

Healthy aging and mortality: the Italian Longitudinal Study on Aging

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Introduction

The major difficulty in studying healthy aging and comparing findings across studies lies both in the operational definition of health itself and in the different predictors investigated. Rowe and Kahn¹, in order to distinguish between the effect of diseases from the aging process itself, introduced the concept of successful aging as the ability to maintain three key behavioural characteristics: low risk of disease and disease-related disability, high mental and physical function and active engagement with life. Successful aging could, generally, be defined on the basis of the WHO definition of health: an optimal state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.

This study analyses the concept of healthy ageing and evaluates at what extent vitality explains mortality in a cohort of 5632 older Italians.

Materials and methods

The Italian Longitudinal Study on Aging² (ILSA) considered a random sample of 5,632 individuals aged 65-84 years, both community-dwelling and institutionalised persons, stratified by age and sex, identified on the demographic lists of the registry office of eight municipalities from northern, central and southern regions of Italy. The survey had two phases: a first phase, administered to all participants, that included 1) a personal interview to obtain information on socio-demographic characteristics, health habits and status for the investigated conditions (cardiovascular diseases, diabetes, parkinsonism, stroke, dementia and peripheral neuropathy); 2) a nurse visit; 3) a physician examination, including a general clinical assessment, the

administration of the Mini Mental State Examination³ (MMSE) the Italian version of the Geriatric Depression Scale⁴ (GDS), activities of daily living⁵ (ADL), instrumental activities of daily living⁶ (IADL), and performance tests. A second phase, administered to participants who screened positive to the first phase, consisted of the clinical confirmation of suspected cases of cardiovascular diseases, diabetes, parkinsonism, stroke, dementia and peripheral neuropathy by a specialist (internist or neurologist) through a visit and the review of medical records. The criteria for the diagnosis and the prevalence ratios were previously published⁷.

Vital status

Data on mortality were collected during the 1996 follow-up and a copy of the death certificate, reporting date and cause of death, was obtained from the national registry.

Assessment of mental status

Mental status score was calculated as a ratio of the number of questions answered correctly to the number of questions (if all questions were applicable), or an adjusted score (number of questions answered correctly divided by the number of answered questions, if some of the questions were not applicable) on the MMSE. If more than six items were missing, the total score was set to missing. The total score is then a number ranging between 0 and 1; the first quartile results to be equal to 0.86 and the third quartile is equal to 0.97.

Assessment of depressive symptoms

The GDS total score was calculated by dividing the number of positive answers with respect to the number of answered questions. If six item or more were missing, the total score was set to missing. The total score is a number ranging between 0 and 1 and the cut-off to classify a depressive symptomatology was set to 0.33.

Assessment of physical functioning

The ADLs score, as developed by Kats⁴, vary between 1 to 3; a score of 1 indicates that the subject is completely independent, while a score of 3 indicates a total dependence. We used an adjusted score varying between 0.33 and 1, obtained dividing the total score in the items answered by the sum of scores of the same items in the hypothesis of complete dependence. A score of 0.33 means that the subject is completely independent; a score between 0.33 and 0.56 indicates a dependence in two ADLs at most; a score between 0.56 and 0.78 indicates a dependence in three ADLs at most, and between 0.78 and 1 a dependence in four or more ADLs.

Definition of vitality level

We have defined as "high vitality group" those falling in the 75th percentile or more for the MMSE and with no impairments in ADL. "Poor vitality group" was defined by the lower 25th percentile of MMSE and impairments in all ADL's. All the others were considered in the "medium vitality group".

Statistical analysis

The design effect was taken into account by weighting each participant according to the age distribution of the Italian reference population (1991 Census) and the sample fraction.

Associations between demographic variables, health habits and conditions with vitality level were investigated with the chi-square test for trend; the chi-square test was performed to verify associations with the vital status.

The comparison of group mean age and Body Mass Index (BMI) with vitality status was evaluated through the *Generalized Linear Model (GLM)* procedure. Levene's test was used to test the homoscedasticity of variances; where the assumption of homoscedasticity was not met, Welch's test was performed.

The adjusted relative risks and 95% confidence intervals were calculated using the *Cox proportional hazards model* to estimate the strength of association of vitality levels with the vital status, controlling for those variables that were distributed unevenly across vitality levels (confounders) and could increase mortality. The assumption of proportionality was assessed through the graphical approach (log-log plot) and the analysis of Schoenfeld residuals of each covariate introduced in the model.

The inspection of potential confounders was assessed among the following variables: age, sex, marital status, education, occupation, smoking and drinking habits, BMI, health conditions (Angina, Myocardial Infarction, Congestive Heart Failure, Cardiac Arrhythmia, Hypertension, Diabetes,

Stroke, Parkinsonism, Distal Symmetric Neuropathy of Lower Limbs), comorbidity, and depressive symptomatology.

Results

At the 1992 baseline, among the 5632 subjects 1010 (17.8%) did not participate at the survey. Complete baseline information on all characteristics investigated in this study (socio-demographics, health habits and conditions) was available for 3439 subjects. The prevalence ratio of "poor vitality" was 3.6% versus 17.4% of the "high vitality". The low vitality group was significantly older, less educated; about 18% had heart failure, 33% stroke, 18% distal symmetric neuropathy of lower limb, 26% Parkinsonism and 83% presence of depressive symptomatology, compared to 2%, 3%, 5%, 1% and 25% of the high vitality group, respectively (table 1.).

Table 1. Distribution of socio-demographic, health habits and conditions at the baseline. Weighted data, ILSA 1992

	High vitality (n=600)	Medium vitality (n=2,715)	Low Vitality (n=124)	p value
Socio-demographic variables (%)				
Sex (males)	49.6	43.1	31.5	*** (1)
Age (mean±sd)	69.5±4.4	72.5±5.5	78.1±4.4	*** (2)
Education (elementary school or less)	40.7	78.4	90.0	*** (1)
Marital status (married)	69.8	60.7	36.6	*** (1)
Occupation (manual or farmer or housewife)	38.6	63.3	80.4	*** (1)
Health habits (%)				
Smoking habit (smoker or ex-smoker)	57.1	43.4	30.9	*** (1)
Alcohol habit (daily wine drinker)	76.7	79.3	77.5	n.s. (1)
BMI (mean±sd)	26.6±0.2	27.2±0.1	26.4±0.6	n.s. (3)
Health conditions (%)				
Arrhythmia	28.6	26.2	23.3	n.s. (1)
Angina	9.7	7.3	5.7	n.s. (1)
Myocardial infarction	7.6	8.4	9.5	n.s. (1)
Congestive Heart failure	2.2	7.3	17.5	*** (1)
Hypertension	59.3	66.0	61.3	* (1)
Diabetes	12.4	13.7	17.3	n.s. (1)
Stroke	2.9	6.3	32.4	*** (1)
Distal symmetric neuropathy of lower limbs	4.9	8.1	18.2	*** (1)
Parkinsonism	0.7	2.8	25.7	*** (1)
Comorbidity (2+ conditions)	35.2	42.0	56.7	*** (1)
Depressive symptomatology	25.6	39.6	82.6	*** (1)

1. χ^2 test for trend

2. Welch's ANOVA (assumption of homoscedasticity violated); not weighted data

3. GLM (assumption of homoscedasticity satisfied)

*** = $p < 0.0001$; ** = $p < 0.001$; * = $p < 0.05$ ns= not significant

Predictors of mortality

During the four-years follow-up period, 3010 were found alive, 710 were found dead and 891 were lost to follow up. This latter group was mainly composed by females, had a higher prevalence ratio of depressive symptomatology although a lower prevalence ratios of all health conditions (data not shown).

In table 2 main characteristics by vital status are shown. Significant associations were found with BMI and all health conditions (except hypertension), depressive symptomatology, cognitive impairment and ADL disability were more prevalent among the deceased group. At follow-up, 14.7% of deceased subjects had a low vitality level at baseline, versus a 2.1% of the alive subjects.

Table 2. Distribution of socio-demographic, health habits and conditions by vital status. ILSA, weighted data.

	Alive (n=3,010)	Deceased (n=719)	p value
Socio-demographic variables (%)			
Sex (females)	56.5	50.6	0.0041
Age (mean±sd)	71.7±5.5	75.7±5.0	<.0001
Marital status (married)	61.8	53.8	0.0002
Education (≤elementary)	70.4	74.0	ns
Occupation (manual or housewife)	59.8	58.3	ns
Health habits (%)			
Smoking status (smoker or ex)	44.3	47.4	ns
Wine drinker (daily)	77.7	75.5	ns
BMI (%)			
Normal	23.1	27.5	<.0001
Underweight	4.1	10.6	
Overweight/obese	72.8	61.9	
Health conditions (%)			
Arrhythmia	24.0	28.0	0.0411
Angina	7.2	7.7	ns
Heart failure	5.1	15.5	<.0001
Myocardial Infarction	7.6	11.2	0.0030
Hypertension	62.8	58.2	0.0334
Diabetes	12.2	16.9	0.0012
Stroke	5.8	14.0	<.0001
Distal Symmetric Neuropathy of Lower Limbs	6.3	10.9	<.0001
Parkinsonism	2.3	7.9	<.0001
Comorbidity (2+ pathology)	36.8	52.1	<.0001
Depressive symptomatology	35.5	53.9	<.0001
MMSE (mean±sd)	0.91±0.10	0.86±0.11	<.0001
ADL disability (mild, moderate or severe)	28.9	55.8	<.0001

Vitality level			<.0001
high	19.0	8.0	
medium	78.9	77.4	
low	2.1	14.7	

To investigate to what extent lack of vitality accounted for survival, after taking into account underlying health habits and conditions, we constructed 3 hierarchical models: the first model including socio-demographic variables, the second model comprising the health habits and conditions and last model including depressive symptomatology.

The Hazard Ratios, estimated by the Cox proportional-hazards model, are shown in table 4. Individuals who had the highest risk of all-cause mortality were those who belonged to the low vitality group, with more than three-fold increase. Significant relative risks were observed with age, male sex and being underweight. Among the investigated conditions, association with mortality was found for heart failure, with more than two-fold increase and diabetes with 79% increase, and subjects with depressive symptomatology were about 60% more likely to die.

Table 4. Hazard ratio and 95% CI of death, hierarchical models. ILSA, data not weighted.

	Model 1		Model 2		Model 3	
	HR	95% CI	HR	95% CI	HR	95% CI
<i>Medium vitality</i>	1.39	0.92-2.11	1.27	0.83-1.94	1.22	0.80-1.87
<i>Low vitality</i>	3.60	1.59-8.17	4.03	1.71-9.52	3.20	1.35-7.60
Age (continuous)	1.11	1.09-1.14	1.10	1.07-1.13	1.10	1.07-1.12
Sex (females)	0.65	0.48-0.87	0.72	0.50-1.01	0.65	0.45-0.93
BMI (underweight)			2.17	1.44-3.27	2.18	1.45-3.29
BMI (overweight/obese)			0.75	0.57-0.99	0.77	0.58-1.02
Heart failure			2.64	1.84-3.77	2.50	1.75-3.59
Diabetes			1.76	1.25-2.48	1.79	1.27-2.52
Depressive symptomatology					1.58	1.22-2.03

Model 1: including sociodemographic variables (marital status, education and lifetime occupation).

Model 2: including sociodemographic variables, health habits and conditions (smoking status, alcohol consumption, BMI, arrhythmia, angina, heart failure, myocardial infarction, diabetes, stroke, distal symmetric neuropathy of lower limbs, parkinsonism and comorbidity).

Model 3: including sociodemographic variables, health habits and conditions, and depressive symptomatology.

All models are stratified for hypertension

CONCLUSIONS

In our study the term "healthy aging" is based on both physical and cognitive functioning and people belonging to the low vitality group (lowest quartile of cognitive functioning and being dependent in all ADL's) are those at higher risk of mortality. An interesting finding is the two-fold increase in mortality for the underweight elderly, which could reflect a malnutrition effect more prevalent among cognitive impaired subjects. The inspection of the characteristics associated to mortality provide some insights into which life-course preventive measures could be implemented, possibly addressed to the impaired functioning.

BIBLIOGRAPHY

1. Rowe JW and Kahn RL. Successful aging. Ed. by Rowe JW and Kahn RL, Pantheon Books, NY, 1998.
2. Maggi S, Zucchetto M, Grigoletto F, et al, for the ILSA group. The Italian Longitudinal Study on Aging (ILSA): design and methods. *Aging Clin Exp Res* 1994; 6: 464-473.
3. Folstein MF, Folstein SE, Mc Hugh PR. Mini Mental State: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; 12:189-198.
4. Brink TL, Yesavage JA, Lum O, Heersema PH, Adey M, Rose TL. Screening tests for geriatric depression. *Clinical Gerontologist*. 1982; 1:37-43.
5. Katz S et al. Studies of illness in the aged. The Index of ADL. A standardized measure of biological and physiological function. *JAMA*. 1963; 185:914.
6. Lawton MP, Brody IAMB. Assessment of older people: self maintaining and instrumental activities of daily living. *Gerontologist*. 1969; 9: 179-186.
7. The Italian Longitudinal Study on Aging Working Group. Prevalence of chronic diseases in older Italians: comparing self-reported and clinical diagnoses. *Int J Epidemiol*. 1997, 26: 995-1002.