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Original Study

Development of a Healthy Aging Score in the Population-Based Rotterdam Study: Evaluating Age and Sex Differences



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ABSTRACT

Objectives: To develop a healthy aging score (HAS), to assess age and sex differences in HAS, and to evaluate the association of the HAS with survival. *Design:* Prospective population-based cohort. *Setting:* Inhabitants of Ommoord, Rotterdam, The Netherlands. *Participants:* A total of 1405 men and 2122 women, mean (standard deviation) age 75.9 (6.4) years.

Main measures: We included 7 domains in the total score of HAS: chronic diseases, mental health, cognitive function, physical function, pain, social support, and quality of life; each scored 0, 1, or 2 in each domain. A total score (range 0–14) was constructed and was assessed continuously and in tertiles (13–14: healthy aging, 11–12: intermediate aging, 0–10: poor aging). Sex-specific change in the mean HAS was computed for the age categories of 65–69, 70–74, 75–79, 80–84, and \geq 85 years. The association between HAS and mortality was assessed with Cox proportional hazards models.

Results: Mean follow-up was 8.6 (3.4) years. Men had poorer scores in the chronic disease domain than women. However, women had poorer mental health, worse physical function, more pain, and lower quality of life compared with men. The prevalence of healthy aging was higher in men (n = 396, 28.2%), than in women (n = 526, 24.8%). The mean (standard deviation) HAS was 11.1 (2.2) in men and 10.7 (2.3) in women. Mean HAS was higher in men than in women for all age categories. The β for change in mean HAS across the 5 increasing age categories was -0.55 (-0.65 to -0.45) in men and -0.65 (-0.73 to -0.57) in women. The age-adjusted hazard ratio per unit increase in HAS with mortality was 0.86 (0.83-0.89) in men, and 0.89 (0.87-0.91) in women.

Oscar H. Franco and Maryam Kavousi contributed equally to this work.

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Conclusions: Levels of HAS were lower in women compared with men, in all age categories. The HAS declined with increasing age for both sexes, albeit slightly steeper in women. The HAS was strongly associated with mortality in both sexes. A better understanding of population healthy aging and sex differences in this regard could aid to implement strategies for sustainable healthcare in aging populations. © 2016 AMDA – The Society for Post-Acute and Long-Term Care Medicine.

Our population is aging.^{1,2} Between 2008 and 2040, the proportion of people aged 65 years and older is projected to increase from 7% (506 million) to 14% (1.3 billion) of the world's population.³ In addition, the number of oldest old (aged 80 years and over) is expected to increase by 233% in this time period.³ This demographic shift can be explained by better living standards and improvements in both preventive and curative healthcare.⁴ Simultaneously, the main causes of death have shifted from infectious diseases toward age-related chronic diseases.⁵ These observed trends have led to aging, and particularly healthy aging, to become one of the top public health challenges,^{6,7} and resulted in the first World Report on Aging and Health from the World Health Organization in 2015.⁸

Focusing on health as a multidimensional state could facilitate prevention and treatment strategies.⁹ Theoretical frameworks have been formulated,^{10–14} and various operational definitions have been applied to populations.^{15,16} For example, Rowe and Kahn introduced a model for successful aging that included avoiding disease and disability, high cognitive and physical function, and engagement with life.^{13,14} This model has been critiqued for being too unidimensional, with its strong focus on physiological constructs for successful aging.¹⁷ Therefore, recent applications have comprehensively included psychosocial constructs, such as mental health and self-perceived health.^{18–20} In addition, it has been suggested that continuum-based measures for healthy aging might better capture the heterogeneity of the phenotype, as opposed to the more widely adopted dichotomous approaches.^{19,21} However, to date, no consensus for the measurement of healthy aging exists.

Worldwide, women outlive men by 6 to 8 years. However, these years are often spent with more disease and disability: "men die quicker, women get sicker."^{9,22} Although the operationalization of healthy aging measures is upcoming, no studies have comprehensively assessed age and sex differences. Within the population-based Rotterdam Study, comprehensive and detailed information on subjective and objective measures, which are necessary to construct a healthy aging score, are available. In addition, the vital status of all participants has been precisely adjudicated in this cohort of middle-aged and elderly men and women. Therefore, we aimed to develop a healthy aging score (HAS) within the population-based Rotterdam Study and to assess

Scheme 1		
Definition	of Healthy	Agir

Definition of Healthy Aging Score

age and sex differences. Furthermore, for illustrative purposes, we aimed to evaluate the association of the HAS with survival.

Methods

Study Population

This study was embedded within the Rotterdam Study: a prospective, population-based cohort among subjects 55 years and older in the municipality of Rotterdam, The Netherlands. The rationale and study design have been described elsewhere.²³ The baseline examination of the original cohort was completed between 1990 and 1993 (RS-I, visit 1). In the fourth visit of RS-I (2002-2004), assessments of social support and quality of life were introduced. Therefore, the current study included all participants alive at the fourth visit of RS-I. Of the 5.008 participants available for inclusion, 1.481 were excluded due to missing data in more than 5 domains of the HAS. Hence, 1.405 men and 2.122 women were included in the current study. The Rotterdam Study has been approved by the Medical Ethics Review Board of Erasmus Medical Center and by the Ministry of Health, Welfare and Sport of the Netherlands, implementing the Wet Bevolkingsonderzoek: ERGO (Population Studies Act: Rotterdam Study). All participants provided written informed consent to participate in the study and to obtain information from their treating physicians.

Assessment of Healthy Aging Score

In line with previously defined conceptual frameworks and applications,^{10–21} we included 7 biopsychosocial domains in the development and construction of the healthy aging score. These domains involved: chronic diseases, mental health, cognitive function, physical function, pain, social support, and quality of life. In each domain, the status was graded as low (0, corresponding to a worse status within the domain), moderate (1), or high (2, corresponding to an optimal status within the domain); Scheme 1. A total score, ranging from 0 to 14 was constructed, by summing up the values of these 7 domains. An extensive description of the HAS construction can be found in Supplemental Methods 1A.

Domain	Low (Score of 0)	Moderate (Score of 1)	High (Score of 2)	
Chronic diseases*	>1 disease, "multimorbidity"	1 disease	0 diseases	
Mental health CES-D	Score of 23 to 60	Score of 17 to 22	Score of 0 to 16 (no depressive symptoms)	
Cognitive functioning MMSE	Score of 0 to 20	Score of 21 to 25	Score of 26 to 30	
Physical functioning bADL/iADL	Severe disability on either bADL or iADL	Everything in between	Mild disability on bADL and iADL	
Pain	(Very) severe pain in hands, knees, hips or back for at least 1 activity	Everything in between	No or mild pain in hands, knees, hips and back in all activities	
Social support	'Agree' in 0–2 statements	'Agree' in 3-4 statements	'Agree' for all 5 statements	
QoL	Low QoL on 5–8 items	Low QoL on 1–4 items	High QoL on all 8 items	

bADL, basic activities of daily living; CES-D, Center for Epidemiologic Studies Depression Scale; iADL, instrumental activities of daily living; MET, metabolic equivalent; MMSE, Mini-Mental State Examination; QoL, quality of life.

*Chronic diseases included myocardial infarction, revascularization, heart failure, stroke, Parkinson disease, diabetes mellitus, chronic obstructive pulmonary disease, cancer, and chronic kidney disease.

Assessment of All-Cause Mortality

To ascertain death and cause of death for all participants of the Rotterdam Study, mortality data was obtained via complementary approaches.²³ Data sources included the central registry of the Municipality of Rotterdam, records from collaborating general practitioners, and information from follow-up rounds. The Central Registry of Genealogy of The Netherlands was consulted when the vital status of participants were missing. All-cause mortality was available up to October 1, 2015.

Assessment of Covariates

The following socioeconomic and health behavior factors were considered for inclusion as covariates in multivariable adjusted models examining the association of HAS with mortality: baseline age, education, household income, marital status, ethnicity, smoking, physical activity, dietary habits, alcohol intake, and waist-hip ratio. A description of the data collection procedure and coding of each covariate is provided in Supplemental Methods 1B.

Statistical Analyses

Participant characteristics were described using means [standard deviations (SD)] and proportions. All analyses were stratified for sex, given that sex-based differences in health conditions, functioning, behavior, and social relations may differentially affect patterns of healthy aging.⁸

Characteristics of Healthy Aging Score

The correlation between the domains was assessed with Pearson correlation coefficients and was considered high if it was ≥ 0.70 .²⁴ Thereafter, the prevalence of low, moderate, and high categories for each of the 7 included domains was assessed. Differences between men and women were tested using the χ^2 statistic.

The healthy aging score was constructed from the 7 domains as a score ranging from 0 to 14. The HAS was assessed continuously as well as in tertiles. The distribution of HAS on a continuous scale was plotted using histograms. We calculated the mean HAS for men and women and additionally adjusted the mean HAS for age using linear regression analysis. We further evaluated and plotted the change of the mean HAS, stratified for age categories (65–69, 70–74, 75–79, 80–84, and ≥85 years) and sex. To define HAS tertiles, the cut-offs 12 and 10 were used for both men and women. Based on the tertiles, participants were categorized into 3 categories; healthy aging (a score of 13–14), intermediate aging (a score of 11–12), and poor aging (a score of 0–10). Differences between men and women were tested using the χ^2 statistic.

Survival Analyses

In secondary analyses, the association between HAS with mortality was assessed. However, this was only done for illustrative purposes, given that the HAS was developed to assess health status' that extend beyond life or death.

The proportional hazards assumption was tested by evaluating log minus log survival plots. We developed 2 Cox proportional hazards models; an age-adjusted model (model 1) and a model further adjusted for covariates (model 2). To build model 2, we first selected the covariates that were associated with both the exposure (HAS) and the outcome (mortality) with a *P* value below $2.^{25}$ Thereafter, using the likelihood ratio test, covariates were eliminated from the multivariable model via a backward selection approach if their contribution to the model was not significant. Hence, model 2 included the covariates: age, smoking (current vs never), smoking (former vs never),

dietary habits, physical activity, and waist-hip ratio. This model could be considered a conservative model given that these covariates antecedently affect the domains of HAS or could be an intermediate factor in the association between HAS with mortality. We also developed survival plots for tertiles of HAS for men and women. Considering the borderline significant interaction term for HAS*sex (P = .082) and significant interaction term for HAS*age (P = .006), we calculated age and sex-specific hazard ratios (HRs) for HAS with mortality. HRs between the youngest and oldest age categories were compared using a test of interaction.²⁶

Supplementary Analyses

To reduce bias because of selective dropout of less healthy participants, values of the 7 domains and covariates were imputed for everybody alive at the start of the fourth visit of the Rotterdam Study and had values observed in at least 2 domains. None of the imputed variables had more than 35% missing data. Values were imputed using fully conditional specification (Markov chain Monte Carlo method) with a maximum iteration number of 20.

In sensitivity analyses, we compared the descriptive characteristics for the observed data to the data after multiple imputations. Moreover, we performed a comparison between the included participants in the study and the ones excluded. To evaluate the influence of choosing tertiles for categorical analyses of HAS, a second approach using the Youden Index was used. The Youden Index maximizes the sum of specificity and sensitivity, to attain an optimal cut-off value of healthy vs nonhealthy aging for mortality. In this scenario, having a score of 12 to 14 was categorized as healthy aging, whereas the remainder of the score was divided into 2 equal groups (a score of 10 to 11 for intermediate aging and a score of 0 to 9 for poor aging). Further sensitivity analyses included ruling out the possibility of reversed causality by excluding participants who died within the first 3 years after baseline and a complete case analysis.

All analyses were performed using IBM SPSS statistics v 21.0 and R statistical software (http://www.r-project.org) v 3.3.1. Associations with a *P* value below .05 were considered statistically significant.

Results

Among the total population of 3527 participants, 1405 (39.8%) were men and 2122 (60.2%) were women (Table 1). Mean (SD) age was 75.3 (6.0) years and 76.3 (6.6) years in men and women, respectively. Nearly all participants (>97%) were of Caucasian descent. Two hundred seventy-one men (19.3%) completed higher vocational education or university, whereas in women, this number was 103 (4.8%). Furthermore, 1124 men were married or living with a partner (80.0%), compared with 919 women (43.3%).

Characteristics of Healthy Aging Score

The correlation between the separate domains ranged from 0 (correlation between chronic disease and social support) to 0.55 (correlation between mental health and quality of life) (Supplemental Table 1). Table 2 provides the prevalence of the 3 categories (low, moderate, and high) for the 7 domains included in the healthy aging score. Compared with men, more women were in the high category for absence of chronic disease (41.2% in women vs 31.6% in men). However, fewer women were in the high category for adequate mental health (82.2% in women vs 91.1% in men), good physical function (72.9% in women vs 79.5% in men), absence of pain (44.3% in women vs 61.1% in men), and good quality of life (52.2% in women vs 61.2% in men). These differences did not change after adjusting for age. The mean HAS was 11.1 (2.2) and 10.7 (2.3) in men and women, respectively, and remained the same after adjusting for age. The distribution of HAS for men and women was

276.e4

Table 1

Characteristics of the Study Population

Characteristics Men (n = 1405) Women (n Age, years 75.3 (6.0) 76.3 (6.6) Education, n (%) 756 (11.1) 417 (19.7)	
Education, n (%))
Primary education 156 (11.1) 417 (19.7	
	7)
Lower/intermediate general or 440 (31.3) 1070 (50.4	4)
lower vocational education	
Intermediate vocational or higher 538 (38.3) 532 (25.1	1)
general education	
Higher vocational education 271 (19.3) 103 (4.8))
or university	
Household income, in/1000 2.6 (1.1) 2.2 (1.0))
Marital status, n (%)	
Never married 36 (2.6) 181 (8.5))
Married, living together 1124 (80.0) 919 (43.3	3)
Widowed, divorced 245 (17.4) 1022 (48.2	2)
Ethnicity, Caucasian 1372 (97.7) 2088 (98.4	4)
BMI, kg/m ² 27.0 (3.5) 27.8 (4.6))
Waist-hip ratio 0.98 (0.07) 0.86 (0.07)	7)
Smoking, n (%)	
Current 241 (17.1) 281 (13.2	2)
Former 1040 (74.0) 866 (40.8	8)
Never 124 (8.9) 975 (46.0	0)
Physical activity, MET-hours/week 78.6 (43.6) 94.4 (46.0	0)
Dutch Healthy Diet Index, score 0–100 42.3 (9.7) 47.8 (9.8))
Alcohol intake, g/day 15.9 (16.7) 6.9 (9.7))

BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; MET, metabolic equivalents; MI, myocardial infarction; n, number. Values are numbers (percentages) or mean (SD) unless stated otherwise. Decimal values for numbers, originating from the combination of multiple imputation sets, were rounded to integer values.

similar (Figure 1). However, the proportion of favorable healthy aging scores was higher in men than in women. When looking at HAS in tertiles, the proportion of healthy agers was higher in men than in women (Supplemental Table 2). Furthermore, the mean HAS decreased linearly across age categories, with borderline significant evidence for parabolic decline in both men (P = .088) and women (P = .059) (Figure 2). The β for change in mean HAS across the 5 age categories was steeper in women [-0.65 (-0.73 to -0.57)] compared with men [-0.55 (-0.65 to -0.45)], but did not differ significantly by sex (P = .12). Within age categories, the mean HAS was significantly higher in men aged 75–79 years (P = .041) and aged 80–84 years (P = .008) compared with women in the same age category.

Survival Analyses

Overall, 793 men died during mean 8.1 years (SD 3.6) years of follow-up, and 1002 women died during mean 8.9 (SD 3.3) years of follow-up. Whereas cumulative survival in men decreased from the start of follow-up, and the decline was gradual over time, in women cumulative survival remained high and dropped more steeply toward



Fig. 1. Distribution of the healthy aging score for men and women.

the end of follow-up in age-adjusted model 1 (Figure 3A and B). This was the same for survival plots adjusted for covariates in conservative model 2 (Supplemental Figure 1A and B). For model 1 and model 2, the HRs per unit increase in HAS with mortality were 0.86 (0.83–0.89) and 0.87 (0.83–0.90) respectively in men, and 0.89 (0.87–0.91) and 0.90 (0.87–0.92) in women. Analyses were repeated for age and sexstrata (Supplemental Table 3). In women, the HR of the youngest age category was stronger than the HR of the oldest age category (P = .02), whereas no differences were observed in men (P = .77). To further explore this differential effect on mortality, the proportions of low, moderate, and high scores within each of the 7 HAS domains were stratified for sex and age groups (Supplemental Table 4). For the domains mental health and pain, fewer women were in the high category compared with men, and this remained significantly different for all age categories.

Supplementary Analyses

The observed data and the data after multiple imputation did not substantially differ (Supplemental Tables 5 and 6). Moreover, we compared participants included in the study to those excluded. The included participants were younger, slightly higher educated, and had a lower proportion of prevalent chronic disease compared with the excluded participants (Supplemental Table 7).

Using the Youden Index, the optimal cut-off for healthy vs nonhealthy aging was 12. Analyses were repeated using this optimal cutoff for defining the healthy aging categories. The proportion of healthy agers was now 50.9% in men and 44.1% in women. The survival analysis results remained similar to the previous categorization based on tertiles of HAS (Supplemental Figure 2A and B).

Finally, in complete case analyses and in analyses excluding people who died within the first 3 years of follow-up, the direction,

Table	2
Table	4

	Men (n = 1405)		Women (n = 2122)			
	Low (0)	Moderate (1)	High (2)	Low (0)	Moderate (1)	High (2)
Chronic disease	452 (32.2)	508 (36.2)	445 (31.6)	427 (20.1)*	820 (38.7)	875 (41.2)*
Mental health	54 (3.9)	70 (5.0)	1281 (91.1)	172 (8.1)*	204 (9.7)*	1746 (82.2)*
Cognitive function	35 (2.5)	182 (13.0)	1188 (84.5)	81 (3.8)	292 (13.8)	1749 (82.4)
Physical function	54 (3.8)	234 (16.7)	1117 (79.5)	116 (5.5)	459 (21.6)*	1547 (72.9)*
Pain	90 (6.4)	457 (32.5)	858 (61.1)	312 (14.7)*	870 (41.0)*	940 (44.3)*
Social well-being	124 (8.8)	369 (26.3)	912 (64.9)	184 (8.6)	508 (24.0)	1430 (67.4)
Quality of life	78 (5.6)	467 (33.2)	860 (61.2)	176 (8.3)	837 (39.5)*	1109 (52.2)*

Values are numbers (percentages). Decimal values, originating from the combination of multiple imputation sets, were rounded to integer values.

*Difference between men and women, per category of the particular domain, statistically significant at $\alpha < 0.001$.

[†]Difference between men and women, per category of the particular domain, statistically significant at $\alpha < 0.05$.



HAS=healthy ageing score.

Fig. 2. Sex-specific change of the healthy aging score across age groups.

magnitude, and significance of the association between continuous HAS and mortality remained the same.

Discussion

Considering the growing importance of healthy aging as a key public health challenge, we developed a healthy aging score consisting of 7 biopsychosocial domains in the population-based Rotterdam Study. Overall, we found that the HAS was lower in women in all age categories. With regard to the specific domains, more men had multimorbidity (eg, more than 1 chronic disease) compared with women, whereas women had worse mental health, more pain, more disability, and a lower quality of life compared with men. The HAS declined with increasing age, albeit slightly steeper in women. In addition, a higher HAS was strongly associated with lower mortality in both sexes. Whereas the strength of this effect was stable across age groups in men, the association was less strong in older women compared with younger women.

Methodological Considerations

This study developed a HAS in a large population-based sample and explored age and sex differences in great detail. Strengths of our study include the large sample size, availability of detailed information that led to a comprehensive definition for HAS; incorporating physiological constructs, social support, as well as quality of life. The latter 2 have proven to be of particular importance in the elderly, as their subjective attitudes toward health may differ significantly from what is measured objectively.¹⁷ In addition, the multidimensionality of the score allowed us to capture other aspects of healthy aging that have not been explicitly included in the score. For example, we would expect to capture the burden of osteoporosis and fractures in the domains of pain and physical function. Another strength of our study is that our defined healthy aging score is an interesting tool for clinical settings, for several reasons. Importantly, our defined healthy aging score is relatively easy and inexpensive to measure because all domains can be measured using questionnaires. In addition, the 0-14 continuous scale makes it easier to detect changes in healthy aging over time, compared with a conventional dichotomous successful vs nonsuccessful aging approach. Finally, the comprehensive definition of HAS allows for directed interventions targeting the domains that require attention.

Besides these strengths, the limitations also merit careful consideration. Unhealthy persons were less likely to be included in the current study, compared with the more healthy agers. Therefore, as inherent to all cohort studies, the possibility of health selection bias



Fig. 3. (A) Age-adjusted survival plots for healthy aging score in tertiles, for men. (B) Ageadjusted survival plots for healthy aging score in tertiles, for women. The yellow line indicates healthy agers (score of 13–14), the green line intermediate agers (score of 11–12), and the blue line poor agers (score of 0–10). The HRs for age-adjusted model 1, for healthy and intermediate aging, compared with poor aging, were 0.42 (95% CI 0.34–0.52) and 0.63 (95% CI 0.53–0.74) for men, and 0.44 (95% CI 0.36–0.54) and 0.70 (95% CI 0.61–0.82) for women, respectively. Cum survival, cumulative survival; FU, follow-up.

cannot be ruled out. Moreover, nearly all participants were of Caucasian descent. Therefore, the generalizability of our findings may be hampered. Furthermore, severity of disease was not included as a separate domain. Although this could have been captured, to some extent, in the other domains of the HAS, we cannot rule out that this might have led to an underestimation of the levels of morbidity.

Furthermore, given that there is no consensus for the definition of healthy aging or uniform measurement guidelines, the cut-offs used within some of the domains and for the HAS were arbitrary (eg, a score of 0, 1, or 2). Although we could have lost information by categorizing continuous measures, such as the Mini-Mental State Examination for the domain of cognitive function, it prevented the use of complex statistical modelling strategies. Hence, the HAS in its current form allows for straightforward interpretation from a clinical perspective.

Each domain was given an equal weight in the total score. Although we can argue that there is sufficient evidence from literature for inclusion of each of these domains, we cannot judge whether or not all should receive the same weight. If one would want to assess weights of specific domains, a multivariable prediction rule should be created, with an outcome that can serve as an adequate gold standard measure for healthy aging. Because there are different working definitions of healthy aging and various perspectives to which underlying construct is being measured, there is no consensus on the best gold standard for healthy aging measurement tools. Furthermore, the most appropriate gold standard may depend on the objectives and context in which healthy aging is measured. A possible gold standard could be resilience and is the opposite of vulnerability: the underlying construct of frailty.^{10,27,28} How much the concepts of healthy aging and frailty overlap, remains to be elucidated.²⁹ Others have proposed vitality³⁰ or positive health (eg, flourishing)³¹ as underlying constructs of healthy aging. In our study, we did not create such multivariable prediction rule. However, we did assess that the correlation between the domains did not exceed 0.55. Hence, this provides assurance that the overlap between the domains was sufficiently small.

Results in Relation to Other Studies

Both men and women scored high on the healthy aging score (eg, a mean score of above 10 on a scale from 0 to 14). Approximately one-third to one-half of the participants were classified as healthy agers, depending on the cut-off used. This finding is in line with a review summarizing 28 studies, in which the mean reported proportion of successful agers was 35.8% (SD 19.8).¹⁶ In contrast, the large variation in measurement scales among studies resulted in large variation in proportion of successful agers in a second review that varied between 1% and 90%.¹⁵

Sex Differences in Healthy Aging

We observed numerous sex differences in HAS at all ages. Women had a lower proportion of healthy agers compared with men, which was in line with a similar study from Assmann et al.¹⁸ Despite women living longer than men, their extended life expectancy was accompanied by poorer scores in more domains, including worse mental health, more pain, and more disability. Given the weaker relation of these domains with mortality, this may also explain why in older women the association between the HAS and mortality became weaker. These findings are in line with the theory of the "male-female disability-survival paradox," which describes that women live longer than men but with more disability.^{32,33} To explain this paradox several explanations have been proposed. Among others, sex-specific gene expression and differential effects of sex hormones can be related to this paradox.³⁴ Another explanation encompasses behavioral differences between the sexes, in such that men and women differ with regard to their symptom perception and attribution,³⁵ patient delay for consulting healthcare professionals,³⁵ and over reporting of worse health outcomes in women.^{33,36} Also, less pathognomonic symptom presentation in women may lead to diagnostic delays and less timely treatment initiation, which could result in more severe consequences in terms of long-term disability.³⁴ It may also be possible that men have greater severity of disease, resulting in higher mortality.³³

Conclusions

In the current study, we developed a comprehensive score for healthy aging in a population-based study. The score included biological, psychological, and social domains, most of which were easy and inexpensive to measure with questionnaires. We found that levels of the HAS in this elderly population were high and that considerable sex and age differences occurred. These included lower levels of HAS and steeper decline across age categories in women and the differential importance of the different health domains between the sexes.

Future research is needed to further understand which factors are associated with healthy aging and which interventions are effective for maintaining, improving, and recovering healthy aging. In this regard, a sex-sensitive approach needs to be adopted. In addition, more research is needed to assess changes in healthy aging over time, within individuals and between populations. From a conceptual perspective, a better understanding of which gold standard underlying constructs should be used, could aid the establishment of a strong contemporary field of healthy aging research.

The importance of keeping people healthy throughout their life course is evident, particularly when taking into account that our population is aging. This study adds to the body of research by expanding the existing theoretical frameworks and incorporating experiences from other operational definitions, to define a practical application. The findings of our study have implications for researchers, clinicians, and policy makers, for all of whom a sexsensitive perspective is essential.¹⁹ For researchers, this is an interesting tool to adopt given its theoretical and experience-based foundation. Clinicians could benefit from monitoring healthy aging in their patients over time. Finally, the measurement of healthy aging in populations could help policy makers to allocate funds to keeping people healthy.

Supplementary Data

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.jamda.2016.11.021.

References

- Oeppen J, Vaupel JW. Demography. Broken limits to life expectancy. Science 2002;296:1029–1031.
- 2. Vaupel JW. Biodemography of human ageing. Nature 2010;464:536-542.
- Kinsella K, He W. U.S. Census Bureau, International Population Reports, P95/ 09–1, An Aging World: 2008, U.S. Government Printing Office, Washington, DC, 2009.
- Riley J. Rising Life Expectancy: A Global History. Cambridge: Cambridge University Press; 2001.
- Omran AR. The epidemiologic transition. A theory of the epidemiology of population change. Milbank Mem Fund Q 1971;49:509–538.
- 6. Cutler RG, Mattson MP. The adversities of aging. Ageing Res Rev 2006;5: 221–238.
- 7. Franco OH, Kirkwood TB, Powell JR, et al. Ten commandments for the future of ageing research in the UK: A vision for action. BMC Geriatr 2007;7:10.
- 8. World Report on Ageing and Health. World Health Organization, 2015.
- Jaspers L, Daan NM, van Dijk GM, et al. Health in middle-aged and elderly women: A conceptual framework for healthy menopause. Maturitas 2015;81:93–98.
- **10.** Franco OH, Karnik K, Osborne G, et al. Changing course in ageing research: The healthy ageing phenotype. Maturitas 2009;63:13–19.
- 11. Lara J, Cooper R, Nissan J, et al. A proposed panel of biomarkers of healthy ageing. BMC Med 2015;13:222.
- Lara J, Godfrey A, Evans E, et al. Towards measurement of the Healthy Ageing Phenotype in lifestyle-based intervention studies. Maturitas 2013;76:189–199.
- 13. Rowe JW, Kahn RL. Human aging: Usual and successful. Science 1987;237: 143–149.
- 14. Rowe JW, Kahn RL. Successful aging. Gerontologist 1997;37:433-440.
- **15.** Cosco TD, Prina AM, Perales J, et al. Operational definitions of successful aging: A systematic review. Int Psychogeriatr 2014;26:373–381.
- Depp CA, Jeste DV. Definitions and predictors of successful aging: A comprehensive review of larger quantitative studies. Am J Geriatr Psychiatry 2006;14:6–20.
- 17. Martinson M, Berridge C. Successful aging and its discontents: A systematic review of the social gerontology literature. Gerontologist 2015;55:58–69.
- Assmann KE, Andreeva VA, Jeandel C, et al. Healthy aging 5 years after a period of daily supplementation with antioxidant nutrients: A post hoc analysis of the French randomized trial SU.VI.MAX. Am J Epidemiol 2015;182(8):694–704.
- Cosco TD, Stephan BC, Brayne C. Validation of an a priori, index model of successful aging in a population-based cohort study: The successful aging index. Int Psychogeriatr 2015;27:1971–1977.
- Young Y, Fan MY, Parrish JM, et al. Validation of a novel successful aging construct. J Am Med Dir Assoc 2009;10:314–322.

- Cosco TD, Stephan BC, Brayne C. (Unsuccessful) binary modeling of successful aging in the oldest-old adults: A call for continuum-based measures. J Am Geriatr Soc 2014;62:1597–1598.
- 22. Van Oyen H, Nusselder W, Jagger C, et al. Gender differences in healthy life years within the EU: An exploration of the "health-survival" paradox. Int J Public Health 2013;58:143–155.
- 23. Hofman A, Brusselle GG, Darwish Murad S, et al. The Rotterdam Study: 2016 objectives and design update. Eur J Epidemiol 2015;30:661–708.
- Searle SD, Mitnitski A, Gahbauer EA, et al. A standard procedure for creating a frailty index. BMC Geriatr 2008;8:24.
- 25. Hosmer D, Lemeshow S, May S. Chapter 5.2 Purposeful selection of covariates. Applied Survival Analysis: Regression Modeling of Time to Event Data. 2nd Ed. New York, NY: A Wiley-Interscience Publication, John Wiley and Sons inc; 2008.
- Altman DG, Bland JM. Interaction revisited: The difference between two estimates. BMJ 2003;326:219.
- Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: Evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146–M156.
- Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. SciWorld J 2001;1:323–336.

- Friedman SM, Shah K, Hall WJ. Failing to focus on healthy aging: A frailty of our discipline? J Am Geriatr Soc 2015;63:1459–1462.
- Westendorp RG, Schalkwijk FH. When longevity meets vitality. Proc Nutr Soc 2014;73:407–412.
- Westendorp RG, van Dunne FM, Kirkwood TB, et al. Optimizing human fertility and survival. Nat Med 2001;7:873.
- Case A, Paxson C. Sex differences in morbidity and mortality. Demography 2005;42:189–214.
- 33. Oksuzyan A, Petersen I, Stovring H, et al. The male-female health-survival paradox: A survey and register study of the impact of sex-specific selection and information bias. Ann Epidemiol 2009;19:504–511.
- **34.** EugenMed, Cardiovascular Clinical Study Group, Regitz-Zagrosek V, Oertelt-Prigione S, Prescott E, et al. Gender in cardiovascular diseases: Impact on clinical manifestations, management, and outcomes. Eur Heart J 2016;37: 24–34.
- 35. Kingston A, Davies K, Collerton J, et al. The contribution of diseases to the malefemale disability-survival paradox in the very old: Results from The Newcastle 85+ study. PLoS One 2014;9:e88016.
- **36.** Kroenke K, Spitzer RL. Gender differences in the reporting of physical and somatoform symptoms. Psychosom Med 1998;60:150–155.