**Research Paper** 

## Profiles of behavioral, social and psychological well-being in old age and their association with mobility-limitation-free survival

Marguerita Saadeh<sup>1,2</sup>, Xiaonan Hu<sup>1</sup>, Serhiy Dekhtyar<sup>1</sup>, Anna-Karin Welmer<sup>1,3,4</sup>, Davide L. Vetrano<sup>1,4</sup>, Weili Xu<sup>1</sup>, Laura Fratiglioni<sup>1,4</sup>, Amaia Calderón-Larrañaga<sup>1,4</sup>

 <sup>1</sup>Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Solna, Sweden
<sup>2</sup>SWEAH, Department of Health Sciences, Lund University, Lund, Sweden
<sup>3</sup>Functional Area Occupational Therapy and Physiotherapy, Karolinska University Hospital, Stockholm, Sweden
<sup>4</sup>Stockholm Gerontology Research Center, Stockholm, Sweden

Correspondence to: Marguerita Saadeh; email: marguerita.saadeh@ki.seKeywords: mobility, survival, well-being, successful aging, older adultsReceived: January 6, 2022Accepted: July 11, 2022Published: July 18, 2022

**Copyright:** © 2022 Saadeh et al. This is an open access article distributed under the terms of the <u>Creative Commons</u> <u>Attribution License</u> (CC BY 3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

## ABSTRACT

Introduction: Successful aging is a multidimensional construct covering behavioral, social, and psychological domains of well-being. We aimed to identify well-being profiles and their association with mobility-limitation-free survival.

Methods: A total of 1488 healthy individuals aged 60+ from the Swedish National study on Aging and Care in Kungsholmen (SNAC-K) were followed-up for 15 years. Mobility limitation was defined as a walking speed <0.8m/s and vital status information was obtained from the National Cause of Death Register. Well-being profiles were derived from different behavioral, social and psychological indicators using latent class analysis among men and women. Cox and Laplace regression models were applied to examine the association with the incidence of a composite endpoint of mobility limitation or death.

Results: At baseline, three well-being profiles (i.e., worst, intermediate, best) were identified, which followed a clear gradient in all behavioral, social and psychological indicators. Compared to those in the worst profile, men and women in the intermediate profile had 27% (HR 0.73; 95% CI 0.56-0.94) and 23% (HR 0.77; 95% CI 0.59-1.00) lower hazard of developing mobility limitation/death. An even greater protective effect was seen among individuals in the best versus worst profile (HR 0.47; 95% CI 0.31-0.70 in men; HR 0.60; 95% CI 0.46-0.78 in women). Men in the intermediate and best profiles survived 1 and 3 years longer without mobility limitation, respectively; these figures were 2 and 3 years for women.

Conclusions: Better profiles of behavioral, social and psychological well-being may prolong mobility-limitationfree survival by at least one year among older adults. Our findings strengthen the evidence-base to achieve successful aging through multi-domain interventions.

## **INTRODUCTION**

Successful aging is a multidimensional construct covering behavioral, social, and psychological domains of well-being, all amenable to individual actions and public health interventions [1–4]. Even if the multifaceted understanding of older people's health and

well-being is on the rise [5], most studies still focus on single well-being domains. For example, the protective effect of lifestyle factors such as Mediterranean diet [6–8], smoking [9, 10] and leisure activity [11–14] on physical frailty and survival has been extensively explored. Studies have also shown that better social and psychological well-being are associated with a slower

decline in physical function [15], lower risk of disability [16], and longer survival [17] among older adults.

Nevertheless, none of these factors alone seems sufficient to explain the great heterogeneity in aging phenotypes, and successful aging may rather result from simultaneously adhering to several of these protective factors [18, 19]. In spite of this, few studies have addressed the complexity and multidimensionality of successful aging by accounting for the coexistence and interactions among several factors and their contribution to old-age health [15, 20–23]. This requires methodological approaches that integrate multiple interrelated indicators to identify those that are shared by groups of older adults with a given aging phenotype [24].

In this study, we used latent class analysis to detect data-driven subgroups of people with similar well-being profiles according to behavioral (diet, smoking, and physical and mental leisure activities), social (social participation, connections, and support) and psychological (life satisfaction, positive and negative affect) well-being indicators, as defined by the Centers for Disease Control and Prevention (CDC) [25]. Given that men and women tend to behave differently on several well-being factors, we performed our analyses stratified by sex. For instance, women are more likely to engage in protective health behaviors (e.g., healthy diet, non-smoking, routine physical checkups), participate in social events and report higher life satisfaction [26, 27], while men tend to be more physically active, feel less lonely and report better psychological well-being, in general [15, 26, 28, 29]. Men and women have also different healthy life expectancies [30].

Most studies looking at indicators of well-being in old age have focused on single outcomes such as frailty, disability or death [31, 32]. Unlike previous studies, we created a mobility-survival aggregate endpoint to convey the importance of not only living longer but also healthier, in consonance with the widespread claim of adding years to life and life to years [33]. Mobility decline precedes disability and premature death, and is therefore considered an optimal early indicator of physical function decay among older adults [34].

The specific aims of this study were: 1) to identify distinct well-being profiles among men and women separately, by using latent class analysis; 2) to determine which of these profiles are associated with the greatest benefit in terms of mobility-limitation-free survival; and 3) to quantify these potential benefits in absolute terms by calculating differences in median age at onset of mobility limitation or death across profiles.

## **MATERIALS AND METHODS**

#### **Study population**

Data were gathered from the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K; https://www.snac-k.se/), an ongoing population-based study. SNAC-K includes a random sample of adults aged 60 years or older living at home or in institutions in the Kungsholmen district of Stockholm, Sweden, between 2001 and 2004. A random sample of individuals from 11 age cohorts (ages 60, 66, 72, 78, 81, 84, 87, 90, 93, 96 and ≥99 years) were invited to participate in the study. The baseline SNAC-K population included 3363 individuals (73.3% participation rate) who have been followed up regularly: every six years for the young-old cohorts (<78 years) and every three years for the older cohorts ( $\geq$ 78 years). At each study wave, physicians, nurses, and psychologists conducted extensive clinical examinations, interviews, and assessments following standard procedures. SNAC-K data has been linked to the National Patient Register and the Swedish Cause of Death Register to obtain information on medical history and vital status.

This study included data from baseline and four followups of SNAC-K, extending until December 2015 (whereas the death register coverage extended until December 2016). Out of the 3363 participants from SNAC-K baseline, we first excluded 322 individuals (9.6%) with a definite or questionable dementia diagnosis according to the Diagnostic and Statistical Manual of Mental Disorders (4th edition) and 55 individuals (1.8% of the remaining sample) with a Mini-Mental State Examination (MMSE) score <24 because of the limited reliability of their self-reported exposures. We further excluded 704 individuals (23.6% of the remaining sample) with mobility limitation at baseline, i.e., walking speed <0.8 meters per second (m/s), according to an established clinical cut-off [35]. Finally, we excluded 794 individuals (34.8% of the remaining sample) with missing data on any variable (42 individuals with missing data on walking speed, 301 additional individuals with >20% missing data on diet, 9 additional individuals with missing data on smoking, 9 additional individuals with missing data on social connections, 116 additional individuals with missing data on life satisfaction, 285 additional individuals with missing data on positive affect, 32 additional individuals with missing data on negative affect). After applying all exclusion criteria, 1488 functionally healthy participants remained in the study sample (Supplementary Figure 1).

SNAC-K was approved by the Swedish Ethical Review Authority in Stockholm, and written informed consent was obtained from participants or their next of kin.

#### **Outcome: mobility-limitation-free survival**

Walking speed was assessed by trained nurses, whereby participants were asked to walk 6m or 2.4m at a selfselected speed and using a walking aid if needed. The length of the walk was determined by asking participants how fast they normally walked (i.e., normal/fast walkers did the longer walk and slow/very slow walkers did the shorter walk). It was reported as meters per second (m/s), reflecting the speed for whichever length walked [15]. Mobility limitation was defined as having a walking speed below 0.8 m/s, a well-established and clinically validated cut-off [15, 35]. Information on death date was obtained from the National Cause of Death Register hosted and updated annually by the Swedish National Board of Health and Welfare, and linked to SNAC-K data through the personal identification number assigned to Swedish residents.

A composite endpoint, considered to be an indicator of mobility-limitation-free survival, was operationalized by taking into account the time from study entry until the development of mobility limitation (i.e., walking speed <0.8m/s) or death, whichever occurred first.

#### Exposures

#### Behavioral well-being

#### Mediterranean diet

Usual dietary intakes were assessed using a validated self-administered 98-item semi-quantitative food frequency questionnaire (SFFQ). Participants were asked to report their average intake frequency of each food and beverage over the past 12 months on a fixed 9-level scale ranging from never to  $\geq 4$  times per day. Zero imputation was applied to replace SFFQ missing items [22]. This is considered a reasonable technique to use with the FFQ, especially for those foods that are not eaten frequently and are thus likely to represent a null consumption [36]. Frequencies were converted into daily consumption and the energy intake was calculated by multiplying these frequencies by a portion size value and by the energy content, based on a food composition database from the National Food Administration using MATs software Version 4.03 (Rudans Lättdata, Västerås, Sweden) [37]. A score indicating the degree of adherence to Mediterranean Diet (MDS: range 0-9) [22] was calculated according to the formula proposed by Trichopoulou et al. [38]. The score was adjusted for total energy intake using the residual method [39]. We further categorized MDS into low, moderate and high adherence according to its tertiles.

#### Smoking

Information was obtained from baseline data and smokers and former smokers were asked how long they

had smoked and the number of cigarettes smoked per day. Former smokers were also asked at what age they had stopped smoking. We further categorized smoking into current, former and never smokers.

#### Physical and mental leisure activities

Participants were asked to specify the type and frequency (i.e., monthly, weekly, less frequently, never) of the leisure activities they regularly engaged in. We grouped the reported activities into physical, mental, and social according to the category they predominantly belonged to, following a procedure described elsewhere [40]. The scores for each type of activity were standardized (i.e., z-scores) based on the baseline mean and standard deviation and were further categorized into low, moderate and high levels according to their tertiles.

Physical leisure activities included: gardening, hiking in the forest/pick berries or mushrooms, hunting/fishing, doing home repairs, and carrying out light exercise (e.g., walking along roads/in parks, walking in the woods, short bicycle rides, light aerobics, golf) or moderate to intense exercise (e.g., jogging, long power walks, heavy duty gardening, long bicycle rides, high intensity aerobics, long distance ice skating, swimming, ball sports other than golf, or other similar activities). Mental leisure activities included: using the internet/playing computer games, painting/drawing/working with clay/ pottery, carrying out car or mechanical repairs, and reading books.

## Social well-being

#### Social leisure activities (i.e., social participation)

Based on the same procedure described above, the following activities were identified: playing a musical instrument, listening to music, going to sports events, participating in study circles/courses, attending church/ revival meetings, participating in volunteer work, going to restaurants/pubs/cafés, dancing, watching TV, playing chess/card games, going to the cinema/theatre/ concert, knitting/weaving/sewing, participating in associations/clubs, traveling, reading the newspaper, reading a magazine/journal, going to the bingo and museum/art exhibition. Scores were standardized and further categorized into low, moderate and high according to tertiles.

#### Social connections

Participants were asked about their marital status, cohabitation status, parenthood, friendships, and the frequency of direct or remote contacts with parents, children, relatives, neighbors, and friends [15, 41]. Each of these measures were standardized (i.e., z-scores) based on the baseline mean and standard deviation and a global score was obtained by averaging all z-scores. We further categorized social

connections into low, moderate and high levels according to tertiles.

#### Social support

Participants were asked about the satisfaction concerning their contacts with subjects from their social network, perceived material and psychological support, sense of affinity with potential associations, relatives, and residence area, and feeling part of a group of friends [15, 41]. Each of these measures were standardized (i.e., zscores) based on the baseline mean and standard deviation and a global score was obtained by averaging all z-scores. We further categorized social support into low, moderate and high levels according to tertiles.

#### Psychological well-being

#### Life satisfaction

Life satisfaction was assessed through the validated self-reported Life Satisfaction Index A (LSI-A) that captures five different components: zest versus apathy, resolution and fortitude, congruence between desired and achieved goals, positive self-concept, and mood tone. The LSI-A consists of 20 items with an "agree," "disagree," or "uncertain" response (range 0-100). A high score indicates that the person takes pleasure from the round of activities that constitutes his or her everyday life, regards life as meaningful and resolutely accepts life as it has been, feels he or she has succeeded in achieving his or her major goals, holds a positive self-image, and maintains happy and optimistic attitudes and mood [15, 41]. We further categorized life satisfaction into low, moderate and high levels according to tertiles.

## Negative affect

Negative affect reflects the extent to which a person feels guilt, anger, or fear, and it considers the following features: distressed, upset, scared, nervous, and afraid. Respondents were asked to report whether and to what extent they had felt in the above-mentioned affective states during the last four weeks. The response options were "not at all," "a little," "somewhat," "quite a bit," and "very much" (range 5-25) [15, 41]. We further categorized negative affect into low, moderate and high levels according to tertiles.

#### Positive affect

Positive affect considers the following affective features: active, inspired, determined, alert, and enthusiastic. Respondents were asked to report whether and to what extent they had felt in the above-mentioned affective states during the last 4 weeks. The response options were "not at all," "a little," "somewhat," "quite a bit," and "very much" (range 5-25) [15, 41]. We further categorized positive affect into low, moderate and high levels according to tertiles.

#### Covariates

Several covariates were considered as possible confounders and measured at baseline: age (continuous), highest level of formal education (elementary school, high school, or university and above), number of chronic diseases (continuous) [42], and Mini-Mental State Examination score (MMSE). In SNAC-K, personality traits (extraversion, neuroticism, and openness to experience) were assessed with a short version of the self-reported NEO Five-Factor Inventory (NEO-FFI) questionnaire [43].

#### Statistical analysis

Latent class analysis (LCA) was used to derive the wellbeing profiles based on the 10 indicators of behavioral, social and psychological well-being assessed at baseline. LCA is a statistical person-centered approach which groups individuals into unobserved classes based on responses to manifest variables. This results in subgroups of individuals similar to each other and distinct from those in other classes [44]. We used the Stata command gsem lclass to estimate the latent class models using the maximum-likelihood estimation. Analyses were run separately in men and women. We started with 2 class-solutions, incrementally increasing the number of classes. The ideal number of classes was determined using statistical criteria and interpretations based on theoretical knowledge. Goodness-of-fit indices included Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC). Participants were assigned to one specific class according to their highest posterior probability. Subsequently, the distribution of all behavioral, social, and psychological factors across the derived classes was examined.

The association between the well-being profiles and the incidence rate of the composite endpoint (i.e., mobility limitation or death) was analyzed through multivariate Cox proportional hazards regression models, from which hazard ratios (HRs) and 95% confidence intervals (CIs) were obtained. The proportional hazard assumption was assessed by regressing the scaled Schoenfeld residuals against survival time. No deviation from the proportional hazard assumption was detected. The models were first adjusted for age and education, and additionally by baseline number of chronic diseases and MMSE score in a second phase. We used Laplace regressions to quantify the differences (in years) in median age at onset of mobility limitation or death (so-called median mobilitylimitation-free survival), according to the well-being profiles. In other words, we analyzed the differences in age when 50% of subjects in each well-being profile had developed the composite endpoint. Populationattributable fractions (PAFs) were calculated to estimate

the proportion of the composite outcome that would be avoided if all subjects belonged to the best profile, a measure that is valuable from the public health perspective. Because the interpretation of PAFs is more straightforward with binary exposures, all profiles were compared against the one with the greatest mobilitylimitation-free survival.

We carried out the following sensitivity analyses. First, in order to verify the robustness of the classes derived from LCA, we performed a data dimension reduction using multiple correspondence analysis (MCA), a generalization of principal component analysis (PCA) for categorical data. We used the obtained dimensions to plot the coordinates for every category of the 10 wellbeing indicators and their corresponding sum of squared Cosine  $(\cos^2)$ . Second, we further plotted the original data on a reduced two-dimensional grid, while labelling the observations with their corresponding well-being profiles obtained from LCA. Finally, we repeated the Cox and Laplace regression analyses: a) additionally adjusting by personality traits, b) excluding participants who were only interviewed at baseline, and c) excluding participants who dropped-out without developing mobility limitation or death.

All analyses were performed using Stata version 15 and R version 3.6.1. with the level of statistical significance set at p < 0.05.

## RESULTS

The study population consisted of 1488 individuals with a mean age of 69 years (standard deviation, SD: 8.3) at baseline. The majority were female (59%) and had at least high-school level education (91%) (Table 1). At baseline, the study sample had a median of three chronic diseases (inter-quartile range, IQR: 2;4) and a median MMSE score of 29 (IQR: 29;30). Eligible participants that were excluded due to missingness in any variable (n=794) were older (mean age (SD): 71.8 (8.3)), had a lower education level, more chronic diseases (median: 3: IQR: 2-5) and lower MMSE score (median: 29; IQR: 28-30). Weak-to-moderate correlations were found within and between behavioral, social, and psychological wellbeing indicators (Table 2). About 47% of the study population developed the composite endpoint during the follow-up (mean: 11 years, SD: 4.0 years) (Table 1). Participants with a walking speed <0.8m/s at baseline, and thus excluded from the sample, were older, had more chronic diseases and reported lower levels of behavioral, social and psychological well-being (Supplementary Table 1).

A three-latent-class solution was identified to be optimal for both men and women, based on the BIC

parameter and the interpretation of the identified profiles (Supplementary Table 2). The worst profile (n=151, 25% in men; n=373, 41.4% in women) was characterized by low adherence to MD, a higher proportion of former/never smokers, lowest levels of leisure activity engagement, and lowest levels of social and psychological well-being (Table 3). The intermediate profile (n=313, 51.2% in men; n=237, 28.9% in women) was characterized by low/moderate adherence to MD, a higher proportion of former/never smokers, and moderate levels of social and psychological well-being. Men in this profile had a low/moderate engagement in leisure activities, while women had moderate/high engagement levels. The best profile (n=145, 23.8% in men; n=269, 29.7% in women) was characterized by high adherence to MD, the lowest proportion of current smokers, high engagement with leisure activities, and highest levels of social and psychological well-being (Table 3). Results from the MCA showed that similar levels (i.e., low, moderate, high) of the 10 well-being indicators clustered together confirming the composition of the profiles identified by the LCA (Figure 1 and Supplementary Figure 2).

Men and women in the best profile were younger, with higher levels of education, had less chronic diseases at baseline, and had a lower incidence of the composite endpoint compared to those in the worst profile (Supplementary Table 3). The associations between the well-being profiles and the incidence of the composite outcome are shown in Figure 2. After adjusting for potential confounders, men and women in the intermediate profile had a 27% (HR 0.73; 95% CI 0.56-0.94) and a 23% (HR 0.77; 95% CI 0.59-1.00) lower hazard of developing the composite endpoint, respectively, compared to those in the worst profile. An even greater protective effect was seen among individuals in the best profile compared to those in the worst profile (HR 0.47; 95% CI 0.31-0.70 in men; HR 0.60; 95% CI 0.46-0.78 in women). We also show the outcome incidence rates across all well-being indicators and covariates in males and females in Supplementary Table 4.

In agreement with the Cox regressions, results from Laplace regressions showed that men in the intermediate and best profiles survived 1 and 3 years longer without mobility limitations, respectively, compared to those in the worst profile after adjustment for potential confounders (Figure 2). Women in the intermediate and best profiles lived 2 and 3 years longer without mobility limitations, respectively, compared to those in the worst profile. The PAFs for belonging to the intermediate and worst versus the best profile was 36% (95% CI 0.14-0.53) for men and 27% (95% CI 0.13-0.39) for women. Similar trends were observed

## Table 1. Baseline characteristics of the study population by sex.

	Total population (n=1488)	Males (n=609)	Females (n=879)	p-value
Age (mean, SD)	69.1 (8.3)	68.6 (8.2)	69.5 (8.4)	0.013
Education (%)				
Elementary	141 (9.5)	58 (9.5)	83 (9.4)	
High school	707 (47.5)	256 (42.2)	451 (51.3)	0.001
University	640 (43.0)	295 (48.3)	345 (39.3)	
Number of chronic diseases, median (IQR)	3 (2;4)	3 (2;4)	3 (2;4)	0.031
MMSE score, median (IQR)	29 (29;30)	29 (29;30)	30 (29;30)	0.196
Mediterranean Diet Score (%)				
Low	705 (47.4)	271 (44.5)	434 (49.4)	
Moderate	331 (22.2)	144 (23.7)	187 (21.3)	0.178
High	452 (30.4)	194 (31.9)	258 (29.4)	
Smoking (%)				
Current	230 (15.5)	86 (14.1)	144 (16.4)	
Former	639 (42.9)	321 (52.7)	318 (36.2)	<0.001
Never	619 (41.6)	202 (33.2)	417 (47.4)	
Physical leisure activity (%)	(	(00)		
No activity	497 (33.4)	164 (26.9)	333 (37.9)	
Mild activity	510 (34.3)	209 (34.3)	301 (34.2)	<0.001
Intense activity	481 (32.3)	236 (38.8)	245 (27.9)	
Mental leisure activity (%)	401 (52.5)	250 (50.0)	245 (21.5)	
No activity	545 (36.5)	172 (28.2)	373 (42.4)	
Mild activity	448 (30.1)	182 (29.9)	266 (30.3)	<0.001
Intense activity	495 (33.3)	255 (41.9)	240 (27.3)	<b>\0.001</b>
Social leisure activity (%)	475 (55.5)	255 (41.5)	240 (27.3)	
Low	496 (33.3)	234 (38.4)	262 (29.8)	
Moderate	496 (33.3)	200 (32.8)	296 (33.7)	0.001
High	496 (33.3)	175 (28.7)	321 (36.5)	0.001
Social connections (%)	490 (33.3)	175 (20.7)	521 (50.5)	
Low	496 (33.3)	175 (28.7)	321 (36.5)	
Moderate	496 (33.3)	199 (32.7)	297 (33.8)	<0.001
High	496 (33.3)	235 (38.6)	261 (29.7)	<0.001
-	490 (55.5)	255 (58.0)	201 (29.7)	
Social support (%)	106 (22.2)	222(26.5)	274(20.0)	
Low	496 (33.3)	222 (36.5)	274 (30.9)	0.104
Moderate	496 (33.3)	193 (31.7)	303 (34.5)	0.104
High	496 (33.3)	194 (31.9)	302 (34.4)	
Life satisfaction (%)	<b>550 (27 0)</b>	200(24.2)	241 (29.9)	
Low	550 (37.0) 572 (28.4)	209 (34.3)	341 (38.8)	0.011
Moderate	572 (38.4)	243 (40.0)	329 (37.4)	0.211
High	366 (24.6)	157 (25.8)	209 (23.8)	
Negative affect (%)	400 (00 1)	170 (00 0)	210 (25.2)	
High	482 (32.4)	172 (28.2)	310 (35.3)	A A4 -
Moderate	356 (23.9)	148 (24.3)	208 (23.7)	0.012
	650 (43.7)	289 (47.5)	361 (41.1)	
Positive affect (%)				
Low	591 (39.7)	243 (39.9)	348 (39.6)	-
Moderate	467 (31.4)	197 (32.4)	270 (30.7)	0.676
High	430 (28.9)	169 (27.8)	261 (29.7)	
Death or mobility limitation during follow-up	699 (47%)	286 (47%)	413 (47%)	0.993
Death without mobility limitation during follow-up	263 (17.7)	133 (21.8)	130 (14.8)	0.001
Mobility limitation (walking speed <0.8 m/s) during follow-up	436 (29.3)	153 (25.1)	283 (32.2)	0.003

SD, standard deviation; IQR, interquartile range; MMSE, Mini Mental State Examination.

p-values for differences observed among males and females estimated using the chi<sup>2</sup> test.

	MDS	Smoking	Physical leisure	Mental leisure	Social leisure	Social connection	Social support	Life satisfaction	Negative affect	Positive affect
MDS	1.00	-	-	-	-	-	-	-	-	-
Smoking	-0.08	1.00	-	-	-	-	-	-	-	-
Physical leisure	0.19	0.04	1.00	-	-	-	-	-	-	-
Mental leisure	0.17	0.12	0.45	1.00	-	-	-	-	-	-
Social leisure	0.15	-0.11	0.31	0.37	1.00		-	-	-	-
Social connection	0.16	-0.05	0.27	0.31	0.23	1.00	-	-	-	-
Social support	0.13	-0.04	0.18	0.25	0.41	0.46	1.00	-	-	-
Life satisfaction	0.13	-0.06	0.29	0.34	0.30	0.37	0.41	1.00	-	-
Negative affect	-0.04	0.06	-0.03	0.08	-0.03	-0.05	-0.16	-0.24	1.00	-
Positive affect	0.14	-0.04	0.32	0.36	0.32	0.25	0.31	0.56	-0.03	1.00

Correlations between and within psychological and social well-being indicators were assessed using the polychoric test. MDS, Mediterranean Diet Score.

when further adjusting by personality traits, and when excluding individuals with only baseline information and/or those who dropped-out without developing the outcome (Supplementary Tables 5–7).

## **DISCUSSION**

In this large community-based cohort study of Swedish older adults aged  $\geq 60$  years, we found strong synergistic effects among different behavioral, social, and psychological indicators of well-being, leading to a clear gradient of well-being both in men and women. We also found that individuals in the intermediate and best well-being profiles lived between one to three years longer without mobility limitation compared to those in the worst profile, independent of potential confounders.

The few previous studies looking at multiple indicators of well-being simultaneously have suggested that these tend to be interrelated and to cluster within individuals [21, 24, 45]. For example, a recent study including 15,771 older adults from the Chinese Longitudinal Health Longevity Survey (CLHLS) identified four latent classes in men and women separately based on increasing levels of social engagement, psychological well-being and adherence to positive health behaviors [21]. The WELL study of Australian older adults identified two classes of lifestyle patterns (i.e., healthy and less healthy) based on concomitantly varying levels of healthy diet, physical activity, sedentary behavior, smoking and alcohol consumption [24]. In accordance with these studies, we found that similar levels across 10 different behavioral, social, and psychological well-being indicators clustered within specific well-being profiles, leading to a clear wellbeing gradient (i.e., worst, intermediate, best) among men and women. Despite the rising evidence

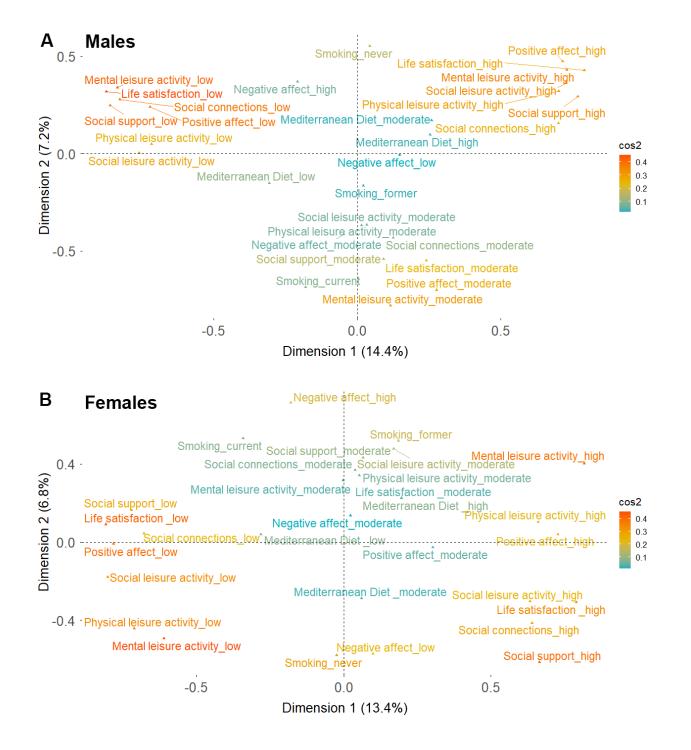
supporting a multidimensional construct of successful aging, most longitudinal studies still fail to cover wellbeing indicators belonging to different domains, as shown by the disproportionate amount of literature focusing exclusively on lifestyle factors [45–48].

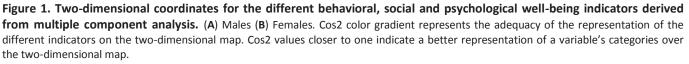
Our finding that well-being profiles may considerably prolong mobility-limitation-free survival among older adults has been partially corroborated by previous evidence. Studies carried out with populations from the blue zones constitute a relevant example. These populations are characterized by a high adherence to a healthy diet and physical activity, increased satisfaction with social ties, high social support and psychological well-being, and exceptional longevity without severe disability [49]. A recent study from the seniors-ENRICA cohort concluded that the joint effect of Mediterranean diet, physical activity, rest, social engagement and conviviality conferred the highest protection against frailty [23]. Similarly, in previous studies from SNAC-K, we showed that a higher adherence to Mediterranean diet, especially in combination with recommended levels of physical activity and high levels of social support, can delay the decline in mobility and muscle strength inherent to aging [22] and, that older adults with high levels in both social and psychological wellbeing have a slower loss of physical function [15]. In another study using SNAC-K, we also found that older adults in the healthiest behavioral profile-concurrently considering lifestyle factors, social network size, and leisure activity participation-lived almost three years longer and developed disability almost four years later compared to those in the least healthy behavioral profile [20]. Compared to the latter study, ours was based on a healthier sample and an outcome (i.e., mobility limitation) that precedes disability. Therefore, our findings further corroborate and complement those from Wu et al. A longitudinal study comprising 10,602

		Males (n=609)		Females (n=879)			
	Worst 25.0%	Intermediate 51.2%	Best 23.8%	Worst 41.4%	Intermediate 28.9%	Best 29.7%	
Mediterranean Diet Score (%)							
Low	61.3	43.9	32.4	59.5	46.4	35.1	
Moderate	14.2	22.8	27.1	21.3	21.5	24.4	
High	24.5	33.3	40.5	19.2	32.1	40.5	
Smoking (%)							
Current	15.1	16.8	9.6	19.8	16.9	11.1	
Former	50.4	52.3	56.0	28.2	46.7	37.0	
Never	34.6	31.9	34.4	52.0	36.3	51.9	
Physical leisure activity (%)							
No activity	56.0	37.8	0.0	60.4	11.8	17.0	
Mild activity	31.0	37.0	27.9	28.9	41.3	31.4	
Intense activity	13.0	25.2	72.1	10.7	47.0	51.6	
Mental leisure activity (%)							
No activity	66.8	32.1	2.4	72.7	17.3	24.8	
Mild activity	20.6	46.8	16.4	21.9	35.8	21.5	
ntense activity	12.7	21.1	81.3	5.4	46.9	53.8	
Social leisure activity (%)							
Low	60.2	35.2	1.2	58.3	22.2	9.3	
Moderate	30.5	37.9	26.7	25.8	45.2	32.6	
High	9.4	26.9	72.2	15.9	32.5	58.1	
Social connections (%)							
Low	74.8	23.9	10.1	50.6	36.1	6.5	
Moderate	20.3	42.4	27.5	29.9	39.9	31.7	
High	5.9	33.7	62.4	19.5	24.0	61.8	
Social support (%)							
Low	78.8	22.9	8.2	50.7	42.5	0.0	
Moderate	17.8	44.7	25.2	30.6	43.3	29.3	
High	3.4	32.5	66.6	18.6	14.2	70.6	
Life satisfaction (%)							
Low	87.3	17.8	14.2	67.2	29.3	9.5	
Moderate	12.3	55.0	36.5	21.4	42.5	25.4	
High	0.4	27.2	49.3	11.5	28.3	66.1	
Negative affect (%)							
High	41.5	20.0	32.2	27.6	33.0	19.4	
Moderate	24.7	23.4	25.8	30.6	38.4	28.5	
LOW	33.8	56.7	42.0	41.8	28.7	52.2	
Positive affect (%)							
LOW	80.2	30.1	17.5	70.4	25.6	10.2	
Moderate	12.8	43.0	30.0	19.4	40.7	36.8	
High	7.0	26.3	52.5	10.2	33.8	53.0	

Table 3. Distribution of behavioral, social, and psychological well-being indicators across well-being profiles in males and females.

participants aged 40-64 years from the Atherosclerosis Risk in Communities (ARIC) study concluded that those with a healthy lifestyle, defined as following a healthy diet, moderate alcohol and coffee consumption, being physically active, having a normal body weight, and not smoking, had a significantly reduced risk of impaired lower extremity function, and limitations in basic and instrumental activities of daily living than participants with an unhealthy lifestyle [50]. Another longitudinal study of 5,248 American older adults showed that simultaneously adhering to multiple healthy lifestyle factors such as never smoking, moderate alcohol





consumption, physical activity, healthy diet, low body mass index, intense social networks, and social support, can compress the number of years lived with disability [51]. Our results advance previous findings by integrating multiple indicators across the behavioral, social and psychological domains of well-being, highlighting their synergistic effects and targeting them as potential modifiable sources of resilience against age-related declines in physical function. Moreover, we created a mobility-survival aggregate endpoint highlighting the importance of not only living longer, but also healthier [33].

Although previous research suggests that nonpharmacological multi-domain interventions can help preserve mental health and cognitive function among older adults [52], there is a clear lack of intervention studies combining behavioral, social and psychological well-being domains in the context of mobility decline prevention in healthy older adults. Instead, most physical function interventions have been based solely on the improvement of nutrition and physical activity and have incorporated well-being and quality of life as primary or secondary outcomes [53-55]. This reflects, among others, the existing asymmetry towards observational studies looking at the reverse association, i.e., impact of physical function on well-being, even if the opposite causal pathway may also be plausible. Along these lines, there is preliminary evidence suggesting that interventions targeting well-being through purposeful activity, i.e., activities that cultivate the pursuit of personal and social goals, feelings of usefulness, and structured community engagement, also impact behavioral, social, and emotional domains [56], but their effect on physical function has not been extensively evaluated. In addition, longitudinal studies exploring the complex mechanisms triggered by the synergies among behavioral, social and psychological well-being factors are warranted, looking beyond their isolated roles in the pathogenesis of functional decline and mortality.

#### Strengths and limitations

The strengths of our study include the longitudinal study design, with a relatively large sample size, and with comprehensive information on a number of behavioral, social and psychological well-being indicators. Thanks to the availability of repeated measures of walking speed and vital status throughout the 15-year follow-up, we were able to create a composite endpoint of mobility-limitation-free survival. Moreover, the use of Laplace regressions allowed for the quantification of the years gained in association with belonging to different well-being profiles, enriching the interpretation of our results.

However, several limitations should be considered. Our exposures were assessed only at baseline to avoid reverse causality, which could be challenging among subjects who are less likely to maintain similar levels

	Well-being profiles	Cases/at risk	IR per 1000/py	Difference in median survival (95% CI)	PAF (95% CI)	HR (95% CI)
	Best	37/145	19.95	2.98 (1.04;4.93)	0.36 (0.14;0.53)	0.47 (0.31;0.70)
Males	Intermediate	150/313	43.64	0.94 (-0.11;1.99)	-	0.73 (0.56;0.94)
	Worst	99/151	71.15	ref	-	ref
Se	Best	83/269	25.27	2.96 (1.61;4.32)	0.27 (0.13;0.39)	0.60 (0.46;0.78)
Females	Intermediate	86/237	30.39	1.90 (0.49;3.31)	-	0.77 (0.59;1.00)
Ľ	Worst	244/373	69.28	ref	-	ref
						0.1 1 Males Females

**Figure 2.** Associations between well-being profiles and mobility-limitation-free survival in males and females. IR: incidence rates; PY: person-years; CI: confidence interval; PAF: population attributable fraction; HR: hazard ratio. Models are adjusted for age, education, number of chronic diseases and MMSE score at baseline.

over time. Additionally, a subsample of the eligible population (35%) lacked data for any study variables, which could lead to selection bias as those with missing data were sicker. Nevertheless, this may be less problematic in our study given that the sample was purposefully selected to be functionally healthy at baseline. Information on all well-being indicators was self-reported, which might have led to misclassification of the exposures. Participants in this study were cognitively healthier and able to self-report their exposure levels, which might have led to an underestimation of the associations in the general population. Finally, our findings, and especially those referring to the well-being profiles, may have a limited transferability beyond the exceptionally healthy and socioeconomically affluent SNAC-K population.

#### **CONCLUSIONS**

While theoretical insights into different models of successful aging are on the rise, empirical evidence from population-based longitudinal data on the complex interplay among the distinct well-being domains and their association with person-centered outcomes, such as mobility-limitation-free survival, is currently lacking. This study addresses such an important gap and provides further evidence to better understand and promote functional independence in community-dwelling older adults through primary prevention multi-domain interventions.

## **AUTHOR CONTRIBUTIONS**

M Saadeh and A Calderón-Larrañaga developed the study concept and design. M Saadeh performed the data analysis (with help from X Hu) and drafted the manuscript. M Saadeh, X Hu, S Dekhtyar, AK Welmer, DL Vetrano, W Xu, L Fratiglioni and A Calderón-Larrañaga interpreted the data. All authors provided critical revisions and approved the final version of the manuscript for submission.

#### ACKNOWLEDGMENTS

We thank the SNAC-K participants and the SNAC-K Group for their collaboration in data collection and management.

## **CONFLICTS OF INTEREST**

The authors declare that they have no conflicts of interest.

#### ETHICAL STATEMENT AND CONSENT

Swedish National Study on Aging and Care in Kungsholmen (SNAC-K) was approved by the Swedish

Ethical Review Authority in Stockholm, and written informed consent was obtained from participants or their next of kin.

#### FUNDING

This work was supported by the funders of The Swedish National study on Aging and Care (SNAC): the Ministry of Health and Social Affairs, Sweden; the participating county councils and municipalities; and the Swedish Research Council. Specific grants were obtained from the Swedish Research Council (2016-00981, 2021-06398); the Swedish Research Council for Health, Working Life and Welfare (2017-01764, 2020-01544, 2021-00256); Karolinska Institutet's Strategic Young Scholar Grants in Epidemiology or Biostatistics (SFO-EPI); Lindhés Advokatbyrå Foundation; and the Swedish National Graduate School on Ageing and Health (SWEAH). The financial sponsors played no role in the design, execution, analysis and interpretation of data, or writing of the study.

#### REFERENCES

 Anton SD, Woods AJ, Ashizawa T, Barb D, Buford TW, Carter CS, Clark DJ, Cohen RA, Corbett DB, Cruz-Almeida Y, Dotson V, Ebner N, Efron PA, et al. Successful aging: Advancing the science of physical independence in older adults. Ageing Res Rev. 2015; 24:304–27. https://doi.org/10.1016/j.arr.2015.09.005

PMID:26462882

- Michel JP, Sadana R. "Healthy Aging" Concepts and Measures. J Am Med Dir Assoc. 2017; 18:460–4. <u>https://doi.org/10.1016/j.jamda.2017.03.008</u> PMID:<u>28479271</u>
- Sabia S, Singh-Manoux A, Hagger-Johnson G, Cambois E, Brunner EJ, Kivimaki M. Influence of individual and combined healthy behaviours on successful aging. CMAJ. 2012; 184:1985–92. https://doi.org/10.1503/cmaj.121080 PMID:23091184
- Fernández-Ballesteros R, Sánchez-Izquierdo M. Are Psycho-Behavioral Factors Accounting for Longevity? Front Psychol. 2019; 10:2516. <u>https://doi.org/10.3389/fpsyg.2019.02516</u> PMID:<u>31798494</u>
- 5. World Health Organization. World Report on Ageing and Health. 2015.
- Struijk EA, Guallar-Castillón P, Rodríguez-Artalejo F, López-García E. Mediterranean Dietary Patterns and Impaired Physical Function in Older Adults. J Gerontol A Biol Sci Med Sci. 2018; 73:333–9. <u>https://doi.org/10.1093/gerona/glw208</u>

PMID:28329809

 Sánchez-Sánchez ML, García-Vigara A, Hidalgo-Mora JJ, García-Pérez MÁ, Tarín J, Cano A. Mediterranean diet and health: A systematic review of epidemiological studies and intervention trials. Maturitas. 2020; 136:25–37.

https://doi.org/10.1016/j.maturitas.2020.03.008 PMID:<u>32386663</u>

- Silva R, Pizato N, da Mata F, Figueiredo A, Ito M, Pereira MG. Mediterranean Diet and Musculoskeletal-Functional Outcomes in Community-Dwelling Older People: A Systematic Review and Meta-Analysis. J Nutr Health Aging. 2018; 22:655–63. <u>https://doi.org/10.1007/s12603-017-0993-1</u> PMID:29806854
- Brandts L, van den Brandt PA. Sex-specific associations between smoking habits and reaching longevity: Netherlands Cohort Study. Geriatr Gerontol Int. 2018; 18:1249–58. https://doi.org/10.1111/ggi.13468 PMID:29978559

 Gellert C, Schöttker B, Brenner H. Smoking and allcause mortality in older people: systematic review and meta-analysis. Arch Intern Med. 2012; 172:837–44. <u>https://doi.org/10.1001/archinternmed.2012.1397</u> PMID:<u>22688992</u>

- Liu X, Ruan Y, Huang L, Guo Y, Sun S, Chen H, Gao J, Shi Y, Xiao Q. Cognitive leisure activity and all-cause mortality in older adults: a 4-year community-based cohort. BMC Geriatr. 2021; 21:236. <u>https://doi.org/10.1186/s12877-021-02180-3</u> PMID:<u>33836660</u>
- Pressman SD, Matthews KA, Cohen S, Martire LM, Scheier M, Baum A, Schulz R. Association of enjoyable leisure activities with psychological and physical wellbeing. Psychosom Med. 2009; 71:725–32. <u>https://doi.org/10.1097/PSY.0b013e3181ad7978</u> PMID:<u>19592515</u>
- Haider S, Grabovac I, Dorner TE. Fulfillment of physical activity guidelines in the general population and frailty status in the elderly population : A correlation study of data from 11 European countries. Wien Klin Wochenschr. 2019; 131:288–93. <u>https://doi.org/10.1007/s00508-018-1408-γ</u> PMID:<u>30421283</u>
- 14. Mok A, Khaw KT, Luben R, Wareham N, Brage S. Physical activity trajectories and mortality: population based cohort study. BMJ. 2019; 365:I2323. <u>https://doi.org/10.1136/bmj.I2323</u> PMID:<u>31243014</u>
- 15. Saadeh M, Welmer AK, Dekhtyar S, Fratiglioni L, Calderón-Larrañaga A. The Role of Psychological and

Social Well-being on Physical Function Trajectories in Older Adults. J Gerontol A Biol Sci Med Sci. 2020; 75:1579–85.

https://doi.org/10.1093/gerona/glaa114 PMID:<u>32384140</u>

- James BD, Boyle PA, Buchman AS, Bennett DA. Relation of late-life social activity with incident disability among community-dwelling older adults. J Gerontol A Biol Sci Med Sci. 2011; 66:467–73. <u>https://doi.org/10.1093/gerona/glq231</u> PMID:<u>21300745</u>
- Lacruz ME, Emeny RT, Baumert J, Ladwig KH. Prospective association between self-reported life satisfaction and mortality: results from the MONICA/KORA Augsburg S3 survey cohort study. BMC Public Health. 2011; 11:579. <u>https://doi.org/10.1186/1471-2458-11-579</u> PMID:21774793
- Rizzuto D, Fratiglioni L. Lifestyle factors related to mortality and survival: a mini-review. Gerontology. 2014; 60:327–35. <u>https://doi.org/10.1159/000356771</u> PMID:24557026
- Buettner D, Skemp S. Blue Zones: Lessons From the World's Longest Lived. Am J Lifestyle Med. 2016; 10:318–21. <u>https://doi.org/10.1177/1559827616637066</u> PMID:30202288
- 20. Wu W, Xu W, Englund S, Shang Y, Pan KY, Rizzuto D. Can health behaviours prolong survival and compress the period of survival with the disability? A populationbased cohort study. Age Ageing. 2021; 50:480–7. <u>https://doi.org/10.1093/ageing/afaa143</u> PMID:32706849
- Shi Z, Lin J, Xiao J, Fang Y. Sex differences in the association between latent class of lifestyle and disability among older adults in China. BMC Geriatr. 2021; 21:188. https://doi.org/10.1186/s12877-021-02087-z

https://doi.org/10.1186/s12877-021-02087-PMID:<u>33736602</u>

- 22. Saadeh M, Prinelli F, Vetrano DL, Xu W, Welmer AK, Dekhtyar S, Fratiglioni L, Calderón-Larrañaga A. Mobility and muscle strength trajectories in old age: the beneficial effect of Mediterranean diet in combination with physical activity and social support. Int J Behav Nutr Phys Act. 2021; 18:120. <u>https://doi.org/10.1186/s12966-021-01192-x</u> PMID:34496869
- Maroto-Rodriguez J, Delgado-Velandia M, Ortolá R, García-Esquinas E, Martinez-Gomez D, Struijk EA, Lopez-Garcia E, Rodriguez-Artalejo F, Sotos-Prieto M. A Mediterranean lifestyle and frailty incidence in older

adults: the Seniors-ENRICA-1 cohort. J Gerontol A Biol Sci Med Sci. 2021. [Epub ahead of print]. <u>https://doi.org/10.1093/gerona/glab292</u> PMID:<u>34614144</u>

 Södergren M, Wang WC, Salmon J, Ball K, Crawford D, McNaughton SA. Predicting healthy lifestyle patterns among retirement age older adults in the WELL study: a latent class analysis of sex differences. Maturitas. 2014; 77:41–6. <u>https://doi.org/10.1016/j.maturitas.2013.09.010</u> PMID:24144958

25. Centers for Disease Control and Prevention. Well-Being Concepts. 2018. <u>https://www.cdc.gov/hrqol/wellbeing.htm</u>

- 26. Rogers RG, Everett BG, Onge JM, Krueger PM. Social, behavioral, and biological factors, and sex differences in mortality. Demography. 2010; 47:555–78. <u>https://doi.org/10.1353/dem.0.0119</u> PMID:<u>20879677</u>
- Joshanloo M, Jovanović V. The relationship between gender and life satisfaction: analysis across demographic groups and global regions. Arch Womens Ment Health. 2020; 23:331–8. <u>https://doi.org/10.1007/s00737-019-00998-w</u> PMID:31482245
- Kemperman A, van den Berg P, Weijs-Perrée M, Uijtdewillegen K. Loneliness of Older Adults: Social Network and the Living Environment. Int J Environ Res Public Health. 2019; 16:406. <u>https://doi.org/10.3390/ijerph16030406</u> PMID:<u>30708985</u>
- 29. Carmel S. Health and Well-Being in Late Life: Gender Differences Worldwide. Front Med (Lausanne). 2019; 6:218. <u>https://doi.org/10.3389/fmed.2019.00218</u> PMID:31649931
- 30. Eurostat statistics Explained. Healthy life years statistics. 2021. <u>https://ec.europa.eu/eurostat/statistics-</u> explained/index.php?title=Healthy life years statistics
- 31. Feng Z, Lugtenberg M, Franse C, Fang X, Hu S, Jin C, Raat H. Risk factors and protective factors associated with incident or increase of frailty among communitydwelling older adults: A systematic review of longitudinal studies. PLoS One. 2017; 12:e0178383. <u>https://doi.org/10.1371/journal.pone.0178383</u> PMID:<u>28617837</u>
- 32. Zhang YB, Pan XF, Chen J, Cao A, Xia L, Zhang Y, Wang J, Li H, Liu G, Pan A. Combined lifestyle factors, all-cause mortality and cardiovascular disease: a systematic review and meta-analysis of prospective cohort studies. J Epidemiol Community

Health. 2021; 75:92–9. https://doi.org/10.1136/jech-2020-214050 PMID:<u>32892156</u>

- Rodriguez-Mañas L, Rodríguez-Artalejo F, Sinclair AJ. The Third Transition: The Clinical Evolution Oriented to the Contemporary Older Patient. J Am Med Dir Assoc. 2017; 18:8–9. <u>https://doi.org/10.1016/j.jamda.2016.10.005</u> PMID:27887892
- 34. Ferrucci L, Cooper R, Shardell M, Simonsick EM, Schrack JA, Kuh D. Age-Related Change in Mobility: Perspectives From Life Course Epidemiology and Geroscience. J Gerontol A Biol Sci Med Sci. 2016; 71:1184–94. https://doi.org/10.1093/gerona/glw043
  - PMID:26975983
- 35. Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, Brach J, Chandler J, Cawthon P, Connor EB, Nevitt M, Visser M, Kritchevsky S, et al. Gait speed and survival in older adults. JAMA. 2011; 305:50–8. <u>https://doi.org/10.1001/jama.2010.1923</u> PMID:<u>21205966</u>
- 36. Fraser GE, Yan R, Butler TL, Jaceldo-Siegl K, Beeson WL, Chan J. Missing data in a long food frequency questionnaire: are imputed zeroes correct? Epidemiology. 2009; 20:289–94. <u>https://doi.org/10.1097/EDE.0b013e31819642c4</u> PMID:<u>19177024</u>
- Shakersain B, Rizzuto D, Larsson SC, Faxén-Irving G, Fratiglioni L, Xu WL. The Nordic Prudent Diet Reduces Risk of Cognitive Decline in the Swedish Older Adults: A Population-Based Cohort Study. Nutrients. 2018; 10:229.

https://doi.org/10.3390/nu10020229 PMID:29462973

 Trichopoulou A, Orfanos P, Norat T, Bueno-de-Mesquita B, Ocké MC, Peeters PH, van der Schouw YT, Boeing H, Hoffmann K, Boffetta P, Nagel G, Masala G, Krogh V, et al. Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study. BMJ. 2005; 330:991. https://doi.org/10.1136/bmj.38415.644155.8F

PMID:<u>15820966</u>

- Willett WC, Howe GR, Kushi LH. Adjustment for total energy intake in epidemiologic studies. Am J Clin Nutr. 1997; 65:1220S–8S. <u>https://doi.org/10.1093/ajcn/65.4.1220S</u> PMID:9094926
- 40. Köhncke Y, Laukka EJ, Brehmer Y, Kalpouzos G, Li TQ, Fratiglioni L, Bäckman L, Lövdén M. Three-year changes in leisure activities are associated with concurrent changes in white matter microstructure and

perceptual speed in individuals aged 80 years and older. Neurobiol Aging. 2016; 41:173–86. https://doi.org/10.1016/j.neurobiolaging.2016.02.013 PMID:27103530

- Straatmann VS, Dekhtyar S, Meinow B, Fratiglioni L, Calderón-Larrañaga A. Unplanned Hospital Care Use in Older Adults: The Role of Psychological and Social Well-Being. J Am Geriatr Soc. 2020; 68:272–80. <u>https://doi.org/10.1111/jgs.16313</u> PMID:<u>31956993</u>
- 42. Calderón-Larrañaga A, Vetrano DL, Onder G, Gimeno-Feliu LA, Coscollar-Santaliestra C, Carfí A, Pisciotta MS, Angleman S, Melis RJ, Santoni G, Mangialasche F, Rizzuto D, Welmer AK, et al. Assessing and Measuring Chronic Multimorbidity in the Older Population: A Proposal for Its Operationalization. J Gerontol A Biol Sci Med Sci. 2017; 72:1417–23. <u>https://doi.org/10.1093/gerona/glw233</u>

PMID:<u>28003375</u>

- 43. Rennemark M, Berggren T. Relationships between work-status and leisure lifestyle at the age of 60 years old. Eur J Ageing. 2006; 3:82–8. <u>https://doi.org/10.1007/s10433-006-0029-x</u> PMID:<u>28794753</u>
- 44. Hagenaars JA, McCutcheon AL, Eds., Applied Latent Class Analysis. Cambridge University Press. 2002.
- Li Y, Pan A, Wang DD, Liu X, Dhana K, Franco OH, Kaptoge S, Di Angelantonio E, Stampfer M, Willett WC, Hu FB. Impact of Healthy Lifestyle Factors on Life Expectancies in the US Population. Circulation. 2018; 138:345–55. https://doi.org/10.1161/CIRCULATIONAHA.117.032047

nttps://doi.org/10.1161/CIRCULATIONAHA.117.032047 PMID:29712712

- 46. Nyberg ST, Singh-Manoux A, Pentti J, Madsen IE, Sabia S, Alfredsson L, Bjorner JB, Borritz M, Burr H, Goldberg M, Heikkilä K, Jokela M, Knutsson A, et al. Association of Healthy Lifestyle With Years Lived Without Major Chronic Diseases. JAMA Intern Med. 2020; 180:760–8. <u>https://doi.org/10.1001/jamainternmed.2020.0618</u> PMID:32250383
- Zhang S, Tomata Y, Discacciati A, Otsuka T, Sugawara Y, Tanji F, Tsuji I. Combined Healthy Lifestyle Behaviors and Disability-Free Survival: the Ohsaki Cohort 2006 Study. J Gen Intern Med. 2019; 34:1724–9. <u>https://doi.org/10.1007/s11606-019-05061-z</u>

PMID:31144283

48. Zaninotto P, Head J, Steptoe A. Behavioural risk factors and healthy life expectancy: evidence from two longitudinal studies of ageing in England and the US. Sci Rep. 2020; 10:6955. https://doi.org/10.1038/s41598-020-63843-6 PMID:<u>32332825</u>

- 49. Fastame MC, Hitchcott PK, Mulas I, Ruiu M, Penna MP. Resilience in Elders of the Sardinian Blue Zone: An Explorative Study. Behav Sci (Basel). 2018; 8:30. <u>https://doi.org/10.3390/bs8030030</u> PMID:29495425
- Li D, Jia Y, Yu J, Liu Y, Li F, Liu Y, Wu Q, Liao X, Zeng Z, Zeng R, Wan Z. Adherence to Healthy Lifestyle and the Risk of Function Limitations in Late Life: The Atherosclerosis Risk in Communities Study. Front Aging Neurosci. 2021; 13:698699.

https://doi.org/10.3389/fnagi.2021.698699 PMID:<u>34413768</u>

- Jacob ME, Yee LM, Diehr PH, Arnold AM, Thielke SM, Chaves PH, Gobbo LD, Hirsch C, Siscovick D, Newman AB. Can a Healthy Lifestyle Compress the Disabled Period in Older Adults? J Am Geriatr Soc. 2016; 64:1952–61. https://doi.org/10.1111/jgs.14314 PMID:27603679
- 52. Whitty E, Mansour H, Aguirre E, Palomo M, Charlesworth G, Ramjee S, Poppe M, Brodaty H, Kales HC, Morgan-Trimmer S, Nyman SR, Lang I, Walters K, et al. Efficacy of lifestyle and psychosocial interventions in reducing cognitive decline in older people: Systematic review. Ageing Res Rev. 2020; 62:101113. https://doi.org/10.1016/j.arr.2020.101113

https://doi.org/10.1016/j.arr.2020.101 PMID:<u>32534025</u>

 Dedeyne L, Deschodt M, Verschueren S, Tournoy J, Gielen E. Effects of multi-domain interventions in (pre)frail elderly on frailty, functional, and cognitive status: a systematic review. Clin Interv Aging. 2017; 12:873–96.

https://doi.org/10.2147/CIA.S130794 PMID:28579766

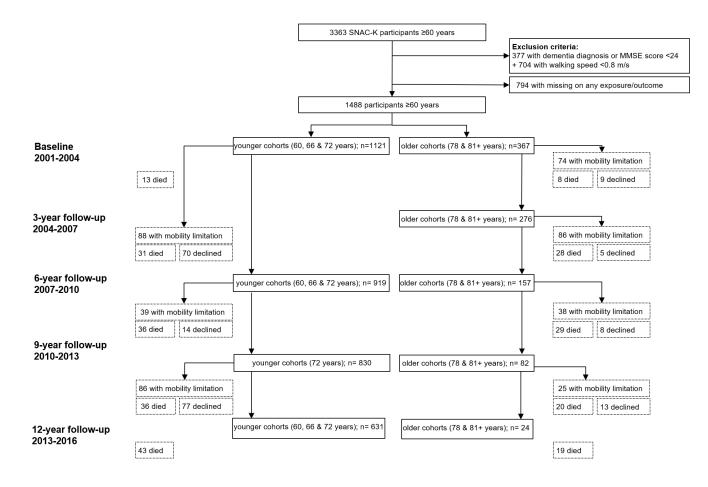
- 54. Daniels R, van Rossum E, de Witte L, Kempen GI, van den Heuvel W. Interventions to prevent disability in frail community-dwelling elderly: a systematic review. BMC Health Serv Res. 2008; 8:278. https://doi.org/10.1186/1472-6963-8-278 PMID:<u>19115992</u>
- 55. Frost R, Belk C, Jovicic A, Ricciardi F, Kharicha K, Gardner B, Iliffe S, Goodman C, Manthorpe J, Drennan VM, Walters K. Health promotion interventions for community-dwelling older people with mild or prefrailty: a systematic review and meta-analysis. BMC Geriatr. 2017; 17:157.

https://doi.org/10.1186/s12877-017-0547-8 PMID:<u>28728570</u>

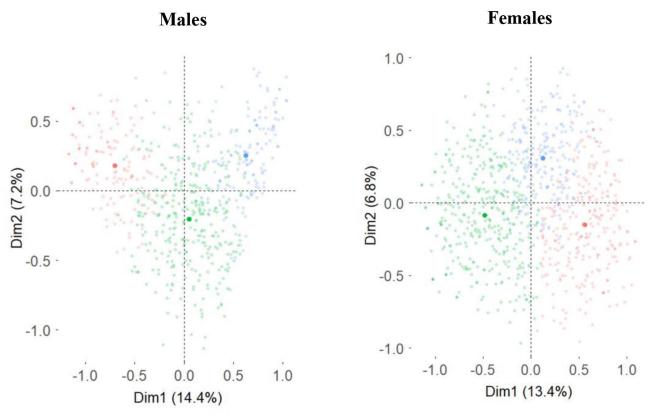
56. Owen R, Berry K, Brown LJ. Enhancing Older Adults' Well-Being and Quality of Life through Purposeful Activity: A Systematic Review of Intervention Studies. Gerontologist. 2021. [Epub ahead of print]. <u>https://doi.org/10.1093/geront/gnab017</u> PMID:<u>33558898</u>

## SUPPLEMENTARY MATERIALS

## **Supplementary Figures**



Supplementary Figure 1. Population flow-chart for baseline and follow-up assessments.



- Worst well-being profile
- Intermediate well-being profile
- Best well-being profile

**Supplementary Figure 2. Two-dimensional coordinates for all observations in the study sample derived from multiple component analysis.** The dot color is assigned in accordance with the well-being profile (derived from LCA) corresponding to that observation. The thickness of the dots is proportional to the number of observations located on a given area of the two-dimensional map.

## **Supplementary Tables**

Supplementary Table 1. Baseline characteristics of the study population by walking speed.

	<0.8 m/s (n=230)	≥0.8 m/s (n=1488)	p-value
Age (mean, SD)	79.3 (8.4)	<b>69.1</b> (8.3)	<0.001
Sex (%)			
Male	66 (28.7)	609 (40.9)	<0.001
Female	164 (71.3)	879 (59.1)	<0.001
Education (%)			
Elementary	44 (19.1)	141 (9.5)	
High school	131 (57.0)	707 (47.5)	<0.001
University	55 (23.9)	640 (43.0)	
Number of chronic diseases, median (IQR)	5 (4;7)	3 (2;4)	<0.001
MMSE score, median (IQR)	29 (28;29)	29 (29;30)	<0.001
Mediterranean Diet Score (%)			
Low	144 (62.6)	684 (46.0)	
Moderate	51 (22.2)	335 (22.5)	<0.001
High	35 (15.2)	469 (31.5)	
Smoking (%)			
Never	127 (55.2)	619 (41.6)	
Former	78 (33.9)	639 (42.9)	<0.001
Current	25 (10.9)	230 (15.5)	
Physical leisure activity (%)			
No activity	170 (73.9)	403 (27.1)	
Mild activity	42 (18.3)	534 (35.9)	<0.001
Intense activity	18 (7.8)	551 (37.0)	
Mental leisure activity (%)			
No activity	166 (72.2)	545 (36.6)	
Mild activity	40 (17.4)	395 (26.6)	<0.001
Intense activity	24 (10.4)	548 (36.8)	
Social leisure activity (%)	· /	· /	
Low	135 (58.7)	438 (29.4)	
Moderate	56 (24.4)	518 (34.8)	<0.001
High	39 (17.0)	532 (35.8)	
Social connections (%)	× /	· /	
Low	110 (47.8)	463 (31.1)	
Moderate	84 (36.5)	489 (32.9)	<0.001
High	36 (15.7)	536 (36.0)	
Social support (%)	× /	· /	
Low	116 (50.4)	457 (30.7)	
Moderate	67 (29.1)	506 (34.0)	<0.001
High	47 (20.4)	525 (35.3)	
Life satisfaction (%)	` '	× /	
Low	137 (59.6)	442 (29.7)	
Moderate	62 (27.0)	538 (36.2)	<0.001
High	31 (13.5)	508 (34.1)	
Negative affect (%)	(10.0)	()	
High	86 (37.4)	482 (32.4)	
Moderate	58 (25.2)	356 (23.9)	0.175

Positive affect (%)			
Low	156 (67.8)	471 (31.7)	
Moderate	50 (21.7)	587 (39.5)	<0.001
High	24 (10.4)	430 (28.9)	

SD, standard deviation; IQR, interquartile range; MMSE, Mini Mental State Examination.

Supplementary	Table	2.	Goodness-of-fit	indices	of	latent	class
models with 2-4	class s	olut	tions.				

	Ma	les	Females			
	AIC	BIC	AIC	BIC		
2-class solution	12571.9	12752.8	18303.5	18499.4		
<b>3-class solution</b>	12473.3	12746.8	18242.5	18538.9		
4-class solution	12448.82	12815.0	18172.9	18569.6		

AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion. Smaller values indicate improved model fit.

Supplementary Table 3. Baseline characteristics of the study population across well-being profiles in males and females.

		Male (n=	:609)		<b>Female</b> ( <b>n=879</b> )			
	Worst (n=151)	Intermediate (n=313)	Best (n=145)	p-value	Worst (n=373)	Intermediate (n=237)	Best (n=269)	p-value
Age (mean, SD)	71.3 (9.3)	68.8 (7.9)	65.1 (6.0)	0.648	73.0 (8.9)	66.7 (7.1)	67.3 (6.8)	0.457
Education (%)								
Elementary	27 (17.9)	27 (8.6)	4 (2.8)		56 (15.0)	13 (5.5)	14 (5.2)	
High school	72 (47.7)	144 (46.0)	40 (27.6)	<0.001	215 (57.6)	119 (50.2)	117 (43.5)	<0.001
University	52 (34.4)	142 (45.4)	101 (69.7)		102 (27.4)	105 (44.3)	138 (51.3)	
Number of chronic diseases, median (IQR)	3 (2;5)	3 (2;4)	2 (1;3)	0.014	4 (2;5)	3 (2;4)	3 (2;4)	<0.001
MMSE score, median (IQR)	29 (29;30)	29 (29;30)	30 (29;30)	<0.001	29 (29;30)	30 (29;30)	30 (29;30)	<0.001
Death or mobility limitation during follow-up	99 (65.6)	150 (47.9)	37 (25.5)	<0.001	244 (65.4)	86 (36.3)	83 (30.9)	<0.001
Death without mobility limitation during follow-up	51 (33.8)	66 (21.1)	16 (11.0)	<0.001	79 (21.2)	27 (11.4)	24 (8.9)	<0.001
Mobility limitation during follow- up (walking speed <0.8 m/s)	48 (31.8)	84 (26.8)	21 (14.5)	0.002	165 (44.2)	59 (24.9)	59 (21.9)	<0.001

SD, standard deviation; IQR, interquartile range; MMSE, Mini Mental State Examination.

p-values for differences observed among worst, intermediate and best profiles estimated using the chi<sup>2</sup> test.

		( <b>n=609</b> )	Females (n=879)			
	Cases/at risk	IR per 1000/py	Cases/at risk	IR per 1000/py		
Age (years)						
<78	158/472	27.5	214/649	27.0		
≥78	128/137	137.1	199/230	116.2		
Education (%)						
Elementary	35/58	59.3	57/83	77.0		
High school	133/256	49.2	243/451	51.8		
University	118/295	34.8	113/345	26.9		
Number of chronic diseases						
<2	92/282	26.9	88/344	20.2		
<u>≥</u> 2	194/327	59.4	325/535	61.7		
 MMSE score						
<27	13/16	122.7	14/18	81.2		
≥27	273/593	41.5	399/861	42.2		
Mediterranean Diet Score	210/070	11.0	577/001	12.2		
Low	143/277	47.9	232/426	52.5		
Moderate	52/132	34.5	89/196	41.0		
High	91/200	41.6	92/257	30.2		
-	91/200	41.0	92/237	50.2		
Smoking	15/00	49.0	CO/144	40.2		
Current	45/86	48.0	68/144	42.3		
Former	147/321	41.8	134/318	37.2		
Never	94/202	42.2	211/417	47.7		
Physical leisure activity						
No activity	128/203	66.7	193/294	69.9		
Mild activity	80/203	34.4	133/292	40.7		
Intense activity	78/203	32.0	87/293	24.1		
Mental leisure activity						
No activity	140/205	74.4	237/373	66.1		
Mild activity	95/201	42.2	99/227	38.2		
Intense activity	51/203	20.0	77/279	22.3		
Social leisure activity						
Low	121/203	59.9	162/293	54.7		
Moderate	91/203	40.4	122/294	36.6		
High	74/203	30.7	129/292	38.6		
Social connections						
Low	114/203	55.9	165/293	54.7		
Moderate	91/203	40.3	137/293	42.5		
High	81/203	33.9	111/293	32.7		
Social support						
Low	120/203	59.4	157/293	51.0		
Moderate	82/203	35.2	127/298	37.8		
High	84/203	36.0	129/288	40.3		
Life satisfaction	0 1/200	20.0	127/200	10.5		
Low	120/209	58.1	202/341	58.9		
Moderate	113/243	41.6	118/252	43.4		
moderate						
High	53/157	27.9	93/286	26.7		

Supplementary	Table	4.	Outcome	incidence	rates	by	baseline	characteristics	and	well-being
indicators in ma	les and	fe	males.							

High	71/172	37.2	112/235	43.5
Moderate	70/148	42.4	115/283	35.3
Low	145/289	46.5	186/361	48.9
Positive affect				
Low	142/243	59.7	218/348	64.5
Moderate	89/197	39.3	109/270	35.1
High	55/169	26.9	86/261	27.3

IR, incidence rates; py, person-years; MMSE, Mini Mental State Examination.

# Supplementary Table 5. Hazard ratios (HR) and differences in median mobility-limitation-free survival in males and females, and by well-being profiles.

	Males (n=609)							Females (n=879)							
	Model I Model I		III	II Model III		Model I		Model II		Model III					
Results from Cox regressions															
	HR (95%CI)	p-value	HR (95%CI)	p- value	HR (95%CI)	p- value	HR (95%CI)	p- value	HR (95%CI)	p- value	HR (95%CI)	p- value			
Well-being pr	rofiles														
Worst	Ref	-	Ref	-	Ref	-	Ref	-	Ref	-	Ref	-			
Intermediate	0.74 (0.57;0.95)	0.021	0.73 (0.56;0.94)	0.017	0.75 (0.56;0.99)	0.048	0.76 (0.59;0.99)	0.043	0.77 (0.59;1.00)	0.050	0.95 (0.74;1.22)	0.692			
Best	0.46 (0.31;0.69)	<0.001	0.47 (0.31;0.70)	<0.001	0.48 (0.31;0.74)	0.001	0.58 (0.45;0.76)	<0.001	0.60 (0.46;0.78)	<0.001	0.55 (0.37;0.80)	0.002			
Results from	Laplace regre	ssions													
	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value			
Well-being pr	rofiles														
Worst	Ref	-	Ref	-	Ref	-	Ref	-	Ref	-	Ref	-			
Intermediate	1.50 (0.13;2.89)	0.032	0.94 (-0.11;1.99)	0.080	0.93 (-0.04;1.90)	0.060	1.95 (0.07;3.82)	0.042	1.90 (0.49;3.31)	0.008	0.10 (- 1.49;1.70)	0.899			
Best	3.32 (0.88;5.76)	0.008	2.98 (1.04;4.93)	0.003	2.99 (1.38;4.60)	<0.001	3.06 (1.60;4.52)	<0.001	2.96 (1.61;4.32)	<0.001	2.63 (0.67;4.59)	0.008			

HR, Hazard Ratio; CI, Confidence Interval.

Model I: adjusted for age and education.

Model II: additionally adjusted for number of chronic diseases and MMSE score at baseline.

Model III: additionally adjusted for personality traits (openness, extraversion and neuroticism).

Supplementary Table 6. Hazard ratios (HR) and differences in median mobility-limitation-free survival in males and females and by well-being profiles, after excluding subjects interviewed only at baseline.

	Males (n=543)							Females (n=818)							
	Model I		Mode	Model II		Model III		Model I		Model II		Model III			
Results from	Cox regression	s													
	HR (95%CI)	p-value	HR (95%CI)	p- value	HR (95%CI)	p- value	HR (95%CI)	p- value	HR (95%CI)	p- value	HR (95%CI)	p- value			
Well-being pr	ofiles														
Worst	Ref	-	Ref	-	Ref	-	Ref	-	Ref	-	Ref	-			
Intermediate	0.81 (0.60;1.09)	0.170	0.79 (0.58;1.07)	0.122	0.84 (0.60;0.16)	0.290	0.80 (0.60;1.06)	0.117	0.82 (0.62;1.08)	0.154	0.87 (0.64;1.16)	0.331			
Best	0.55 (0.35;0.86)	0.009	0.54 (0.35;0.85)	0.008	0.58 (1.12;1.17)	0.027	0.57 (0.43;0.75)	<0.001	0.59 (0.44;0.79)	<0.001	0.66 (0.48;0.90)	0.009			
Results from	Laplace regres	sions													
	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value			
Well-being pr	ofiles														
Worst	Ref	-	Ref	-	Ref	-	Ref	-	Ref	-	Ref	-			
Intermediate	0.83 (-0.08;1.74)	0.074	0.59 (-1.00;2.23)	0.477	0.44 (-1.43;2.32)	0.645	1.74 (0.09;3.38)	0.038	1.71 (0.42;3.01)	0.010	1.22 (-0.02;2.46)	0.053			
Best	2.15 (0.06;4.24)	0.043	2.04 (-0.47;4.56)	0.112	1.92 (-0.56;4.41)	0.130	2.94 (1.63;4.26)	<0.001	2.85 (1.46;4.24)	<0.001	2.25 (0.99;3.52)	<0.001			

HR, Hazard Ratio; CI, Confidence Interval.

Model I: adjusted for age and education.

Model II: additionally adjusted for number of chronic diseases and MMSE score at baseline.

Model III: additionally adjusted for personality traits (openness, extraversion and neuroticism).

Supplementary Table 7. Hazard ratios (HR) and differences in median mobility-limitation-free survival in males and females and by well-being profiles, after excluding subjects who dropped-out without developing the outcome.

	Males (n=549)							Females (n=768)							
	Model I		Model	Model II		Model III Mode		el I Model II			Model III				
Results from	Cox regressio	ns													
	HR (95%CI)	p-value	HR (95%CI)	p- value	HR (95%CI)	p- value	HR (95%CI)	p- value	HR (95%CI)	p- value	HR (95%CI)	p- value			
Well-being p	rofiles														
Worst	Ref	-	Ref	-	Ref	-	Ref	-	Ref	-	Ref	-			
Intermediate	0.76 (0.59;0.98)	0.036	0.77 (0.60;0.99)	0.048	0.80 (0.59;1.07)	0.125	0.70 (0.54;0.91)	0.007	0.69 (0.53;0.90)	0.006	0.70 (0.53;0.93)	0.013			
Best	0.47 (0.31;0.71)	<0.001	0.49 (0.33;0.73)	<0.001	0.50 (0.32;0.78)	0.002	0.48 (0.37;0.63)	<0.001	0.49 (0.38;0.64)	<0.001	0.51 (0.38;0.68)	<0.001			
Results from	Laplace regre	ssions													
	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value	β (95%CI)	p-value			
Well-being p	rofiles														
Worst	Ref	-	Ref	-	Ref	-	Ref	-	Ref	-	Ref	-			
Intermediate	1.38 (-0.02;2.79)	0.054	0.80 (-0.16;1.75)	0.103	0.70 (-0.33;1.73)	0.184	2.16 (0.83;3.48)	0.001	1.85 (0.37;3.32)	0.014	1.35 (0.20;2.51)	0.022			
Best	3.22 (0.86;5.59)	0.008	2.86 (1.15;4.56)	0.001	2.78 (1.07;4.48)	0.001	3.44 (2.13;4.77)	<0.001	3.22 (2.12;4.32)	<0.001	2.90 (1.75;4.04)	<0.001			

HR, Hazard Ratio; CI, Confidence Interval.

Model I: adjusted for age and education.

Model II: additionally adjusted for number of chronic diseases and MMSE score at baseline.

Model III: additionally adjusted for personality traits (openness, extraversion and neuroticism).