent research has linked nutritional status to cognitive, neuropsychiatric, and functional decline in persons with dementia (PWD).³⁻⁶ In a clinic-based French cohort of 523 persons with AD, Vellas et al.³ reported individuals at risk of malnutrition had worse cognitive performance and greater impairment in Activities of Daily Living (ADL) compared to those who were well-nourished. Additionally, malnourished individuals had significantly worse cognitive and neuropsychiatric symptoms than well-nourished individuals at one-year follow-up.⁴ In an Italian clinic-based sample of 49 hospitalized persons with dementia (PWD), Spaccavento et al.⁵ found that those at-risk of malnutrition experienced more impairment in ADLs and behavioral symptoms than those who were well-nourished at entry. In the Cache County population-based cohort, PWD with poorer nutritional status had worse functional status and faster cognitive decline over six years.⁶

The clinical endpoint of "severe dementia" is an important milestone in the course of the condition due to its association with greater ADL limitations and degree of disability,⁷ higher formal and informal costs of care,⁸⁻¹⁰ hospitalizations,¹¹ and increased risk of institutionalization. One analysis from the Cache County cohort reported that with increasing dementia severity, there was a 6-fold higher cost of informal care.¹² In the Predictors Study, a longitudinal study of persons with AD, each unit increase on the Blessed Dementia Rating Scale (BDRS) increased the probability of receiving informal care by 29.5% and increased the average hours of informal care by 5.4%.¹³ Similarly, a one-point increase on the BDRS was associated with 7.6% and 3.9% increases in formal medical and non-medical costs, respectively.⁸

Previous research has identified risk factors predictive of progression to severe dementia. In the Cache County cohort, newly identified persons with AD who were female, had less than a high school education, worse overall health, and at least one clinically significant neuropsychiatric symptom at baseline were 1.38 to 2.48 times more likely to progress to severe dementia.¹⁴ However, age of onset exhibited a U-shaped relationship with risk, with older and younger persons exhibiting the highest hazard of severe dementia.¹⁴ These factors were similar to those identified as predictors of more rapid cognitive and functional decline in the same cohort.^{15,16} Data pooled from 14 randomized clinical trials indicated that baseline cognitive, global, and behavioral status were independent predictors of faster rates of cognitive decline in persons with AD.¹⁷ While these clinical and demographic variables may be useful in prognosis, they are not modifiable. By contrast, indicators of nutritional status represent anthropomorphic, dietary, mobility, and medical variables that may provide points of intervention through medical and caregiving practices. Thus, the present study investigated the association between baseline nutritional status and the clinical endpoints of

severe dementia or death in the Cache County Dementia Progression Study (DPS). To our knowledge, this is the first study to date to evaluate nutritional status in relation to these clinical endpoints using a longitudinal design. Further, the present study evaluates subcomponents of nutritional status to identify the strongest predictors of these outcomes and thereby increase the specificity of possible interventions.

METHODS

Three hundred and twenty-eight participants were diagnosed with dementia at one of three *incidence* waves of the Cache County Study on Memory in Aging (CCSMSA) and enrolled in DPS. The methods for these studies are detailed elsewhere.^{15,18} Briefly, 5092 individuals were recruited and completed a multi-staged dementia screening and evaluation protocols in CCMS over four triennial waves. In each wave, dementia was diagnosed based on a clinical assessment that included a nurse's medical and neurological exam, detailed clinical history of cognitive and functional decline, medical history, and neuropsychological assessment. Causes of dementia were further evaluated with a physician examination, neuroimaging (brain MRI), and a common panel of blood lab assays and urinalysis to rule out other medical conditions.¹⁸ Final diagnoses of dementia and dementia type (e.g., AD, vascular dementia, etc.) were determined by consensus of an expert panel of geropsychiatrists, neuropsychologists, neurologists, and a cognitive neuroscientist.¹⁸ Individuals diagnosed with dementia at each incidence wave, and their caregivers, were invited to participate in the DPS.

At semi-annual visits, participants completed a battery of neuropsychological tests and caregivers provided information about the health, cognitive status, functional ability, and neuropsychiatric symptoms of their care-recipient. Nutritional status was assessed at baseline and at each odd numbered visit. Baseline nutritional status was used as a predictor and cognitive and functional assessments conducted at each visit were used to assess the outcome of severe dementia (see below). Study procedures were approved by the Institutional Review Boards of Utah State and Johns Hopkins Universities.

Measures

Nutritional status was assessed using a modification of the Mini Nutritional Assessment (mMNA) as reported previously in this cohort.⁶ The Mini Nutritional Assessment (MNA)¹⁹ is a well-established, 30-point measure of nutritional status in the elderly using rubrics of anthropometric, dietary, medical, and subjective items. The MNA was adapted to this population by eliminating items associated with dementia (presence of dementia or depression and self-estimation of nutritional status) and henceforth referred to as the mMNA.⁶ Data used in the derivation of the mMNA were collected during the nurse's health interview and evaluation, including a general health survey (GMHR),²⁰ ADLs (physical self-maintenance scale), medication inventory, behavioral disturbances (i.e. weight loss via the NPI),²¹ nutritional intake, and direct measures of blood pressure, height, weight, and neurological status. Two items, regarding calf circumference and presence of pressure sores or skin ulcers, were not collected during the original interviews and are not included in this version. Thus, the mMNA consisted of the following sub-items with maximum point values

in parentheses: maintenance of food intake (2), weight loss (3), mobility (2), Body Mass Index (BMI) (3), lives independently (not institutionalized) (1), prescription drugs (1), daily meals (2), daily consumption of protein (1), fruit/vegetables (1), and fluids (1), mode of feeding (2), health status (2), and mid-arm circumference (1). New threshold values for the clinical categories of the mMNA were calculated to be proportionally equivalent to the original and are as follows: (22 pt max): 12.5=malnourished, 13–17.5= risk for malnutrition, and 17.5=well-nourished.

Participants were assessed to have severe dementia according to procedures described previously,¹⁴ if they received a global rating of “severe” on the Clinical Dementia Rating Scale (CDR)²² or a score ≤ 10 on the Mini-Mental State Exam (MMSE)²³. CDR is a rating of dementia severity based on the person’s cognitive and functional status in six domains: memory, orientation, judgment & problem-solving, community affairs, home & hobbies, and personal care.²² Based on clinical interviews with participants and caregivers as well as cognitive testing, nurses assigned a CDR score of 0 (no impairment), 0.5 (questionable impairment), 1 (mild impairment), 2 (moderate impairment), 3 (severe impairment), 4 (profound impairment), and 5 (terminal status). An established algorithm was followed to produce a global score.²² The MMSE is an 11-item assessment of global cognitive performance with well-documented reliability and validity.²³ Trained psychometrists administered the MMSE to participants, measuring orientation, memory, attention, verbal skills, and visuospatial reasoning for a maximum score of 30 points.²³ MMSE scores were adjusted for sensory-motor impairments for up to 10% of items affected.¹⁵ Time to severe dementia was measured as the time elapsed (in years) from the baseline visit to the visit at which the participant met criteria for severe dementia.

Mortality was monitored through daily review of obituaries and contacts with participants’ caregivers and family members. Date of death was recorded as the date of the event. Time to death was measured as the time elapsed from the baseline visit to date of death. The following covariates were selected based on their significance in the literature and theoretical importance: sex, education, dementia type, age of dementia onset, dementia duration, genotype at apolipoprotein E (APOE), and co-residence with a caregiver at baseline. APOE status was represented as carrying at least one e4 allele or not. Formal education was analyzed as a continuous variable (i.e. in years ranging from 0 to 20). Dementia was categorized as Alzheimer’s disease (AD), vascular dementia (without AD), or other.

Statistical Methods

All analyses excluded participants missing data on the predictor variables at baseline. Of 328 persons enrolled in DPS, 241 with complete mMNA and covariate data were included in the analyses modeling time to death. In models of severe dementia, 70 more participants were excluded at baseline due to prevalent severe dementia or lack of follow-up; thus, the sample consisting of 171 participants was included in mMNA models of severe dementia. To maximize use of the data in subcomponent analyses, participants were included if they had complete data for that specific component ($N = 200\text{--}300$), regardless of missing total mMNA score. See Table 3 for specific sample size of each analysis. In order to investigate

baseline differences between those with and without complete data, *t*-tests and Pearson's Chi-Square tests of independence were conducted. Cox proportional hazards regression was used to estimate time to severe dementia or death. The primary predictors were baseline mMNA category (well-nourished, at-risk for malnutrition, malnourished) or its components, in separate models. Of note, we elected to use baseline mMNA as a fixed factor and not time-varying due to missingness at subsequent visits. Covariates were added in a step-wise fashion and removed based on significance ($p < 0.05$) to develop the most parsimonious models. Log-minus-log (LML) plots were examined for each predictor variable to ensure that the proportional hazards assumptions were met. All analyses used SPSS version 24.

RESULTS

Two hundred and forty-one PWD (71% AD and 52% female) had complete mMNA and other baseline predictors. These participants had mean (SD) education of 13.24 (3.02) years, baseline age of 85.60 (5.56), and dementia duration of 3.44 (1.82). The majority of participants were in the well-nourished (48.96%) and at-risk for malnutrition (37.34%) categories at baseline. Additionally, 54.77% of participants were living with their caregiver at the start of the study. Individuals included in the analyses differed from those missing data ($N = 87$) on some baseline characteristics. Those with missing data were more likely to be female and not residing with a caregiver at baseline ($p < .05$). Approximately 86% of 241 died during the study period and 21% of 171 participants developed incident severe dementia. Table 1 displays baseline demographic characteristics of those included and excluded from the mMNA analyses and Table 2 gives a summary of the survival times for each outcome.

In Cox proportional hazards models, baseline mMNA category significantly predicted hazard of severe dementia ($p = .025$) and death ($p < .001$). Compared to the well-nourished, malnourished individuals were over 4 times as likely to reach severe dementia ($HR = 4.31$, 95% $CI = 1.34-13.87$, $p = .014$) and approximately 3 times as likely die ($HR = 3.04$, 95% $CI = 1.96-4.72$, $p < .001$) over the study period. Similarly, those at risk for malnutrition were twice as likely to reach severe dementia (trend; $HR = 1.98$, 95% $CI = 0.96-4.09$, $p = .064$) and 1.5 times as likely die over the study period ($HR = 1.46$, 95% $CI = 1.08-1.98$, $p < .001$) than the well-nourished participants. Statistically significant covariates predicting time to death included dementia onset age, baseline dementia duration, and dementia type (with AD having higher risk). None of the covariates were statistically significant in models of mMNA and time to severe dementia and thus were dropped from the final model. Table 3 shows the results of the Cox regression models for both outcomes and Figures 1 and 2 display the survival plots by nutritional status.

Component Analyses

Bivariate correlations demonstrated that maintenance of food intake was positively associated with weight ($r = .52$), mobility ($r = .19$), BMI ($r = .16$), independent living (not institutionalized) ($r = .11$), mid-arm circumference ($r = .12$), independent mode of feeding ($r = .16$), and fruit/vegetable ($r = .17$) and fluid intake ($r = .13$), all $p < .05$. Greater variety in protein intake was associated with greater number of daily meals ($r = .21$) and higher fruit/

vegetable intake ($r = .25$), all $p < .05$. Better health status was associated with fewer prescribed drugs ($r = .25$), weight ($r = .13$), greater mobility ($r = .30$), and living independently (not institutionalized) ($r = .16$), all $p < .05$. When examined individually as predictors, the following components of the baseline mMNA predicted time to both severe dementia and death in Cox proportional hazards regression: decline in food intake, reduction in mobility, smaller mid-arm circumference, moderately varied consumption of protein (i.e. consumed 2 of 3 protein options daily), though the latter was only marginally significant after controlling for caregiver co-residence. The following additional components were associated with time to death (but not severe dementia): weight loss, lower BMI, and poor/fair health status. Dementia onset age, duration of dementia, caregiver co-residence status, sex, and dementia type were significant covariates in predicting time to death. In statistical analyses of time to severe dementia, all covariates were non-significant except for caregiver co-residence but this varied by model (i.e. not significant when mobility was accounted for and marginally significant when modeled with mid-arm circumference). Table 3 shows the results of the mMNA component analysis.

DISCUSSION

The findings presented here suggest that poor nutritional status is associated with shortened lifespan and faster time to severe dementia in persons with dementia. This is consistent with previous literature, which demonstrated the association between poorer nutritional status and worse clinical features of dementia, such as cognitive and functional impairments, and neuropsychiatric symptoms.^{3–6} Therefore, screening for malnutrition is useful in predicting clinical outcomes of dementia. These findings extend that of a recent cross-sectional study within a clinical setting in Brazil,²⁴ which demonstrated negative correlations between MNA and severe dementia. Thus, nutritional status may serve as an important target for intervention in its own right and as an indirect path directed at maintenance of cognitive health.

As a multi-faceted construct encompassing diet, body composition, and overall health, nutritional status offers several opportunities of intervention in order to lengthen time of spent in milder stages of dementia for those afflicted with the condition. In fact, the present analyses showed that particular components of nutritional status may be particularly relevant for this purpose. Generally, dietary and anthropometric factors associated with frailty, such as reduction in food intake, weight loss, and lower BMI and smaller mid-arm circumference (MAC), were associated with time to severe dementia, mortality or both outcomes. These results are consistent with the current literature, which indicates that frailty is associated with cognitive impairment²⁵ and mortality²⁶ in older adults.

It is well established that eating behaviors change during the course of dementia and vary by type,²⁷ possibly related to differences in regional brain atrophy among underlying diseases causing dementia. While weight loss and BMI have been previously associated with dementia severity,^{28,29} they were only predictive of mortality in the present study. Previous studies used specific criteria to measure clinically significant weight loss (i.e. 10 or more pounds in the past 3 months²⁸ or weight loss $> 4\%$ in 1 year²⁹ whereas weight change in the current analyses were represented in the context of the mMNA, which relied on a crude

estimate of weight loss (i.e. persons experienced “some” weight loss versus persons who maintained weight). With respect to BMI, a recent cross-sectional investigation of 82 Italian older adults with dementia found that lower BMI ($<25 \text{ kg/m}^2$) was significantly associated with higher risk of moderate-severe cognitive impairment (OR=2.96; 95% CI: 1.16–7.55).³⁰ These researchers proposed an “alarm” BMI cut-off of 25 for preventing severe dementia.³⁰ Monitoring both weight loss and BMI outside of the context of nutritional status may be helpful in this regard. Lastly, smaller MAC has been negatively correlated with level of care, hospitalization, and prevalence of dementia in community-dwelling German older adults receiving home-care assistance³¹ and higher ADL dependence in a population-based Swedish cohort.³² Further, a cross-sectional, multi-national survey demonstrated that MAC was significantly associated with dementia prevalence and severity.³³ The current findings extend the findings from previous studies and utilize longitudinal data with a sample of persons with dementia of varied etiologies. We found that compared to persons who have a MAC of 22 centimeters or greater, those with a MAC less than 22 are twice as likely to die and 7 times as likely to reach severe dementia. While the other studies cited above examined MAC as a continuous variable, our study suggests that a “cut-off” value of 22 may be useful in predicting clinical outcomes of dementia.

An important indicator of disability, reduced mobility, was highly predictive of both clinical endpoints of severe dementia and death. Persons who were bed or chair-bound were 15 times as likely to reach severe dementia and 1.6 times more likely to die, compared to freely ambulating individuals. It is well established that functional impairment typically follows cognitive decline in dementia;³⁴ however the functionally related construct of mobility has not been well studied as a predictor of severe dementia. Based on our findings, level of mobility is a simple, robust predictor of severe dementia. Interestingly, persons who ambulated with assistance were slightly less likely to reach severe dementia than their freely ambulating peers. Though not statistically significant, this result may represent differences in level of care between groups – i.e. persons reporting assistance with walking may receive additional supports in maintaining beneficial social/cognitive stimulation³⁵ and overall health.

Protein consumption is an important dietary marker of nutritional status^{19,36} and relative to other macronutrients, is a modifiable risk factor for developing MCI or dementia.³⁷ In their longitudinal, population-based study, Roberts et al.³⁷ demonstrated that persons with a higher proportion of caloric intake from proteins and fats compared to carbohydrates were at reduced risk for later MCI and dementia. Results from the present analysis underscore the importance of protein intake (over other nutrients) in predicting clinical outcomes in dementia. Compared to persons who consumed a largely varied protein diet (e.g. meat, legumes, and dairy), persons who consumed a moderately varied protein diet (e.g. 2 of 3 protein options daily) were 2.39 times more likely to reach severe dementia (marginally significant). Previous research from the broader Cache County Memory Study demonstrated that a balanced, diverse diet of recommended foods was associated with better cognitive outcomes in persons without dementia.³⁸ The current analyses suggests the same may be true for protein intake alone. Though the group with the least variation in protein consumption (e.g. 1 of the 3 protein options) was also at greater risk for increased mortality and severe dementia, these effects were not statistically significant.

The strengths of this study include the longitudinal, population-based design with high participation rates (excluding death) for up to 6 years of follow-up. However, the current sample was comprised primarily white, older adults with prevalence rates of drinking and smoking lower relative to the general population of the United States.³⁹ These characteristics may limit the generalizability of the current findings. Inclusion of non-AD dementias may be seen as a possible weakness of the study's specificity, though this was examined in the analyses and thus increased the relevance and strength of the study findings. Additionally, statistical power was compromised in analyses of severe dementia due to low incidence (N = 36) of severe dementia during the period of observation. While causation cannot be determined based on our observational study, use of baseline mMNA that predated severe dementia is consistent with the notion that worse nutritional status predicts worse outcomes in dementia.

In conclusion, we found nutritional status was a significant predictor of severe dementia and shorter lifespan, and therefore, represents an important *modifiable* clinical factor to monitor and potentially guide interventions to affect patient outcomes. Particular components of the mMNA were more predictive than others, providing specific areas to possibly address in multi-faceted interventions. Current evidence is limited in supporting recommendations for overcoming malnutrition in older adults with dementia⁴⁰ and randomized controlled trials are needed to validate these claims.

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REFERENCES

1. APA. Diagnostic and statistical manual of mental disorders: DSM-5. Washington, D.C: American Psychiatric Association; 2013.
2. 2016 Alzheimer's disease facts and figures. Alzheimer's & dementia : the journal of the Alzheimer's Association. 2016;12(4):459–509.
3. Vellas B, Lauque S, Gillette-Guyonnet S, et al. Impact of nutritional status on the evolution of Alzheimer's disease and on response to acetylcholinesterase inhibitor treatment. Journal of Nutrition, Health & Aging. 2005;9(2):75–80.
4. Guerin O, Soto ME, Bocker P, et al. Nutritional status assessment during Alzheimer's disease: results after one year (the REAL French Study Group). Journal of Nutrition, Health & Aging. 2005;9(2):81–84.
5. Spaccavento S, Del Prete M, Craca A, Fiore P. Influence of nutritional status on cognitive, functional and neuropsychiatric deficits in Alzheimer's disease. Archives of gerontology and geriatrics. 2009;48(3):356–360. [PubMed: 18448178]
6. Sanders C, Behrens S, Schwartz S, et al. Nutritional status is associated with faster cognitive decline and worse functional impairment in the progression of dementia: The cache county dementia progression study. Journal of Alzheimer's Disease. 2016;52(1):33–42.
7. Arrighi HM, Gelinas I, McLaughlin TP, Buchanan J, Gauthier S. Longitudinal changes in functional disability in Alzheimer's disease patients. Int Psychogeriatr. 2013;25(6):929–937. [PubMed: 23406898]
8. Zhu CW, Leibman C, McLaughlin T, et al. Patient dependence and longitudinal changes in costs of care in Alzheimer's disease. Dementia and geriatric cognitive disorders. 2008;26(5):416–423. [PubMed: 18946219]

9. Andersen CK, Lauridsen J, Andersen K, Kragh-Sorensen P. Cost of dementia: impact of disease progression estimated in longitudinal data. *Scandinavian journal of public health*. 2003;31(2):119–125. [PubMed: 12745762]
10. Leicht H, Heinrich S, Heider D, et al. Net costs of dementia by disease stage. *Acta psychiatrica Scandinavica*. 2011;124(5):384–395. [PubMed: 21838738]
11. Zhu CW, Cosentino S, Ornstein K, Gu Y, Andrews H, Stern Y. Use and cost of hospitalization in dementia: longitudinal results from a community-based study. *International journal of geriatric psychiatry*. 2015;30(8):833–841. [PubMed: 25351909]
12. Rattinger GB, Schwartz S, Mullins CD, et al. Dementia severity and the longitudinal costs of informal care in the Cache County population. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*. 2015;11(8):946–954.
13. Zhu CW, Scarmeas N, Torgan R, et al. Clinical characteristics and longitudinal changes of informal cost of Alzheimer's disease in the community. *Journal of the American Geriatrics Society*. 2006;54(10):1596–1602. [PubMed: 17038080]
14. Rabins PV, Schwartz S, Black BS, et al. Predictors of progression to severe Alzheimer's disease in an incidence sample. *Alzheimer's & Dementia*. 2013;9(2):204–207.
15. Tschanz JT, Corcoran CD, Schwartz S, et al. Progression of cognitive, functional, and neuropsychiatric symptom domains in a population cohort with Alzheimer dementia: The Cache County Dementia Progression Study. *The American Journal Of Geriatric Psychiatry*. 2011;19(6):532–542. [PubMed: 21606896]
16. Leoutsakos J-MS, Han D, Mielke MM, et al. Effects of general medical health on Alzheimer's progression: The Cache County Dementia Progression Study. *International Psychogeriatrics*. 2012;24(10):1561–1570. [PubMed: 22687143]
17. Lopez OL, Schwam E, Cummings J, et al. Predicting cognitive decline in Alzheimer's disease: An integrated analysis. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*. 2010;6(6):431–439.
18. Breitner JS, Wyse BW, Anthony JC, et al. APOE-ε4 count predicts age when prevalence of AD increases, then declines. *Neurology*. 1999;53(2):321–331. [PubMed: 10430421]
19. Guigoz Y, Vellas B, Garry PJ. Mini Nutritional Assessment: A Practical Assessment Tool for Grading the Nutritional State of Elderly Patients In: Vellas BJ, Guigoz Y, Garry PJ, Albaredo JL, eds. *Facts and Research in Gerontology*. New York, NY: Springer Publishing Company; 1994:15–59.
20. Lyketsos CG, Galik E, Steele C, et al. The General Medical Health Rating: a bedside global rating of medical comorbidity in patients with dementia. *Journal of the American Geriatrics Society*. 1999;47(4):487–491. [PubMed: 10203127]
21. Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology*. 1994;44(12):2308–2314. [PubMed: 7991117]
22. Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. *British Journal of Psychiatry*. 1982;140:566–572. [PubMed: 7104545]
23. Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State" A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*. 1975;12:189–198.
24. Marino LV, Ramos LF, Chiarello PG. Nutritional status according to the stages of Alzheimer's disease. *Aging clinical and experimental research*. 2015;27(4):507–513. [PubMed: 25539973]
25. Robertson DA, Savva GM, Coen RF, Kenny RA. Cognitive function in the prefrailty and frailty syndrome. *Journal of the American Geriatrics Society*. 2014;62(11):2118–2124. [PubMed: 25370593]
26. Matusik P, Tomaszewski K, Chmielowska K, et al. Severe frailty and cognitive impairment are related to higher mortality in 12-month follow-up of nursing home residents. *Archives of gerontology and geriatrics*. 2012;55(1):22–24. [PubMed: 21764151]
27. Kai K, Hashimoto M, Amano K, Tanaka H, Fukuhara R, Ikeda M. Relationship between eating disturbance and dementia severity in patients with Alzheimer's disease. *PloS one*. 2015;10(8):e0133666. [PubMed: 26266531]

28. Albanese E, Taylor C, Siervo M, Stewart R, Prince MJ, Acosta D. Dementia severity and weight loss: a comparison across eight cohorts. The 10/66 study. *Alzheimer's & dementia : the journal of the Alzheimer's Association*. 2013;9(6):649–656.
29. Guerin O, Andrieu S, Schneider SM, et al. Different modes of weight loss in Alzheimer disease: a prospective study of 395 patients. *The American journal of clinical nutrition*. 2005;82(2):435–441. [PubMed: 16087990]
30. Coin A, Veronese N, De Rui M, et al. Nutritional predictors of cognitive impairment severity in demented elderly patients: the key role of BMI. *The journal of nutrition, health & aging*. 2012;16(6):553–556.
31. Pohlhausen S, Uhlig K, Kiesswetter E, et al. Energy and Protein Intake, Anthropometrics, and Disease Burden in Elderly Home-care Receivers--A Cross-sectional Study in Germany (ErnSIPP Study). *The journal of nutrition, health & aging*. 2016;20(3):361–368.
32. Gavrilidou NN, Pihlsgard M, Elmstahl S. Anthropometric reference data for elderly Swedes and its disease-related pattern. *European journal of clinical nutrition*. 2015;69(9):1066–1075. [PubMed: 25990690]
33. Taylor CL, Albanese E, Stewart R. The association of dementia with upper arm and waist circumference in seven low- and middle-income countries: the 10/66 cross-sectional surveys. *The journals of gerontology Series A, Biological sciences and medical sciences*. 2012;67(8):897–904.
34. Suh GH, Ju YS, Yeon BK, Shah A. A longitudinal study of Alzheimer's disease: rates of cognitive and functional decline. *International journal of geriatric psychiatry*. 2004;19(9):817–824. [PubMed: 15352138]
35. Treiber KA, Carlson MC, Corcoran C, et al. Cognitive stimulation and cognitive and functional decline in Alzheimer's disease: The Cache County Dementia Progression Study. *The Journals of Gerontology: Series B: Psychological Sciences and Social Sciences*. 2011;66(4):416–425.
36. Guigoz Y, Lauque S, Vellas BJ. Identifying the elderly at risk for malnutrition. The Mini Nutritional Assessment. *Clinics in geriatric medicine*. 2002;18(4):737–757. [PubMed: 12608501]
37. Roberts RO, Roberts LA, Geda YE, et al. Relative intake of macronutrients impacts risk of mild cognitive impairment or dementia. *Journal of Alzheimer's disease : JAD*. 2012;32(2):329–339. [PubMed: 22810099]
38. Wengreen HJ, Neilson C, Munger R, Corcoran C. Diet quality is associated with better cognitive test performance among aging men and women. *The Journal of nutrition*. 2009;139(10):1944–1949. [PubMed: 19675102]
39. Wengreen HJ, Munger RG, Corcoran CD, et al. Antioxidant intake and cognitive function of elderly men and women: the Cache County Study. *The journal of nutrition, health & aging*. 2007;11(3):230–237.
40. Droogsma E, van Asselt D, De Deyn PP. Weight loss and undernutrition in community-dwelling patients with Alzheimer's dementia: From population based studies to clinical management. *Zeitschrift fur Gerontologie und Geriatrie*. 2015;48(4):318–324. [PubMed: 25990006]

Figure 1. mMNA predicts time to severe dementia. Compared to those who are well-nourished at baseline, persons at risk for malnutrition are twice as likely and malnourished individuals are nearly three times as likely to die over the study follow-up.

Figure 2. mMNA predicts time to death. Compared to those who are well-nourished at baseline, persons at risk for malnutrition are about 1.5 times as likely and malnourished individuals are 3 times as likely to reach the endpoint of death.

Table 1Baseline Characteristics[‡] of DPS Participants With and Without Complete Data

	Complete (N=241)	Incomplete (N=87)	Chi ² , p value
Female N (%) *	126 (52.28)	64 (73.56)	11.88, <i>p</i> = .001
Dementia Type N (%)			0.85, <i>p</i> = .654
AD	171 (70.95)	65 (74.71)	
VaD	31 (12.86)	8 (9.20)	
Other dementia	39 (16.18)	14 (16.09)	
mMNA group N (%)			3.041, <i>p</i> = .219 [‡]
Malnourished	33 (13.69)	1 (1.15)	
At-risk for malnutrition	90 (37.34)	4 (4.60)	
Well-nourished	118 (48.96)	12 (13.79)	
Missing	-	70 (80.46)	
Presence of APOE e4 N (%)	109 (45.23)	36 (41.38)	0.29, <i>p</i> = .589
Missing	-	1 (1.15)	
Caregiver co-residence N (%) *			8.83, <i>p</i> = .003
Co-resides	132 (54.77)	20 (22.99)	
Does not co-reside	109 (45.23)	40 (45.98)	
Missing	-	27 (31.03)	
BMI N (%)			0.55, <i>p</i> = .760
<19	13 (5.39)	5 (5.75)	
19–23	57 (23.65)	19 (21.84)	
23	171 (70.95)	48 (55.17)	
Missing	-	15 (17.24)	
Weight loss since last visit N (%)			0.49, <i>p</i> = .486
Some or don't know	29 (12.03)	13 (14.94)	
None	212 (87.97)	74 (85.06)	
GMHR Health Status N (%)			1.06, <i>p</i> = .589
Poor/fair	51 (21.16)	16 (18.39)	
Good	161 (66.80)	57 (65.52)	
Excellent	29 (12.03)	14 (16.09)	
<i>t, p value</i>			
Age M (SD)	85.60 (5.56)	86.91 (6.14)	-1.82, <i>p</i> = .068
Dementia onset age M (SD)	82.16 (5.92)	83.01 (6.19)	-1.14, <i>p</i> = .257
Dementia duration M (SD)	3.44 (1.82)	3.90 (2.08)	-1.92, <i>p</i> = .055
Education M (SD)	13.24 (3.02)	13.57 (2.69)	-0.88, <i>p</i> = .379

[‡]Baseline characteristics of participants with complete data for all baseline predictor variables, including full mMNA, compared to excluded participants with incomplete data. Significant differences were evaluated using Pearson Chi-Square tests of independence and *t*-test analyses for categorical and continuous variables, respectively.

* $p < .05$ in t -test and Pearson's Chi-Square tests of independence.

Note that approximately 80% of excluded persons were missing on mMNA.

AD=Alzheimer's Disease; VaD=Vascular Dementia; mMNA=modified Mini Nutritional Assessment; APOE=Apolipoprotein E; BMI=Body Mass Index; GMHR=General Medical Health Rating.

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Table 2

Survival Summary[‡]

Event	N (%) reached event	Mean (st. error) survival time	95% CI for mean survival		Median (st. error) survival time	95% CI for median survival	
			Lower Bound	Upper Bound		Lower Bound	Upper Bound
Severe dementia	36 (21.05)	6.13 (0.34)	5.46	6.80	6.67 (0.55)	5.59	7.75
Death	208 (86.31)	3.47 (0.19)	3.09	3.84	2.54 (0.19)	2.17	2.92

[‡]Survival summaries based on Kaplan-Meier analyses with log-rank tests of total mMNA predicting time to severe dementia and death

Table 3

mMNA and Components[‡] Predict Time to Severe Dementia & Death

Severe Dementia											Death			
95% CI for Exp(β)											95% CI for Exp(β)			
	N	β	SE	p	Exp(β)	Lower	Upper	N	β	SE	p	Exp(β)	Lower	Upper
Total mMNA														
Well-nourished (ref)	171							241						
Malnourished		1.46	0.60	.014	4.31	1.34	13.87		1.11	0.22	<.001	3.04	1.96	4.72
At-risk for malnutrition		0.68	0.37	.064	1.98	0.96	4.09		0.38	0.16	.015	1.46	1.08	1.98
mMNA Component Analysis														
Stable Food Intake (ref)	207							291						
Decline in Food Intake		1.06	0.33	.001	2.88	1.50	5.53		0.41	0.16	.008	1.51	1.12	2.05
Ambulates freely (ref)	207							291						
Chair Bound		2.70	0.56	<.001	14.94	5.02	44.51		0.68	0.23	.003	1.97	1.26	3.06
With Assistance		-0.36	0.33	.280	0.70	0.37	1.34		0.50	0.14	<.001	1.65	1.24	2.18
MAC (ref: > 21)	200							282						
MAC < 21		1.97	0.53	<.001	7.14	2.55	19.97		0.87	0.25	.001	2.39	1.45	3.94
Protein Intake (ref: 3 Types)	203							285						
0-1 Types		0.42	0.56	.450	1.52	0.51	4.52		0.32	0.23	.152	1.38	0.89	2.15
2 Types		0.87	0.46	.058	2.39	0.97	5.89		0.51	0.20	.010	1.66	1.13	2.45
Weight Loss (ref: none)								300						
Some Weight Loss									0.54	0.18	.003	1.71	1.20	2.44
BMI (ref: 23 or greater)								287						
<19									0.92	0.26	<.001	2.50	1.50	4.17
19-22									0.30	0.15	.054	1.34	1.00	1.81
Health Status (ref: excellent)								300						
Poor/Fair									0.72	0.23	.002	2.06	1.31	3.23
Good									0.35	0.20	.080	1.43	0.96	2.12

Categories were collapsed within the following components: food intake, MAC, BMI, and health status. N sizes for each analysis are displayed in the table. Covariates are not displayed. Please see text for significant covariates retained in final models.

mMNA=modified Mini-Nutritional Assessment; MAC = Mid-Arm Circumference; BMI = Body Mass Index.