Prospective Change in Health-Related Quality of Life and Subsequent Mortality Among Middle-Aged and Older Women

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Objectives. We sought to determine prospective changes in health-related quality of life (HRQoL) measures and subsequent mortality in middle-aged and older women.

Methods. We obtained data from 40 337 healthy women from the Nurses' Health Study aged 46 to 71 years in 1992. We used Cox proportional hazards regression to evaluate associations of changes in self-assessed physical and mental component summary (PCS and MCS) scores from the Short Form 36 Health Survey between 1992 and 1996 and between 1996 and 2000, with all-cause mortality through 2004.

Results. Women with low HRQoL (PCS and MCS scores) and the greatest HRQoL declines had higher mortality than did women with stable scores. Change in PCS score predicted mortality across the range of 4-year change: severe decline (relative risk [RR]=3.32; 95% confidence interval [CI]=2.45, 4.50), moderate decline (RR=1.44; 95% CI=1.16, 1.79), slight decline (RR=1.35; 95% CI=1.12, 1.63), no change (reference category), improvement (RR=0.72; 95% CI=0.56, 0.91; continuous $P<.001$). MCS score results were similar. Score increases were associated with lifestyle improvements, especially increased physical activity.

Conclusions. Observed associations demonstrate the predictive validity of changes in self-assessed HRQoL for subsequent mortality in healthy populations. Future research should examine determinants of patterns of change. (*Am J Public Health.* 2008;98:2085–2091. doi:10.2105/AJPH.2007.114041)

Studies have demonstrated that lower levels of physical and mental function or self-rated health-related quality of life (HRQoL) predict higher mortality in healthy, older population samples[1–5] in analyses adjusted for risk factors and diagnosed conditions and in samples of patients with coronary heart disease,[6] arthritis,[7] lung disease,[8] and kidney disease.[9] However, few studies have examined whether changes in self-reported HRQoL predict mortality, and those that have, have occurred in patient samples,[3,10] not in healthy populations.

It is generally assumed that HRQoL undergoes a steady decline as people age. However, data on population norms for HRQoL suggest,[11] and a Nurses' Health study[12] of middle-aged and older women has demonstrated, that HRQoL may improve with age for some women, particularly in the domains of mental well-being and emotional functioning, and among those with and without disease. Generic measures of HRQoL, such as the Short Form 36 Health Survey (SF-36; Medical Outcomes Trust, Inc, Waltham, MA) instrument, have been proposed as useful approaches for monitoring trends and variations in population health status. Although some studies have documented declines in HRQoL following the onset of serious illness,[13] few studies have examined whether changes in self-reported HRQoL predict mortality,[3,10] no studies have examined whether changes in HRQoL predict mortality among healthy individuals, and no studies have examined whether changes in HRQoL predict mortality explicitly among healthy women. Knowing whether changes in generic HRQoL predict mortality may be useful not only for population health forecasts but also within clinical settings.

We prospectively examined associations between HRQoL and subsequent mortality in a large cohort of healthy women. We hypothesized that lower baseline HRQoL and greater declines in HRQoL would predict higher subsequent mortality among women independent of the diagnosis of several serious and life-threatening conditions. However, to enable comparison with previous studies, we also evaluated this hypothesis among women both diagnosed and not diagnosed with these conditions. Finally, because some middle-aged and older women experience improvement in HRQoL over time, we examined whether improvements in HRQoL might predict lower mortality compared with stable or declining HRQoL.

METHODS

Study Population

The Nurses' Health Study (NHS) is an ongoing prospective study of 121 700 female nurses in the United States. At baseline in 1976, and biennially thereafter, participants provided health behavior and medical history information via mailed questionnaires.

Our study population consisted of women from the NHS who were aged 46 to 71 years in 1992, with follow-up from 1992 to 2004. For analyses of cross-sectional HRQoL and mortality, the study sample included women who had responded to HRQoL assessments in 1992 (n=72 141). For analyses of change, the study sample included women who responded to HRQoL assessments in 1992 and 1996 (n=63 527). To ensure the same number of women in all analyses, at each follow-up (in 1992, 1996, and 2000), we excluded, as data were updated, women who were missing HRQoL summary score data. (In additional analyses that allowed reentry of women into the sample with each follow-up, leading to different sample sizes in each analysis, results were qualitatively similar to those presented below [data not shown].)

We also excluded participants previously reporting any of the following serious illnesses or medical procedures: diabetes, cancer, cardiovascular disease (myocardial infarction, angina, stroke, coronary artery bypass graft, congestive heart failure, peripheral artery disease, peripheral venous thrombosis, carotid endarterectomy), lung disease (pulmonary embolism,

emphysema), debilitating bone fracture (vertebral fracture, hip fracture), chronic kidney disease, and neurological disorders (multiple sclerosis, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease). After exclusions, 50 490 women remained in our analyses of cross-sectional HRQoL and subsequent mortality. Of these women, 40 337 provided HRQoL data in 1992 and 1996 and were included in our analyses of 4-year HRQoL change and subsequent mortality.

We further excluded women with diagnoses which may either precede serious illness (e.g., colorectal polyps, transient ischemic attacks) or were chronic and debilitating in nature as well as possibly increasing the risk of mortality through serious complications (e.g., diverticulitis, ulcerative colitis, Crohn's disease, tuberculosis, systemic lupus, interstitial cystitis, asthma, and other diagnoses of other serious illnesses not reported specifically on the NHS questionnaire), leaving a sample of 29 574 women with 768 deaths. Because the results did not substantially change in analyses with the additional exclusions (data not shown), the results we present are for the 40 337 women in our sample after the first round of exclusions. A subsequent longitudinal analysis of the entire sample, including but adjusting for the disease status of women with the aforementioned diagnoses, included 63 527 women. We conducted analyses in this way to enable comparison with population samples that included people with multiple disease conditions.

Data Collection

The SF-36[14] is a self-administered questionnaire that measures 8 domains of HRQoL: physical functioning, role limitations because of physical problems, bodily pain, vitality, social functioning, role limitations because of emotional problems, mental health, and general health perceptions. The physical component summary (PCS) and mental component summary (MCS) scales were constructed from these subscales: PCS from physical functioning, role limitations because of physical problems, bodily pain, and general health perceptions; and MCS from vitality, social functioning, role limitations because of emotional problems, and mental health perceptions.[15] Among the questions on general health perceptions is a measure of self-rated health that asks respondents to rate their health as very poor, poor, fair, good, and excellent. We substituted this item with the close proxy question, "Do you rate your health as excellent?" (definitely true, mostly true, not sure, mostly false, definitely false) and instead used these results in the computation of the PCS score. In NHS II,[12] which involves a younger cohort similar to that of NHS, responses to these questions were highly correlated ($r=0.75$; $P<.001$). Scores for the physical and mental health summary subscales range from 0 to 75 for each of the summary scales, with higher scores signifying better health and with mean scores of 50. This instrument has been extensively tested and validated.[16–22]

Respondent deaths were ascertained from responses to mailed questionnaires by the respondent's family or by postal authorities at each biennial follow-up. Additionally, names of persistent nonresponders were searched in the National Death Index.[23] Respondent's family members were asked for permission to obtain further information from medical records and were interviewed about the circumstances surrounding the respondent's death if not adequately documented in the medical record. Date of death was ascertained from death certificates. Cause of death was assigned by NHS physician reviewers. More than 98% of deaths in the NHS were identified by these methods.[24]

Age was assessed in 1976. Data on biomedical and lifestyle factors including body mass index (BMI; defined as weight in kilograms divided by height in meters squared), smoking, and menopausal status were assessed biennially. Information on serious chronic illnesses and conditions related to exclusions was also collected biennially. Marital status and social networks,[25] a measure of social connection, were assessed every 4 years beginning in 1992. Women's and their husband's education were assessed in 1992 and, for this study, served as a measure of socioeconomic position. Alcohol consumption was assessed in 1992, 1996, and 1998 in grams per day, and physical activity was assessed in 1992, 1996, and 2000 in terms of metabolic equivalents per week (METs). We chose our covariates on the basis of previously published findings regarding factors related to HRQoL.[12,26–30]

Statistical Analyses

Using a linear regression procedure (PROC GLM) in SAS version 8.0 (SAS Institute Inc, Cary, NC) and adjusting for continuous age, we regressed potential confounding variables (menopausal status, BMI, physical activity, smoking status, marital status, level of social integration, education level, and husband's education level) as well as physical function, physical role function, bodily pain, energy and vitality, social function, emotional role function, and mental health against categories of change in PCS.

We employed Cox proportional hazards models (PROC PHREG) to evaluate associations of HRQoL or change in HRQoL with time to all-cause mortality.[31,32] Person-years of follow-up were counted from the date of each HRQoL questionnaire until the date of death or end of follow-up, whichever came first. For analyses of change, mortality during 1996 to 2000 was regressed on the 1992 to 1996 HRQoL change, and mortality during 2000 to 2004 was regressed on the 1996 to 2000 HRQoL change. Follow-up ranged from 2.8 to 12 years with a median of 8 years (2.6 to 8 years with a median of 4.4 years in change analyses).

We conducted analyses with adjustment for continuous age (and baseline HRQoL in analyses of HRQoL change; model 1) and compared these with analyses with adjustment for continuous age and baseline HRQoL and a range of potential confounding variables: menopausal status, level of social integration, BMI, physical activity, smoking status, education level, husband's education level (model 2). In a third set of models (model 3), we adjusted simultaneously for summary HRQoL scale (PCS or MCS) scores or changes in those scores to determine which scale was more predictive of mortality. We also conducted analyses that included the previously excluded women with prior illness to enable a comparison with other studies of community-based samples.

In all analyses, we employed time-varying independent variables and covariates, with most recent HRQoL status (or change in status) as the independent variable of interest. Covariates were also updated with the most recent follow-up.

Recent Health-Related Quality of Life and Mortality

In analyses of most recent HRQoL and mortality, we categorized the PCS and MCS summary scores into categories of 0 to 30, 31 to 50, 51 to 60, and 61 to 75 points to examine associations across the range of scores and to ensure an adequate distribution. However, rather than present *P* values from a test for trend, we chose to present *P* values for continuous variables to enable comparison with other studies that have reported continuous results. Analyses were adjusted for age, menopausal status, level of social integration, BMI, physical activity, smoking status, educational level, husband's educational level, and simultaneously for PCS and MCS.

Change in Health-Related Quality of Life and Mortality

For analyses of change, we categorized 4-year change in PCS and MCS scores into 5 categories: severe decline (decrease of 20 to 75 points), moderate decline (decrease of 10 to 19 points), slight decline (decrease of 5 to 9 points), no change (decrease of 4 to increase of 5 points), and improvement (increase of 6 to 75 points).

To evaluate whether associations between HRQoL changes and mortality differed by baseline HRQoL, we evaluated differential mortality for women whose self-reported PCS or MCS score decreased (from a score of more than 50 points ["good" health] to a score of 50 or fewer points ["poor" health]), increased (from 50 or fewer to more than 50 points), or was continuously low (remained fewer than 50 points across a 4-year interval), compared with women who continuously reported good health (more than 50 points across any 4-year interval). The cutpoint we used was based on the mean of the summary measures established by Ware et al.[33]

Lifestyle Factors and Change in Health-Related Quality of Life

Finally, we used logistic regression to evaluate the relative risk of improvement in HRQoL versus a decline or no change for each lifestyle factor. We evaluated changes in physical activity, BMI, smoking, alcohol consumption, and social networks, or antidepressant use and adjusted for baseline levels of variables. Because weight loss associated with mortality (i.e., cachexia) might confound associations, we excluded women who died during the study.

All tests of statistical significance were 2-tailed, with α equal to .05.

TABLE 1—Selected Sample Characteristics of Middle-Aged and Older Women (n = 40 337), by 4-Year Change in Physical Component Summary (PCS) Score: Nurses' Health Study, 1996–2000

	Decreasing PCS Score				
	−75 to −20	−19 to −10	−9 to −5	Stable PCS Score (−4 to 5)	Increasing PCS Score (6 to 75)
Person-years	6177	28 321	42 679	176 835	36 274
Deaths	51	112	152	429	97
Mean age, y	64	64	64	63	63
Postmenopausal, %	93	92	92	92	93
Lifestyle factors					
Mean BMI, kg/m^2	27.8	27.4	26.7	25.6	26.2
Physical activity ≥ 18 METs/wk, %	25.9	29.7	34.1	39.9	36.0
Never smoker, %	44.0	44.8	45.8	47.3	46.1
1992 HRQoL scores, mean					
Physical function	89.4	87.9	89.3	91.1	78.3
Physical role function	91.0	84.1	84.9	86.0	41.2
Bodily pain	80.6	77.1	79.6	79.5	57.7
Energy and vitality	61.4	60.9	63.6	68.4	58.7
Social function	85.5	87.5	89.9	93.4	83.3
Emotional role function	73.3	74.7	78.9	89.6	83.1
Mental health	71.4	72.9	74.4	79.5	75.9
1996 HRQoL scores, mean					
Physical function	50.2	67.8	80.5	89.5	86.5
Physical role function	14.7	38.8	68.8	88.3	86.8
Bodily pain	43.8	57.3	68.4	80.7	78.4
Energy and vitality	52.2	57.6	63.4	70.4	65.0
Social function	73.2	85.0	91.6	95.1	91.2
Emotional role function	84.2	82.3	86.0	89.8	79.0
Mental health	77.3	77.5	79.6	81.5	76.2
Psychosocial factors, %					
Married	78.1	77.7	79.9	80.4	79.6
Low level of social integration	7.5	7.6	6.6	6.3	6.9
Less than a college education	10.8	9.2	10.6	11.0	9.7
Husband's educational level ≥ college[a]	56.6	55.3	56.2	57.8	57.2

Note. BMI = body mass index; METs = metabolic equivalents; HRQoL = health-related quality of life.
[a]Among married women.

RESULTS

Compared with women whose PCS scores were stable between 1996 and 2000, women whose PCS scores decreased the most between 1996 and 2000 reported similar HRQoL at baseline but less healthy lifestyle factors in 1996 (e.g., greater BMI, less likely to engage in high levels of physical activity, and less likely to have been never-smokers). Compared with women whose PCS scores remained stable, women whose scores increased had lower baseline HRQoL but reported similar lifestyle as women with stable PCS scores (Table 1).

Recent Health-Related Quality of Life and Mortality

Consistent with our hypothesis, low HRQoL (as measured by PCS and MCS summary scale scores) was associated with

TABLE 2—Relative Risk of Mortality by 4-Year Change in Health-Related Quality of Life (HRQoL) Among Middle-Aged and Older Women (n = 40 337), by Component Summary: Nurses' Health Study, 1992–2004

	Decreasing PCS Score			Stable PCS Score[a] (-4 to 5)	Increasing PCS Score (6 to 75)	Continuous *P*
	-75 to -20	-19 to -10	-9 to -5			
Physical health summary						
Person-years	6 177	28 321	42 679	176 835	36 274	
Deaths	51	112	152	429	97	
Model 1, RR (95% CI)	3.38 (2.52, 4.52)	1.46 (1.19, 1.81)	1.37 (1.14, 1.65)	1.00	0.73 (0.57, 0.92)	<.001
Model 2, RR (95% CI)	3.14 (2.33, 4.21)	1.41 (1.14, 1.74)	1.33 (1.11, 1.61)	1.00	0.75 (0.59, 0.95)	<.001
Model 3, RR (95% CI)	3.32 (2.45, 4.50)	1.44 (1.16, 1.79)	1.35 (1.12, 1.63)	1.00	0.72 (0.56, 0.91)	<.001
Mental health summary						
Person-years	3 128	13 343	25 032	186 845	61 938	
Deaths	19	58	82	509	173	
Model 1, RR (95% CI)	2.35 (1.49, 3.72)	1.52 (1.16, 1.99)	1.18 (0.93, 1.49)	1.00	0.97 (0.79, 1.19)	<.001
Model 2, RR (95% CI)	1.99 (1.26, 3.15)	1.35 (1.03, 1.78)	1.11 (0.88, 1.41)	1.00	0.96 (0.78, 1.18)	.01
Model 3, RR (95% CI)	1.86 (1.17, 2.97)	1.25 (0.95, 1.65)	1.05 (0.83, 1.32)	1.00	0.77 (0.63, 0.95)	<.001

Note. RR = relative risk; CI = confidence interval. Mortality for 1996 to 2000 was regressed on 1992 to 1996 HRQoL change, and mortality for 2000 to 2004 was regressed on 1996 to 2000 HRQoL change. Model 1 was adjusted for age in years and baseline HRQoL. Model 2 was adjusted for age in years (continuous variable), baseline HRQoL (continuous variable), menopausal status (premenopausal [reference], postmenopausal), level of social integration (socially integrated [reference], moderately integrated, moderately isolated, isolated), body mass index (< 21, 21–22 [reference], 23–24, 25–29, ≥ 30 kg/m^2), physical activity (0–2 [reference], 3–17, ≥ 18 metabolic equivalents per week), smoking status (never [reference], past, current 1–14, current 15–24, current ≥ 25 cigarettes/day), educational level (undergraduate degree [reference], registered nurse, master's, doctorate), husband's educational level (< high school, some high school, high-school graduate, college graduate [reference], graduate school). Model 3 was adjusted for the variables in model 2 with simultaneous adjustment for each HRQoL domain, i.e., physical and mental component summary (PCS and MCS) score.

[a]Reference category.

higher subsequent mortality in age- and multivariate-adjusted analyses. In analyses of model 3, which was adjusted for covariates and simultaneously for PCS and MCS, women with PCS scores of 0 to 30 had a relatative risk (RR) of 2.43 (95% confidence interval [CI] = 1.65, 3.58) for subsequent mortality, women with scores of 31 to 50 had an RR of 1.24 (95% CI = 0.87, 1.77), and women with scores of 51 to 60 had an RR of 0.87 (95% CI = 0.61, 1.24) compared with women with PCS scores of 61 to 75 (the reference group; continuous variable $P < .001$).

Women with MCS scores of 0 to 30 had an RR of 1.12 (95% CI = 0.74, 1.67) for subsequent mortality, women with scores of 31 to 50 had an RR of 1.15 (95% CI = 0.96, 1.37), and women with scores of 51 to 60 had an RR of 0.97 (95% CI = 0.83, 1.14) compared with women with MCS scores of 61 to 75 (the reference group; continuous variable $P < .001$). Despite a weak association in categorical MCS, this strong association between continuous MCS and mortality was driven by a higher mortality among women with the very lowest MCS scores (data not shown).

Changes in Health-Related Quality of Life and Mortality

Declines in HRQoL (as measured by PCS and MCS summary scale scores) were associated with higher subsequent mortality in age- and multivariate-adjusted analyses (vs stable scores). Decreases in PCS score were more predictive of mortality than were decreases in MCS score. However, increases in each scale were associated with a lower subsequent mortality versus stable scores (Table 2, model 3).

In stratified analyses, decreases in PCS summary score associated with mortality did not vary by baseline score; decreases in MCS summary score associated with mortality were significant for women whose baseline scores were high (50 or more points). The association between improvements in HRQoL (as measured by both PCS and MCS) and reduced mortality was strongest among women with low baseline scores. Interactions of continuous change and dichotomous baseline scores were not significant (data not shown).

Table 3 presents relative mortality risk for the 4 categories of stability and change in HRQoL. Women whose HRQoL (as measured by PCS and MCS summary scale scores) declined ("declining health") and women whose HRQoL remained poor throughout a 4-year interval ("continued poor health") had significantly higher mortality than did women whose baseline scores were high (more than 50 points) at both times ("continued good health"). On the other hand, women whose baseline scores were low (50 or fewer points) and subsequently increased ("recovering health") had no higher mortality than did women whose self-reported HRQoL was good throughout (Table 3).

In analyses of the sample that included women both with and without serious conditions (N = 63 527), we found associations similar to those found in analyses that excluded women with serious conditions (data not shown).

Lifestyle Factors and Change in Health-Related Quality of Life

Because women whose PCS and MCS scores increased had lower mortality than did women with stable scores, we conducted

TABLE 3—Relative Risk of Mortality by Category of Change in Health-Related Quality of Life (HRQoL) and Prospective Mortality Risk Among Middle-Aged and Older Women (n = 40 337), by Component Summary: Nurses' Health Study, 1992–2004

	Continued Good Health[a] (>50 to >50 points)	Recovering Health (≤50 to >50 points)	Declining Health (>50 to ≤50 points)	Continued Poor Health (≤50 to ≤50 points)
		Physical health		
Baseline score, mean	56.0	44.1	54.1	39.8
Follow-up score, mean	55.3	53.7	42.9	38.3
Person-years, no.	158 571	26 536	44 680	60 499
Deaths, no.	315	63	169	294
Mortality risk, RR (95% CI)	1.00	1.12 (0.85, 1.47)	1.58 (1.30, 1.91)	1.77 (1.49, 2.10)
		Mental health		
Baseline score, mean	56.8	42.6	54.6	39.5
Follow-up score, mean	57.6	55.3	43.3	40.5
Person-years, no.	199 422	38 162	22 052	30 650
Deaths, no.	533	108	95	105
Mortality risk, RR (95% CI)	1.00	1.13 (0.91, 1.39)	1.43 (1.15, 1.78)	1.28 (1.03, 1.59)

Note. RR = relative risk; CI = confidence interval. Mortality for 1996 to 2000 was regressed on 1992 to 1996 HRQoL change and mortality for 2000 to 2004 was regressed on 1996 to 2000 HRQoL change. Models were adjusted for age in years (continuous), menopausal status (premenopausal [reference], postmenopausal), level of social integration (socially integrated [reference], moderately integrated, moderately isolated, isolated), body mass index (<21, 21–22 [reference], 23–24, 25–29, ≥30 kg/m^2), physical activity (0–2 [reference], 3–17, ≥18 metabolic equivalents per week), smoking status (never [reference], past, current 1–14, current 15–24, current ≥25 cigarettes/day), educational level (undergraduate degree [reference], registered nurse, master's, doctorate), husband's educational level (<high school, some high school, high school graduate, college graduate [reference], graduate school), and for each HRQoL domain, i.e., physical and mental component summary (PCS and MCS) score.
[a]Reference category.

additional analyses to determine whether changes in lifestyle factors accounted for improvements in these measures of HRQoL. In these analyses, increased physical activity and weight loss were most strongly associated with PCS score increases. Increased physical activity and level of social integration were associated with increasing MCS scores. By contrast, continued smoking or antidepressant use of any kind was associated with a lower likelihood of an increase in the PCS and MCS scores. Quitting smoking was not related to improvements in HRQoL, and weight loss was associated with lower odds of increasing MCS score (Table 4). Although changes in behaviors were associated with HRQoL, these changes did not explain associations between HRQoL and mortality (data not shown).

DISCUSSION

In a large cohort of healthy women, low baseline HRQoL and declines in HRQoL, after control for baseline HRQoL, predicted higher subsequent mortality. Moreover, women whose general mental health (as determined by MCS score) and physical health (as determined by PCS score) was initially poor and had rebounded by the next follow-up did not experience a higher mortality than did those whose health remained consistently good over the same time period. Positive changes in lifestyle factors, especially increases in physical activity, were related to increases in PCS and MCS score. These findings are consistent with the general notion that, even after declines in health, women can improve HRQoL and functioning later in life, and that such improvement may help to delay mortality. To our knowledge, this is the first study to prospectively examine improvements in HRQoL and subsequent mortality in a healthy population of middle-aged and older women.

Previous studies have documented that poor HRQoL[1–9] and declines[3,10] in HRQoL are predictive of mortality. Other studies have documented HRQoL improvements following declines that occur with disease onset.[34,35] However, no study has examined whether improvements in HRQoL, unrelated to recovery from illness, are associated with differences in mortality. Data from our stratified analyses suggest that women whose self-reported HRQoL is initially poor and later rebounds have little increased risk of mortality relative to those whose health is consistently good, lending support to the notion that aging does not necessarily lead to an inexorable decline in health functioning. Improvements in the lifestyle factors we examined could not explain associations between HRQoL and mortality, which suggests that other factors are more important in how improvements in HRQoL influence mortality. Women who decline and improve in HRQoL may have greater biological reserve or may be constitutionally more robust than women whose HRQoL declines and stays low. Other lifestyle, behavioral, biological, or medically related factors may underlie this relation. Because the US population older than 65 years is projected to double in size by 2020, it will be important to identify these factors and develop interventions that can extend disability-free years.

Previous studies have pointed to PCS score as a more important summary measure than MCS score in predicting mortality.[6,36] Rumsfeld found no association of MCS score with mortality after coronary artery bypass surgery, after adjustment for PCS score.[6] Although Lee et al.[5] used different measures of physical and mental health than those derived using the Medical Outcomes Study SF-36, they also found limited evidence of an association between cross-sectional MCS score and subsequent mortality in a population of community-dwelling people older than 65 years. In our population, we found evidence of a higher mortality rate only among women with the lowest MCS scores. Because numbers of these women were small in our study, studies using a small sample may not effectively detect an association, although this is not uniformly true.[2]

Nonetheless, we found significant linear and monotonic associations of declines in the physical and mental health domains of HRQoL with mortality, with the magnitude

TABLE 4—Relative Odds of Improvement in Physical and Mental Health Summary (PCS and MCS) Scores and Changes in Lifestyle Factors: Nurses' Health Study, 1992–2000 (N = 40 337)

	Person-Years	Deaths	Improvement in PCS Score, OR (95% CI)	Improvement in MCS Score, OR (95% CI)
BMI[a]				
Increase > 0.5 kg/m^2	156 819	369	0.82 (0.78, 0.87)	1.02 (0.97, 1.07)
–0.5 kg/m^2 to 0.5 kg/m^2 (Ref)	31 802	85	1.00	1.00
Decrease > 0.5 kg/m^2	87 930	335	1.11 (1.05, 1.18)	0.91 (0.87, 0.97)
Physical activity				
Increase, METs > 0	129 775	312	1.25 (1.13, 1.38)	1.22 (1.11, 1.33)
No change (Ref)	9 265	49	1.00	1.00
Decrease, METs < 0	149 324	469	0.98 (0.89, 1.08)	1.06 (0.97, 1.17)
Social integration				
Increase ≥ 1 level	43 088	97	1.03 (0.98, 1.09)	1.14 (1.09, 1.20)
No change (Ref)	174 231	522	1.00	1.00
Decrease ≥ 1 level	55 796	170	1.08 (1.03, 1.12)	0.79 (0.76, 0.83)
Smoking status[b]				
Never (Ref)	136 181	307	1.00	1.00
Past	118 471	324	0.97 (0.94, 1.01)	1.02 (0.99, 1.06)
Relapsed	2 174	7	0.91 (0.75, 1.10)	0.99 (0.82, 1.20)
Quit	7 250	40	0.85 (0.76, 0.95)	0.95 (0.86, 1.05)
Continued smokers	25 418	159	0.89 (0.84, 0.95)	0.93 (0.88, 0.99)
Antidepressant use[c]				
No use (Ref)	109 654	301	1.00	1.00
Started antidepressants	8 144	42	0.60 (0.52, 0.68)	0.50 (0.43, 0.57)
Quit using	1 710	3	0.75 (0.60, 0.93)	0.54 (0.43, 0.67)
Continued use	4 962	14	0.76 (0.69, 0.84)	0.46 (0.42, 0.51)

Note. OR = odds ratio; CI = confidence interval; BMI = body mass index; METs = metabolic equivalents per week. ORs higher than 1.00 indicate lifestyle factors associated with improvements in physical function. Models were simultaneously adjusted for age in years (continuous), baseline physical function (continuous), educational level (undergraduate degree [reference], registered nurse, master's, doctorate), husband's educational level (< high school, some high school, high school graduate, college graduate [reference], graduate school), baseline social networks (continuous), change in level of social integration (increase, no change [reference], decrease), baseline BMI (continuous kg/m^2), change in BMI (increase, no change [reference], decrease), baseline physical activity (continuous METS) change in physical activity (increase, no change [reference], decrease), smoking status (never [reference], past, relapse, quit, current), baseline alcohol consumption (continuous g).

[a]Missing data: 13 735 person-years (PY^{-1}) for BMI change, 1921 PY^{-1} for change in physical activity, 792 PY^{-1} for change in smoking status, 17 171 PY^{-1} for change in level of social integration, and 165 816 PY^{-1} for antidepressant use.

[b]Never smokers were respondents who had never smoked. Past smokers were those who had previously smoked but were nonsmokers across a 4-year follow-up. Relapsed smokers were those who had quit but then began smoking again by the end of the 4-year follow-up. Quitters were those who smoked at the beginning of the study but quit by the end of a 4-year follow-up. Continued smokers were those who indicated that they still smoke by the end of the 4-year follow-up.

[c]Reduced model of 1996 to 2000 change only because of lack of data on antidepressant use in 1992. Those who started antidepressants were those who began using antidepressants by the end of the 4-year follow-up. Those who quit using were those who used them at the beginning but quit by the end of the 4-year follow-up. Those who continued use used antidepressants at the beginning and the end of the 4-year follow-up.

of risk being larger for declines in physical health. This appears to be consistent with previous results reported by Fan et al.,[3] who found significant increases in mortality with declines in physical and mental domains of HRQoL in older, mostly male primary-care patients. However, unlike those of previous studies, our findings demonstrate that recovery and improvements in the physical and mental domains of HRQoL are important predictors of mortality. These data furthermore suggest the importance of both physical and mental health domains in understanding HRQoL.

A possible limitation to study validity was the potential misclassification of women with serious disease because of underreporting of serious illness. However, previous tests of validity about health-related information have confirmed the quality of the information provided by the women in the Nurses' Health Study. Moreover, the qualitative nature of our findings did not change with the extent of medical exclusions, suggesting that this potential misclassification should not be a major concern.

To determine whether we omitted any important conditions, we examined the causes of death for participants who had died. Seventy percent died primarily of 2 causes: cancer (50%) and cardiovascular disease (20%). In our study, we excluded participants with preexisting diagnoses of these diseases as well as other causes related to actual causes of death, so nonexcluded diagnoses were not likely to be a major concern. Furthermore, previous studies of self-assessed health and mortality have typically adjusted for a much smaller subset of conditions than those that we included in our analyses.

A related concern is that participants may have had subclinical or undiagnosed disease but failed to seek medical attention. Because women may have delayed seeking medical care, we conducted an analysis excluding women diagnosed with a serious condition in the 4 years (i.e., 1996–2000 and 2000–2004) following the estimation of 4-year change in HRQoL. This analysis did not significantly alter the associations we found.

Declines in the physical and mental health domains of HRQOL predicted higher subsequent mortality in middle-aged and older women in our study. Furthermore, HRQoL improvements, concurrent with lifestyle improvements, predicted lower mortality. Our findings demonstrate the importance of both physical and mental aspects of HRQoL in overall health. Self-rated HRQoL may provide important cues for medical attention or active behavioral interventions to improve health and thus, potentially, longevity. ■

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This article was accepted July 29, 2007.

Acknowledgments

The authors received funding from the Robert Wood Johnson Foundation's Health and Society Scholars Program. The Nurses' Health Study was funded by the National Cancer Institute, National Institutes of Health (grant CA87969). C.H. Kroenke was a Robert Wood Johnson Health and Society Scholar at the University of California in San Francisco and Berkeley during the study.

The authors thank the Nurse's Health Study for access to data.

Human Participant Protection

This research was approved by the institutional review boards of Brigham and Women's Hospital, Harvard Medical School, Boston, MA, and the University of California, San Francisco.

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