1	The Mini Nutritional Assessment-Short Form and mortality in nursing home residents -
2	Results from the INCUR study
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13 Abstract

OBJECTIVES: To examine whether the Mini Nutritional Assessment-Short Form (MNA SF) score and its individual items are predictors of mortality in a nursing home population.

DESIGN: Prospective, secondary analysis from the Incidence of pNeumonia and related
 ConseqUences in nursing home Residents (INCUR) study with 1-year follow-up.

PARTICIPANTS: A total of 773 older persons (women 74.4%) living in 13 French nursing
homes.

MEASUREMENTS: At baseline, nutritional status was assessed with the MNA-SF. Overall mortality rate was measured over a 12-month follow-up period after the baseline assessment visit. Cox proportional hazard models were performed to test the predictive capacity of the MNA-SF score and its single components for mortality.

RESULTS: Mean age of participants was 86.2 (standard deviation, SD 7.5) years. Mean 24 25 MNA-SF score was 9.8 (SD 2.4). Among participants, 198 (25.6%) presented a normal nutritional status (12-14 points), 454 (58.7%) were at risk of malnutrition (8-11 points), and 26 121 (15.7%) were malnourished. After one year of follow-up, 135 (17.5%) participants had 27 28 died. Age, female gender, baseline weight, BMI and MNA-SF were significant predictors of mortality whereas no specific chronic disease was. The total MNA-SF score was a significant 29 30 predictor of mortality (Hazard Ratio=0.81; 95% CI 0.74-0.90; p<0.001), even after adjustment for potential confounders. Four individual items: weight loss, mobility, recent stress and BMI 31 32 were independent predictors of mortality.

CONCLUSIONS: The MNA-SF appears to be an accurate predictor of one-year mortality in
 nursing home residents. Thus, this tool may be regarded not only as a nutritional screening
 tool, but also as an instrument for identifying the most-at-risk individuals in this population.

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37 Key words: Older age; Mini Nutritional Assessment; Nursing Homes.

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Introduction

Malnutrition is associated with adverse health outcomes in older subjects. It predicts hospitalization, infectious diseases (1) and death (2,3). Poor nutritional status is also related to increased health care expenditures (2). On the other hand, nutritional interventions have proven beneficial effects on weight gain and malnutrition-related outcomes such as morbidity and mortality (4). Therefore, there has been a growing interest in assessing the nutritional status of elders in order to facilitate the early detection of malnutrition and structure a proper management.

46 Although many instruments have been developed and validated for nutritional assessment (e.g. involuntary weight loss, Body Mass Index [BMI], albumin concentration, 47 Mini-Nutritional Assessment [MNA] (5)), these tools have rarely been explored in nursing 48 home (NH) residents (6). This population represents a highly vulnerable part of the 49 heterogeneous geriatric patients, characterized by a high prevalence of chronic diseases, 50 51 impaired cognitive and physical functions and limitations of activities of daily living (7). Many risk factors may also increase the risk for malnutrition in these subjects, such as 52 polypharmacy (8) and multiple comorbidities (9). Unsurprisingly, the prevalence of 53 54 malnutrition in NH population has shown to reach 30% (3).

55 The MNA test is a very commonly used assessment tool of nutritional status (5). It has shown great sensitivity, specificity and predictive positive value for malnutrition in elderly 56 subjects (96%, 98% and 97% respectively), but needs 15 minutes to be completed. The MNA 57 short form (MNA-SF) consists of 6 items and takes less than 5 minutes to complete. It was 58 originally elaborated as a first step in the screening of malnutrition. A score of 11/14 or lower 59 indicates a risk for malnutrition and triggers the administration of the full MNA questionnaire. 60 Nevertheless, the MNA-SF has also been validated as an independent tool for nutritional 61 screening in older adults (10). Interestingly, the items composing the MNA-SF are related to 62

functional or cognitive performance, and thus potentially provide information on multiplehealth domains over and above the mere nutritional status.

However, there are still uncertainties regarding the ability of the MNA-SF to predict 65 mortality in older adults. In a systematic review the MNA-SF (as well as the full MNA) was 66 associated with higher mortality (Dent E, Visvanathan R, Piantadosi C, Chapman I 67 Nutritional screening tools as predictors of mortality, functional decline, and move to higher 68 level care in older people: a systematic review. J Nutr Gerontol Geriatr. 2012;31(2):97-145.) 69 70 In a recent population-based study involving elders from Taiwan with a 4-year follow-up, the MNA-SF also appeared as an effective predictor of mortality. (Wang JY, Tsai AC. The short 71 form Mini Nutritional Assessment is as effective as the full-Mini Nutritional Assessment in 72 predicting follow-up 4-year mortality in elderly Taiwanese. J Nutr Health Aging 2013;17: 73 594–598.) On the other hand, another study found that the MNA-SF is not suitable to provide 74 75 prognostic information in older adults with multiple comorbidities (Vischer UM, Frangos E, Graf C et al. The prognostic significance of malnutrition as assessed by the Mini Nutritional 76 77 Assessment (MNA) in older hospitalized patients with a heavy disease burden. Clin Nutr 2012;31:113–117.) In the present study, we conducted longitudinal analyses aimed at 78 examining the relationship between the MNA-SF and mortality in a sample of NH residents, 79 80 over one year of follow-up. We also studied which items of the MNA-SF may independently explain this association. 81

82 Methods

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Study design and participants

Data were from participants recruited as part of the Incidence of pNeumonia and related ConseqUences in nursing home Residents (INCUR) study, a prospective observational cohort study of 800 NH residents. The INCUR rationale, study design, and methodology have been previously described (11). The primary aim of INCUR was to estimate the incidence of pneumonia and the associated health-related expenditures in this population. The 6-month recruitment period started in February 2012. The INCUR project ended on June 2013 after all participants had been followed-up over 12 months.

Main eligibility criteria of INCUR included: age of 60 years and older; a functional 91 status ranging from 2 to 5 at the Autonomie Gérontologie - Groupes Iso-Ressources (AGGIR) 92 scale (i.e. the nationally recognized functional scale on which the allocation of social support 93 is decided by public health authorities in France; a score between 2 and 5 excluded totally 94 disabled patients as well as subjects with no impairment in basic activities of daily living) 95 (12) residents living in the NH for more than 30 days. The design of the INCUR project was 96 consistent with the Declaration of Helsinki and the study protocol was approved by the local 97 Ethics Committee. 98

99 Two follow-up visits were scheduled after 6 and 12 months from the baseline visit. At 100 these visits, besides of repeating the same multidimensional evaluation conducted at the 101 baseline, the possible onset of major health-related events occurred during the past 6 months 102 was ascertained. The present analyses were conducted in 773 subjects, after exclusion of 27 103 subjects with missing key data.

105 Variables of interest

At baseline, socio-demographic information, medical history, and comorbidities were recorded. Chronic diseases of interest were: atrial fibrillation, heart failure, coronary heart disease, respiratory conditions, history of stroke and stroke-related impairment, cancer, diabetes, Parkinson's disease and dementia. Weight and height were measured and BMI was calculated. Current smoking and oxygen therapy were also recorded. Cognitive function was assessed with the Abbreviated Mental Test scale (13). Depression was assessed with the 10item Geriatric Depression Scale (14).

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114 MNA-SF assessment

115 The MNA-SF consists of the first six items, also known as the "screening part" of the full MNA. Briefly these items are: A) food intake; B) involuntary weight loss; C) mobility; D) 116 recent psychological stress or acute disease; E) neuropsychological problem (i.e. dementia or 117 depression); and F) BMI. In case of missing value for this item (as frequently occurring in 118 bed-ridden residents), the BMI item can be replaced by the calf circumference (measured with 119 a tape). The MNA-SF score can range between 0 and 14 points with higher values indicating 120 better nutritional status. The MNA-SF score is also usually categorized into three groups 121 defining "normal" (12-14 points), "at risk" (8-11 points), and "malnutrition" (0-7 points) 122 123 statuses.

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127 Statistical analyses

Chi-squared tests and t-tests were used to describe the categorical and continuous 128 129 characteristics of the study sample according to the outcome of interest, respectively. Cox proportional hazard models were used to evaluate the relationships of the MNA-SF score (as 130 both continuous and categorical variable) and its composing items with mortality. Results are 131 presented as hazard ratios (HR) and 95% confidence intervals (95% CI). Secondary analyses 132 were also conducted using the single items composing the MNA-SF as independent variables 133 of interest in the prediction of mortality. Although weight and height were significantly 134 different between deceased subjects and survivors, these two variables were not included in 135 the adjusted model because strongly correlated with the independent variables of interest. All 136 137 statistical analyses were performed using SPSS statistical software version 18.0.0 (IBM Corp, New York). Statistical significance was defined as P<0.05. For all the single items 138 significantly associated with mortality, sensitivity, specificity, positive and negative 139 140 predictive values and positive and negative likelihood ratios were calculated.

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Results

Descriptive characteristics of the study sample (n=773) according to the study outcome are presented in Table 1. One hundred and thirty five (17.4%) residents died during the 12 months of follow-up. Mean age of the study population was 86.1 (SD 7.5) years, with a higher prevalence (74.6%) of women. The mean MNA-SF score was 9.8 (SD 2.4). In the study sample, 198 persons (25.6%) had a normal nutritional status (MNA-SF 12-14 points), 454 (58.7%) were at risk of malnutrition (8-11 points), and 121 (15.7%) were malnourished.

Among the deceased residents, mean age was 88.5 (SD 6.9) vs. 85.7 (SD 7.5) in survivors (p<0.001). Women represented 76.7% of survivors vs. 63.1% of deceased (p=0.001). None of the chronic diseases was significantly associated with mortality. However, indicators of nutritional status were predictors of 1-year mortality: baseline weight and BMI were lower in NH residents who died (61.3 kg [SD 13.4] vs. 64.4 kg [SD 14.6], p=0.03; and 24.2 [SD 4.3] kg/m² vs. 25.4 [SD 5.3] kg/m², p=0.04 respectively) as well as the MNA-SF score (9.3 vs. 9.9, p=0.02; Table 1).

In Table 2, results from Cox-proportional hazard models examining the MNA-SF and one-year mortality were presented. The MNA-SF (continuous variable) was associated with a significantly lower risk of dying during the follow-up, even after adjustment for age and gender. When the MNA-SF score was categorized, malnourished subjects (0-7 points) showed a significantly higher risk of mortality (HR=4.64, 95%CI 1.79-12.0; p=0.002) compared to the reference group. A trend for association between being at risk of malnutrition and higher risk of mortality (HR=2.40; 95%CI 0.99-5.79; p=0.052) was also observed.

167 Similar results were found in secondary analyses exploring the individual components 168 of the MNA-SF components and mortality (Table 3). Weight loss (p=0.02), BMI<21 kg/m² 169 (or calf circumference<31 cm) (p=0.004), recent disease or psychological stress (p=0.01) and 170 lack of mobility (p=0.048) were all significant predictors of the studied outcome. Their 171 sensitivity, specificity, positive and negative predictive values and likelihood ratios are 172 respectively displayed in Table 4. When considered individually, the four latter items showed 173 poor sensitivity for mortality. In contrast, the MNA-SF with a threshold of 12/14 had a correct 174 sensitivity (88.5%) for mortality. Moreover, only a borderline significance was reported for 175 the decrease in food intake item (p=0.053). The neuropsychological problem item was not 176 associated with mortality (p=0.83). 177

Discussion

In the present prospective study, a low MNA-SF score was a strong predictor of death after one year of follow-up. A low BMI (or calf circumference) or recent weight loss were individual and significant predictors of mortality in our sample. Two other items: "functional impairment" and "recent acute stress", which are likely to reflect a more general status of frailty rather than malnutrition *sensu stricto*, were also significant predictors of mortality. On the other hand, education or clinical conditions, including depression and dementia were not.

Malnutrition dramatically affects the vulnerable older persons, in particular those 184 185 living in institutions. Consistently to prior studies, only one quarter of our sample (25.6%) had a normal (i.e \geq 12) MNA-SF score whereas the other three guarters where either at risk of 186 malnutrition (58.7%) or malnourished (15.7%) (15,16). A recent systematic review has 187 188 examined the predictive validity of the available screening tools for malnutrition in NH populations (17). Authors concluded that none of them emerged as the gold-standard. Another 189 study specifically assessed the usefulness of the MNA-SF for malnutrition screening in a NH 190 population (18). This study considered a smaller sample (n=151) of institutionalized subjects 191 compared to our work, and only 64.4% of undernourished patients were found to be correctly 192 classified using this tool. Nevertheless, the MNA score demonstrated to be feasible and 193 showed the best predictive capacity for survival (compared with Nutritional Risk Screening 194 and the Malnutrition Universal Screening Tool) among well-nourished NH residents (15). 195

The use of the MNA-SF offers several advantages: this tool is standardized, reproducible, non-invasive, and takes only 5 minutes to be completed. Moreover, it is strongly correlated with the full MNA (19,20). Interestingly, the 6 items of the MNA-SF comprise three nutritional criteria (BMI, food intake and weight loss) as well as three criteria related to "geriatric conditions" (mobility, recent acute stress and neuropsychological disorder). Thus, this tool may be specifically tailored for frail older persons and is likely to provide insightsinto the global health apart from the mere nutritional status.

In our study, the MNA-SF appeared as a predictor of mortality. Not only the total 203 score, but also the score categories (i.e. people at risk of malnutrition and malnourished 204 subjects) as well as most of the subitems when individually considered. Our results are 205 206 supported by the study of Tangvik and colleagues who recently investigated the association between nutritional status and clinical outcomes (21). Authors have found that the 207 combination of four criteria from the ESPEN guidelines for nutrition screening 2002 (22) 208 (BMI <20.5 kg/m2 / Weight loss within the last weeks / Reduced dietary intake during the last 209 weeks / Severe illness) was accurate to predict mortality, morbidity and hospitalizations in 210 211 Norway hospital in-patients. Interestingly, such criteria are very similar to 4 MNA-SF items we found in our analyses. Thus, we may draw two main conclusions. First, our results are 212 consistent with the established relationship between nutritional status and survival in 213 214 institutionalized elderly (23,24). Second, the MNA-SF, may be regarded as a multidimensional instrument for identifying the most vulnerable individuals of an elderly 215 population. 216

On the other hand, the absence of chronic conditions related with enhanced 217 mortality might be surprising. This result may be explained by the high prevalence of 218 coexisting chronic diseases in our population. Further, we did not take into consideration the 219 severity of the diseases. Obviously, severe heart failure or dementia are a heavier burden than 220 221 mild stages of these conditions and increase the risk of poor outcomes. Yet, the simple MNA-SF showed an additional value to identify NH residents at higher risk of death whereas 222 223 specific pathological conditions did not. Two NH residents with the same multiple (but often stable) clinical conditions may be at different risk of dying given their nutritional status 224 assessed with the MNA-SF. But the death event can be the consequence of an impaired 225

response to an acute stressor (e.g. infection) in polypathological individuals (25). Thus, the MNA-SF may be considered as multidimensional assessment tool, resembling the frailty ones (26,27), thus overcoming the single nosological entities commonly used in the clinical setting. Consistently, the "mobility" and the "acute stress" items of the MNA-SF both reflect functional performances and were predictors of mortality in our study. As such, our results highlight the relationship between risk of death and functional status rather than comorbidities.

The main strengths of our study were the large sample size and the prospective design. 233 The representativeness of our sample was good, with few missing data (23 subjects i.e. less 234 than four percent) despite one year of follow-up. On the other hand, some limitations have to 235 236 be acknowledged. This study did not analyze biological markers of protein malnutrition (e.g. albumin concentration) that are independent risk factor for mortality in NH residents. We did 237 not consider either the causes of death or some other potential confounding factors to explain 238 the death. Yet, comorbidities, depression and dementia were not significantly associated with 239 death in our analyses. Moreover, the individual items of the MNA-SF have been 240 dichotomized instead of examining each category for each question of the form. Nevertheless, 241 we aimed at preserving the clinical meaningfulness when combining different categories of a 242 single item. 243

244 Conclusion

The MNA-SF and most of its subitems, but not clinical conditions, were significant predictors of overall mortality in NH residents, independently of potential confounders. Our findings support the use of this simple test in this population, not only for malnutrition screening but also for obtaining an overview of the general risk profile of these complex older adults. Therefore, the MNA-SF may pave the way not only for nutritional assessment but also 250 for comprehensive geriatric assessment and management of these vulnerable elders.

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Variable, M±SD	Death		
variable, MESD	No (n=638)	Yes (<i>n</i> =135)	Р
Age (years)	85.7±7.5	88.5±6.9	< 0.001
Gender (women)	76.7	63.1	0.001
Current smoking	2.5	3.1	0.66
Education (years)	8.5±3.3	8.1±3.1	0.28
Height (cm)	159.2±8.6	159.1±7.9	0.89
Weight (kg)	$64.4{\pm}14.6$	61.3±13.4	0.03
Body mass index (kg/m ²)	25.4±5.3	24.2±4.3	0.04
Clinical conditions			
Atrial fibrillation	12.3	17.0	0.25
Heart failure	26.9	33.3	0.26
Coronary heart disease	5.4	8.2	0.34
Respiratory disease	9.6	14.2	0.11
Stroke	7.7	11.9	0.38
Cancer	12.6	9.0	0.13
Diabetes	15.0	14.0	0.79
Parkinson's disease	5.9	5.9	0.98
Dementia	35.3	33.3	0.32
O ₂ therapy	1.8	2.2	0.70
Abbreviated Mental Test score (/10)	5.7±3.6	5.0±3.4	0.06
10-item Geriatric Depression Scale	2.9 ± 2.4	2.9 ± 2.5	0.84
MNA-SF score (/14)	9.9 ± 2.4	9.3±2.4	0.02

Table 1. Baseline characteristics of our population

356 Results are presented as means \pm SDs, or percentages

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Table 2. Relationships of the Mini Nutritional Assessment-Short Form (MNA-SF) score with mortality over one year of follow-up in nursing
 home residents.

	Unadjusted HR (95% CI)	Р	Adjusted* HR (95% CI)	Р
MNA-SF score (continuous), n/N=52/773	0.83 (0.75, 0.91)	< 0.001	0.81 (0.74, 0.90)	< 0.001
MNA-SF score categories				
Normal nutritional status (12-14 points), n/N=6/198	1 (Reference group)		1 (Reference group)	
At risk of malnutrition (8-11 points), n/N=31/454	2.30 (0.96, 5.51)	0.06	2.40 (0.99, 5.79)	0.052
Malnourished (0-7points), n/N=15/121	4.31 (1.67, 11.10)	0.003	4.64 (1.79, 12.00)	0.002

361 CI: confidence interval; HR: Hazard Ratio; MNA-SF: Mini Nutritional Assessment-Short Form; n: number of deceased subjects/N: total number

362 of subjects; *Adjusted for age and gender

	Unadjusted HR for mortality (95% CI)	Р	Adjusted* HR for mortality (95% CI)	Р
Decrease in food intake over the past 3 months				
No decrease in food intake, $n/N=36/627$	1 (Reference group)		1 (Reference group)	
Moderate and severe decrease in food intake, n/N=16/146	1.97 (1.09, 3.55)	0.02	1.82 (0.99, 3.34)	0.053
Weight loss over the past 3 months				
No weight loss, $n/N=26/513$	1 (Reference group)		1 (Reference group)	
Weight loss between 1 and 3 kg, and greater than 3 kg n/N=25/248	2.04 (1.18, 3.54)	0.01	1.93 (1.10, 3.39)	0.02
Mobility				
Goes out, $n/N=25/468$	1 (Reference group)		1 (Reference group)	
Able to get out of bed/chair but does not go out, and bed or chair bound,				
n/N=27/305	1.68 (0.97, 2.89)	0.06	1.75 (1.00, 3.06)	0.048
Acute disease or psychological stress over the past 3 months				
No, n/N=31/593	1 (Reference group)		1 (Reference group)	
Yes, n/N=21/180	2.30 (1.32, 4.00)	0.003	2.12 (1.20, 3.74)	0.01
Neuropsychological problems				
No psychological problems, n/N=17/226	1 (Reference group)		1 (Reference group)	
Mild and severe dementia or depression, n/N=35/547	0.85 (0.47, 1.51)	0.58	0.94 (0.52, 1.70)	0.83
Body mass index (BMI, kg/m2) or calf circumference (CC, cm)**				
BMI \ge 21or CC \ge 31, n/N=33/603	1 (Reference group)		1 (Reference group)	
BMI < 21 or CC < 31, n/N=19/170	2.08 (1.18, 3.66)	0.01	2.34 (1.31, 4.17)	0.004

Table 3. Relationships of individual items composing the MNA-SF score with mortality in nursing home residents.

369 BMI: Body Mass Index; CC: Calf circumference; HR: Hazard Ratio; CI: confidence interval n: number of deceased subjects/N: total number of

370 subjects; *Adjusted for age and gender ; ** if BMI was not available, the CC was used at its place to define the item

Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Positive Likelihood Ratio	Negative Likelihood Ratio
MNA-SF items					
36.5	79.1	11.2	94.5	1.74	0.80
40.4	78.0	11.7	94.8	1.83	0.76
49.0	68.6	10.1	94.9	1.56	0.74
51.9	61.4	8.9	94.7	1.35	0.78
88.5	26.6	8.0	97.0	1.21	0.43
28.9	85.2	12.3	94.3	1.95	0.84
-	36.5 40.4 49.0 51.9 88.5	36.5 79.1 40.4 78.0 49.0 68.6 51.9 61.4 88.5 26.6	Sensitivity (%) Specificity (%) Value (%) 36.5 79.1 11.2 40.4 78.0 11.7 49.0 68.6 10.1 51.9 61.4 8.9 88.5 26.6 8.0	Sensitivity (%)Specificity (%)Value (%)Value (%)36.579.111.294.540.478.011.794.849.068.610.194.951.961.48.994.788.526.68.097.0	Sensitivity (%)Specificity (%)Value (%)Value (%)Ratio36.579.111.294.51.7440.478.011.794.81.8349.068.610.194.91.5651.961.48.994.71.3588.526.68.097.01.21

Table 4. Sensitivity, Specificity, Predictive values and Likelihood ratios for mortality of the MNA-SF and its significant items

BMI: Body Mass Index; CC: Calf circumference; MNA-SF: Mini Nutritional Assessment-Short Form

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