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Effect of chronic disease-related symptoms and impairments on universal health outcomes in older adults

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Abstract

Objectives—To determine the extent to which disease-related symptoms and impairments, which constitute measures of disease severity or targets of therapy, account for the associations between chronic diseases and universal health outcomes.

Design—Cross-sectional

Setting—Cardiovascular Health Study (CHS) and Health ABC.

Participants—5,654 CHS, and 2,706 Health ABC, members.

Measurements—Diseases included heart failure (HF), chronic obstructive pulmonary disease (COPD), osteoarthritis, and cognitive impairment. The universal health outcomes included self-rated health, basic and instrumental activities of daily living (BADLs-IADLs), and death. Disease-related symptoms/impairments included HF symptoms and ejection fraction (EF) for HF; Dyspnea Scale and FEV1 for COPD; joint pain for osteoarthritis, and executive function for cognitive impairment.

Results—The diseases were associated with the universal health outcomes ($p<0.001$) except osteoarthritis with death (both cohorts) and cognitive impairment with self-rated health (Health ABC). Symptoms/impairments accounted for ≥30% of each disease's effect on the universal health outcomes. In CHS, for example, HF, compared with no HF, was associated with one fewer (0.918) BADLs-IADL performed without difficulty; 27% of this effect was accounted for by HF symptoms, only 5% by EF. The hazard ratio for death with HF was 6.5 (95% CI, 4.7, 8.9) with 40% accounted for by EF and only 14% by HF symptoms.

Conclusion—Disease-related symptoms/impairments accounted for much of the significant associations between the 4 chronic diseases and the universal health outcomes. Results support considering universal health outcomes as common metrics across diseases in clinical decision-

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making, perhaps by targeting the disease-related symptoms/impairments that contribute most

Elements of Financial/Personal Conflicts	* Author 1 MT		Author 2 GM		Author 3 SC		Author 4 YN	
	Yes	No	Yes	No	Yes	No	Yes	No
Employment or Affiliation		X		X		X		X
Grants/Funds		X		X		X		X
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Speaker Forum		X		X		X		X
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Personal Relationship		X		X		X		X

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Personal Relationship		X		X		X		X

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For “yes” x mark(s): give brief explanation below:

strongly to the effect of the disease on the universal health outcomes.

Keywords

chronic diseases; universal health outcomes; patient-reported outcomes; clinical decision-making

INTRODUCTION

Clinical decisions currently are aimed at diagnosing and treating individual diseases. Within each disease, treatments may be targeted at different disease-related symptoms, impairments or therapeutic endpoints, increasingly with multiple pharmacologic and nonpharmacologic therapies.[1–3] As the number of diseases and treatment options escalate, decision-making can be confusing and burdensome.[1–3] This concern is particularly relevant for older adults, the majority of whom experience multiple chronic diseases.[4–6] Improving the effectiveness, safety, and efficiency of decision-making in patients with chronic diseases requires determining how individual diseases, and their treatments, contribute to overall health. One method for doing this would be to focus decision-making on a shared set of health outcomes – cross-disease or universal health outcomes - that are affected by most chronic diseases. Determining the effect of treatments on these universal health outcomes would facilitate the identification of those treatments with the greatest overall effects on patients' health.

Previous work supports the existence of universal health outcomes. In addition to survival, an obvious universal health outcome, there is an extensive literature describing health-related quality of life (HRQOL), quality adjusted life years (QALYs), and other patient-reported outcomes (PROs). Some of these are summary measures that incorporate multiple domains; others address a single domain such as affect or physical function.[7–10] A large body of research supports an association between individual chronic diseases and these cross-disease, universal health outcomes.[11–21] Older adults volunteer that they are concerned about specific diseases because of their effect on these cross-disease, universal health outcomes.[22] While there is as yet no single set of universal health outcomes, activities of daily living functioning, self-rated health, and survival are examples of outcomes that have been widely used in clinical research and are often included in disease guidelines.

Despite a compelling body of work linking chronic diseases with HRQOL, activities of daily living, self-rated health, and other PROs, they have not been broadly or systematically incorporated into clinical practice or clinical decision-making. At least one factor that may explain this lack of inclusion is that studies have not yet demonstrated whether diseases are linked to universal health outcomes through their effect on disease-related symptoms or impairments. This linkage is important to establish because disease-related symptoms/impairments, the usual therapeutic targets or measures of disease severity, are the focus of disease-specific decision-making. If disease-related symptoms/impairments account for much of the effect of chronic diseases on universal health outcomes, and patients endorse the central importance of universal health outcomes, then the focus of clinical decision-making might shift to considering the effect of disease-related symptoms and impairments - and their treatments - on universal health outcomes. As an initial step in determining the appropriateness of such a shift, we determined whether and to what extent disease-related symptoms and impairments accounted for significant associations between chronic diseases and universal health outcomes. We studied four common chronic conditions and three representative universal health outcomes.

METHODS

Study Populations

The study population included two cohorts of older adults, the Cardiovascular Health Study (CHS) and the Health, Aging, and Body Composition Study (Health ABC). We chose to study two cohorts to assess the robustness of results. We chose these two community-based cohorts because they have a wealth of disease-related symptom and impairment data. The CHS cohort was recruited from a gender and age-stratified (65–69, 70–74, 75–79, ≥ 80) random sample of Medicare eligible individuals in Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland, and Allegheny County (Pittsburgh), Pennsylvania.[23] Eligibility criteria included age ≥65 years, not living in an institution, expected to remain in the area for 3 years and capable of giving informed consent. Participants needing a wheelchair or receiving hospice care, radiation treatment, or chemotherapy were excluded. The initial sample of 5,201 participants, recruited from 1989 to 1990, was enriched with the addition of 687 African American men and women meeting the same eligibility criteria who were recruited from 1992 to 1993, for a combined cohort of 5888 participants. The 5654 cohort members with data for at least one of our analytical models were included in the current study. Health ABC is a prospective cohort study involving all black and a random sample of white Medicare-eligible community-dwelling individuals living in Memphis, Tennessee or Pittsburgh, Pennsylvania who were aged 70–79 years at recruitment.[24] Eligible participants reported no life-threatening cancers or difficulty walking one-quarter of a mile, climbing 10 steps, or performing activities of daily living (BADL-IADLs) at baseline. Of 3,075 participants, 2,733 (89%) had a year 5 (2001–2002) assessment; the 2,706 participants with data for at least one of our analytical models were included in the current study. The cohorts were followed every six months. All participants provided informed consent; respective Institutional Review Board approvals were received. The study was approved by the Yale School of Medicine's Human Investigation Committee.

Data

Socio-demographic, functional, and health data were obtained from person-level interviews and clinical examinations. Information on diseases was collected via self-report and medical record abstraction for both cohorts and Medicare claims data for CHS. The CHS data were from the publicly-released files.

Chronic diseases of interest—The four chronic diseases, chosen because they are common in older adults and account for a large amount of morbidity, included heart failure (HF), chronic obstructive pulmonary disease (COPD), osteoarthritis, and cognitive impairment/dementia. Adjudicated algorithms were used to define HF in both cohorts.[25,26] The combination of self-report and claims data was used for COPD (chronic bronchitis or emphysema) in CHS; self-report, medications, and medical records were used for Health ABC. Self-reported medical provider diagnosis alone was used for osteoarthritis because osteoarthritis is poorly reported in claims data. Cognitive impairment was defined in CHS by any claims data for dementia or a modified Mini-Mental State Exam (3MS) score that was at least 1.5 standard deviations (SD) below the strata mean for education (less than high school; at least high school) and race (Black; Other), criteria with a high specificity for dementia.[27,28] Medical record data or 3MS score was used for Health ABC.

Disease-related symptoms or impairments—The symptoms (i.e. subjective complaints) and impairments (i.e. physiological or other derangements such as ejection fraction) chosen for study are those considered to result from the disease and represent therapeutic targets and/or measures of disease severity. For the CHS cohort, disease-related symptoms/impairments for HF included the CHS HF symptom score;[29] and ejection fraction

(EF). HF-related impairments were not available in Health ABC. The candidate COPD-related impairments included the American Thoracic Society Dyspnea Scale[30] and spirometry measures which included forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and FEV1/FVC. The candidate osteoarthritis impairments included total number of pain sites and site-specific pain (upper extremity, lower extremity, and back). The Digit Symbol Substitution Test (DSST), a measure of processing speed and executive function,[31] was the cognition-related impairment. Short term memory was also considered but was not included because it was assessed with delayed recall as part of the 3MS, the test used to define cognitive impairment.

Universal health outcomes—The three representative universal health outcomes included self-rated health, basic and instrumental activities of daily living (BADL-IADL) functioning or disability, and death. Self-rated health was included because it represents a simple and reliable measure of self-perceived overall health. Functional disability and death represent widely accepted health outcomes.[7–11] The 5-level self-reported health measure ranged from 1 = excellent to 5 = poor in both cohorts. BADL-IADL functioning, a commonly used measure of disability, was assessed with a scale that ranged from 0–12 in CHS and 0–9 in Health ABC based on the number of BADLs and IADLs with which the participant reported having difficulty or could not perform.[32,33] The 12 activities included in CHS included walking, transferring (out of bed), eating, toileting, dressing, bathing, light housework, and heavy housework, shopping, preparing meals, paying bills, and using the phone. The activities in Health ABC were similar except eating, toileting, paying bills, and using the phone were not asked but any of working, volunteering, or providing care was asked.

Death was ascertained primarily by interviews with the next of kin.

Descriptive and covariate data—The covariates included age, gender, race, education, smoking status, social support, depressive symptoms assessed with the Center for Epidemiologic Studies Depression (CES-D) Scale (10 items, range 0–30),[34] and comorbidity. Comorbidity was measured using the Functional Comorbidity Scale which includes the following 18 conditions, arthritis, osteoporosis, asthma, COPD, angina, HF, myocardial infarction, neurological disease, stroke, peripheral vascular disease, diabetes, upper gastrointestinal disease, depression, anxiety, visual impairment, hearing impairment, degenerative disc disease, and obesity.[35] Cardiovascular diseases, COPD, dementia, and arthritis were excluded for the relevant analyses.

Analysis

Because the relationships of interest are likely to be strongest contemporaneously, cross sectional analyses were performed, except for the outcome of death. The most thorough ascertainment of disease-related impairments for the original CHS cohort was baseline for HF and COPD and first follow-up for osteoarthritis and cognitive impairment; in the African American cohort, first follow-up was used for COPD, cognitive impairment, and osteoarthritis and second follow-up for HF. For Health ABC, Years 5–6 had the best available symptom, impairment, and universal outcome data. For both cohorts, death was ascertained over the two years following the disease ascertainment.

We used multiple linear regression for the analysis of continuous universal health outcomes to quantify each disease's association with a universal health outcome and then to assess how much of this association could be attributed to the disease-related symptoms and impairments. Correlations between candidate disease-related symptoms and impairments were determined. The correlation between FEV1 and ATS Dyspnea scale was .22; all other

correlations were <.20. Multicollinearity was assessed by calculating variance inflation factors for all variables included in the regression models. Variables with values > 5 were excluded from the regression models.

In the multiple regression models, the universal health outcome was the dependent variable. The independent variables were the disease status (1 = present, 0 = absent), the disease-related impairments, and the covariates. Models were fitted hierarchically to the data in the following sequence: 1) disease status alone; 2) disease status adjusted for disease-related impairments, singly and then in combination; and 3) disease status adjusted for disease-related impairments and covariates. To estimate the amount of the association between a disease and a universal health outcome that was accounted for by the disease-related impairments, we calculated the percent change in the regression coefficients for disease status between the models unadjusted for disease-related impairments (β) and the adjusted model (β*). Specifically, percent change was calculated as $[(\beta - \beta^*)/\beta] \times 100\%$, so that positive values represent the amount of a disease effect on the universal health outcome attributed to the impairment. The variance of the percent change was estimated using the Delta method and was used to assess its significance (i.e., percent change/standard error is approximately normally distributed).[34] Regression diagnostics were used to assess the fit of the multiple regression models.

Time to death was analyzed by the Cox model using the same approach as for the multiple regression models. The percent change in the hazard ratio and its variance were calculated as above. The proportional hazard assumption was examined in the Cox models by including time by covariate interaction terms. Model fit was evaluated by graphical techniques and examination of residuals.

RESULTS

Characteristics of the cohorts are presented in Table 1. Compared with the CHS cohort, the Health ABC cohort was older and had a higher percentage of Blacks. The mean age of the CHS cohort was 72.8 (SD 5.6) years; 57.5% were female; and 14.4% were Black. The mean age of the Health ABC at Year 5 was 77.6 (SD 2.9) years; 53% were female; and 39.8% were Black. With the exception of more BADL-IADL difficulties and a lower prevalence of osteoarthritis in Health ABC, the two cohorts were similar in results for the universal health outcomes and in prevalence of the chronic diseases.

The associations between HF and the three universal health outcomes and the contribution of HF-related symptoms and EF to these associations are displayed in Table 2. HF was significantly associated with the three universal outcomes in both cohorts. The percentage of the associations accounted for by disease-related symptoms and EF in CHS varied for the universal health outcomes (Table 2). For example, HF symptoms accounted for 25% of the effect of HF on self-rated health, 27% on BADL-IADL functioning, but did not account for the association with death. Conversely, EF accounted for a marginally statistically significant 40% of the association of HF with death but did not contribute to the association with self-rated health or BADL-IADL functioning. The HF-related symptoms and EF were unavailable Health ABC.

The associations between COPD, osteoarthritis, and cognitive impairment and the universal health outcomes, and the contribution of the disease-related symptoms/impairments to these associations, are displayed in Tables 3–5. Dyspnea contributed over 50% of COPD's effect on self-rated health and BADL-IADLs and a borderline significant 33% percent of COPD's effect on death (Table 3). Although not reaching statistical significance, FEV1 accounted for 20–30% of COPD's effect on each universal health outcome except for BADL-IADLs in

Health ABC. Osteoarthritis was not associated with an increased risk of death (Table 4). Pain accounted for 30–70% of the effect of osteoarthritis on self-rated health and BADL-IADLs (Table 4). Cognitive impairment had a strong association with BADL-IADLs and death in both cohorts (Table 5). DSST accounted for 44% to 95% of these effects. This achieved borderline statistical significance (p=.07).

DISCUSSION

The four chronic diseases were significantly associated with each universal health outcome except, as expected, osteoarthritis with death. These observed effects of chronic diseases on self-rated health, BADL-IADL functioning, and death confirm previous findings in older adults.[12–18, 20–22,37–40] The current study adds to our understanding of the relationship between chronic diseases and universal health outcomes by determining how much of the association is accounted for by the disease-related symptoms and impairments which constitute therapeutic targets and indicators of disease severity.

The percent of disease association with the universal health outcomes attributed to disease-related symptoms and impairments ranged from almost a third to over 95% for the four diseases. The amount contributed by the symptoms/impairments, were similar, although not identical, in the two cohorts for most of the analyses. These similarities were in spite of differences in the populations and in the measures of disease-related symptoms/impairments. The amount that individual symptoms or impairments contributed to each disease's association with the universal health outcomes appeared to vary with some symptoms or impairments accounting for a greater or lesser amount of the relationship for some universal outcome than for others.

Heart failure symptoms accounted for the largest amount of the effect of HF on self-rated health and BADL-IADL functioning while reduced EF had the strongest effect on death. A continuous rather than categorical measure of EF may have shown stronger associations with self-rated health or functioning. Finding that most individuals with HF had normal EFs, [41–43] but that lower EF was associated with a higher risk of death, [37] confirms earlier studies. Some of the findings regarding HF may relate to differences between diastolic and systolic heart failure although we could not address this possibility in the current study. HF-related symptoms/impairments were not assessed in Health ABC so we could not corroborate the relationships in this cohort.

The ATS dyspnea scale accounted for the greatest percentage of the association between COPD and all universal health outcomes except death in Health ABC. The lack of statistical significance for FEV1 in Health ABC may reflect the smaller sample size. There is no current consensus on the best spirometry measure for airflow limitations. FEV1, which is highly correlated with FEV1/FVC ratio, is more reproducible[45] and less affected by effort and cognition than FVC, and has been used as a measure of decline in lung function in observational studies.[38,45,46] Our results do not discern the effects of height and waist circumference on spirometric measurements.

For osteoarthritis, pain was the only symptom assessed in CHS and in the entire Health ABC cohort. No measure of pain severity was available. We cannot comment on osteoarthritis-related impairments such as in range of motion or on radiographic measures. Although we cannot ensure that the pain reported was due to osteoarthritis, we did include only joint sites. While arthritic involvement of specific joints likely have unique effects,[47] the sites of pain (lower extremity, upper extremity, back) were highly correlated and had similar relationships with the universal health outcomes in the current study. These findings suggest

that all joint sites with pain contributed to the effect of osteoarthritis on the universal health outcomes.

Cognitive impairment was the most challenging condition to study but was included because of its frequency and morbidity. There is inherent circularity because the diagnosis of dementia requires impairment in memory and other cognitive domains as well as effect on functioning, one of the universal health outcomes. Using education-race strata cutoffs for the 3MS, a test with good specificity for dementia[27] to define cognitive impairment, avoided tautology with the BADL-IADL functioning outcome. DSST,[31] a measure of executive function and processing speed, contributed much of the effect of cognitive impairment on BADL-IADL functioning and death as has been shown previously.[48–51] The contribution of other cognitive deficits, including short term memory, could not be determined in the current study but have been assessed previously, with variable results. [39,52] Reliability of patient-reported outcomes such as self-rated health and BADL-IADL functioning may be limited in individuals with cognitive impairment. Previous work has shown that, while there is good agreement, cognitively-impaired individuals tend to overestimate their functional abilities relative to proxy reports, suggesting that we may have underestimated the contribution of cognitive impairment to BADL-IADL functioning.[53]

Other methods require comment. The use of two large community-based cohorts with disease and health outcome data was a strength. Diagnostic accuracy is always an issue in epidemiological studies. The combination of medical record or claims data plus self-report likely improved reliability. The similar, albeit not identical, relationships in the two cohorts strengthen confidence in the findings. While precluding determination of temporal precedence, the effect of the disease-related symptoms and impairments on the universal health outcomes is likely to be most potent contemporaneously, supporting cross sectional analysis. For example, current arthritic pain or heart failure symptoms will have a stronger effect on BADL-IADL functioning today than in six months when the universal health outcomes were next ascertained in the cohorts. Because temporal sequence and establishment of causality can only be determined longitudinally, the current analyses only ascertained associations, not causality. A wealth of previous longitudinal research, upon which this work builds, has shown longitudinal associations between the diseases and the universal health outcomes and between disease-related symptoms and impairments and the outcomes.[11–20]

We reported the percent effects, based on the regression coefficients, to determine how much of the disease-universal health outcome association was accounted for by disease-related symptoms and impairments.[54, 55] Our approach is similar to determining the mediating effect of the symptoms and impairments.[54, 55] The focus was on the changes that occurred in the disease-universal outcome association (regression coefficient) not explaining the overall variation in outcomes. Some effect of each disease remained for most of the universal health outcomes after accounting for the disease-related symptoms and impairments. The disease-related symptom and impairment data available for the cohorts were not exhaustive. Accounting for more symptoms or impairments might have explained more disease effects on the universal health outcomes. Furthermore, there likely are physiological, anatomical, and other disease effects that are not yet known or measurable. Not surprisingly, some of the disease effect was reduced after adjusting for covariates suggesting that, as is well accepted, social, psychological, and other factors, influence the effect of diseases on health outcomes. We cannot comment on whether controlling for treatment of the diseases would increase or reduce the effect of the diseases on the universal health outcomes or on the amount of these effects accounted for by the symptoms/impairments. Given the magnitude of the effects, however, it is unlikely that the relationships would be eliminated by controlling for treatments.

Some of the disease-related impairments such as FEV1 could be considered general measures of health as well as disease-related impairments. In addition, some symptoms, such as dyspnea, result from more than one disease. While perhaps not unique to specific diseases, the symptoms and impairments are those clinically ascribed to the diseases we studied.

We limited the current study to four common chronic diseases. It is possible, indeed likely, that similar relationships among diseases, disease-related symptoms/impairments, and universal health outcomes exist with most diseases. We investigated only three universal health outcomes. These are not the only important universal health outcomes. Determining the full set of universal health outcomes remains an important clinical and research challenge. Health-related quality of life, active life expectancy, depression, and symptom burden are examples of other potential universal health outcomes that should be explored. Eventually a set of reliable, valid, reproducible, clinically feasible universal health outcomes will hopefully to be chosen for use in clinical practice. We chose to consider symptoms to be disease-related and to include depression as a comorbidity. The fact that symptoms can be viewed as both specific to individual diseases and common across diseases and that depression is both a disease and a potential universal health outcome exemplifies the overlap between certain disease-specific and universal health outcomes.

In addition to identifying the complete contingent of universal health outcomes, much work is needed before proposing that universal health outcomes should serve as the focus of clinical decision-making. The effects of other diseases and disease-related impairments on universal health outcomes must be verified. Findings must be replicated in other populations. The temporal relationships among the symptoms/impairments and universal health outcomes need to be established.

Eventually, it will need to be determined which diseases or disease-related symptoms/impairments have the strongest effect on each universal health outcome. This latter information, along with knowledge of individuals' outcome priorities, could help to establish treatment priorities. The effects of treatment on the disease-related symptoms/impairments and on the universal health outcomes also must be determined. While in many cases, it is known that a treatment may affect all disease-related symptoms and impairments and universal health outcomes similarly, there are examples in which this is not the case. For example, beta-blockers reduce cardiovascular mortality but their effects on heart failure symptoms, function, and quality of life are less clear.[56] In the case of COPD, bronchodilators, oxygen, and exercise are the treatments most recommended for dyspnea with consideration of anxiolytics to treat the perception of dyspnea.[57] The comparative effectiveness of bronchodilators or steroids at improving dyspnea, FEV1, or function is not yet known. To acquire this evidence, and to ensure that treatment is targeted toward the most important outcome to the patient and to the disease manifestations that affect that outcome, universal health outcome domains as well as disease-related symptoms/impairments will have to be assessed routinely in clinical trials and observational studies.

Once this evidence is acquired, current findings suggest a possible approach to more effective and efficient clinical decision-making for older patients. At the population level, the potential effect of recommended treatments on universal health outcomes could be considered in disease management guidelines. At the patient level, clinical decision-making could begin with the patient prioritizing which universal outcomes, e.g. functioning versus prolonged survival, was most important. The clinician then would choose treatments that target the disease-related symptom or impairment that most strongly affects this priority outcome. For example, treatment might prioritize maximizing EF for patients with HF for whom prolonged survival is most important, while symptoms should be the focus for those

who prioritize function. These decisions will need to be made within the context of an individual's overall disease burden; consideration needs to be given to priorities across as well as within diseases. Focusing on cross-disease, universal health outcomes might constitute one step toward effective and efficient clinical decision-making for older patients.

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None of the funding organizations had any say in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

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Table 1

Characteristics of the Two Cohorts*

Characteristics	Cardiovascular Health Study (CHS) N=5,654†	Health ABC Study (ABC) N=2,706†
Age, mean (SD)	72.8 (5.6)	77.6 (2.9).
Female, n (%)	3,249 (57.5)	1,435 (53.0)
Black, n (%)	815 (14.4)	1,077 (39.8)
Less than high school education, n (%)	1,640 (29.0)	652 (24.1)
Married, n (%)	3,750 (66.4)	1,456 (54.2)
Current smoker, n (%)	673 (11.9)	246 (9.1)
Social support, mean (SD)	8.3 (2.6)	8.4 (1.7)
Depressive symptoms, mean (SD)	4.7 (4.6)	5.0 (4.4)
Functional comorbidity index score, mean (SD)	2.3 (1.8)	3.1 (1.9)
No. BADLS-IADLS does with difficulty or does not perform, mean (SD)	0.5 (1.1)	1.6 (1.6)
Self-reported health, mean (SD)	2.8 (1.0)	2.8 (1.0)
Died over two years follow-up n (%)	282 (5.1)	217 (8.2)
Heart failure, n (%)	262 (4.6)	141 (5.3)
COPD, n (%)	608 (10.8)	288 (10.7)
Osteoarthritis, n (%)	3,344 (59.2)	1,073 (40.0)
Cognitive impairment, n (%)	419 (7.9)	201 (7.7)

BADL-IADL, basic and instrumental activities of daily living; COPD, chronic obstructive pulmonary disease

*The Cardiovascular Health Study cohort includes both the original and the African American cohort as described in the Methods. Characteristics are at baseline for the original cohort and the first follow-up for the African-American cohort for the Cardiovascular Health Study and at Year 5–6 for the Health ABC cohort.

†N reflects the number of participants included in at least one analysis model.

Table 2

Amount of Association between Heart Failure and Universal Health Outcomes Accounted for by Disease-related Symptoms and Impairments in Older Adults

	Cardiovascular Health Study		Health ABC
Universal health outcome models[a]	**Effect of HF on UO**	**% of HF effect on UO contributed by symptoms/impairment(s)**	**Effect of HF on UO**
	β (SE)[†], P-Value	**(SE)[‡], P-Value**	**β (SE)[†], P-Value**
Self-rated health (excellent to poor)			
HF alone	.946 (.066), P<.001	---	.426 (.089), P<.001
HF + HF symptoms[§]	.709 (.066)	25% (8.4%), P=.003	Not available
HF + EF[¶]	.852 (.069)	10% (9.2%), P=.28	Not available
HF + HF symptoms + EF	.627 (.068)	34% (8.3%), P<.001	Not available
HF + HF symptoms + EF + covariates [#]	.489 (.063)	48% (7.4%), P<.001	Not available
No. BADL-IADLs not performed or performed with difficulty			
HF alone	.918 (.073), P<.001	---	.449 (.147), P=.002
HF + HF symptoms	.670 (.073)	27% (9.3%), P=.004	Not available
HF + EF	.869 (.076)	5% (10.4%), P=.63	Not available
HF + HF symptoms + EF	.631 (.076)	31% (9.4%), P=.001	Not available
HF + HF symptoms + EF + covariates	.493 (.071)	46% (8.5%), P<.001	Not available
Death over two years[**]	HR (95% CI)		
HF alone	6.5 (4.7, 8.9), P<.001	---	3.0 (1.9, 4.7), P<.001
HF + HF symptoms	5.6 (4.0, 7.9)	14% (28.7%), P=.63	Not available
HF + EF	3.9 (2.7, 5.6)	40% (22.8%), P=.08	Not available
HF + HF symptoms + EF	3.4 (2.3, 5.0)	47% (20.7%), P=.02	Not available
HF + HF symptoms + EF + covariates	2.9 (2.0, 4.2)	55% (18.1%), P=.002	Not available

Abbreviations: SE, Standard Error; HR, hazard ratio; CI, confidence intervals; BADL-IADL, basic and instrumental activities of daily living; CHS, Cardiovascular Health Study; EF, ejection fraction; HF, heart failure; UO, universal health outcome

[*] Two year death estimates are from Cox models; other estimates are from cross sectional regression models. Heart failure-related symptoms and impairments were not available in Health ABC. Self-rated health ranged from 1 = excellent to 5 = poor. BADL-IADL functioning was the number of basic and instrumental ADLs that participants reported having difficulty with or were unable to perform (range, 0 to 12 in CHS; 0–9 in Health ABC).

[†] The initial Beta (β) coefficient for each universal health outcome can be interpreted as the effect of the disease on the universal health outcome; i.e. the difference in the universal health outcome among those with vs. without heart failure. For example, for CHS, the β coefficient for BADL-IADL functioning is .918 meaning that persons with HF do not do, or perform with difficulty, almost one more BADL-IADL than those without HF.

[‡] This is the percent change in the regression coefficient for heart failure when the disease-related symptoms/impairments and the covariates are added to the model. The percentage change can be interpreted as the amount of the effect of heart failure on the universal health outcomes that is contributed by the heart failure-related symptoms/impairment(s).

[§] CHS heart failure symptom score (0 to 3) - sleeping with pillows, awakening with shortness of breath, and swelling of ankles.

[¶] Ejection fraction categorized by CHS investigators as ≥ 55%; 45–54%; <45%.

[#] Covariates included age, gender, race, social support, education, smoking, depressive symptoms, and Functional Comorbidity Index score with cardiovascular diseases removed.

** Hazard ratios and 95% confidence intervals for death over two years.

Table 3

Amount of Association between COPD and Universal Health Outcomes Accounted for by Disease-related Symptoms and Impairments in Older Adults

	Cardiovascular Health Study		Health ABC	
Universal health outcome models*	**Effect of COPD on UO**	**% of COPD effect on UO contributed by symptoms/ impairment(s)**	**Effect of COPD on UO**	**% of COPD effect on UO contributed by symptoms/ impairment(s)**
	β (SE)†, P-Value	**(SE), P-Value‡**	**β (SE), P-Value**	**(SE), P-Value**
Self-rated health (excellent to poor)				
COPD alone	.556 (.045), P<.001	---	.393 (.069), P<.001	---
COPD + ATS dyspnea scale§	.258 (.044)	54% (6.5%), P<.001	.142 (.068)	64% (11.0%), P<.001
COPD + FEV1¶	.438 (.046)	21% (6.9%), P=.002	.274 (.070)	30% (11.4%), P=.009
COPD + ATS dyspnea + FEV1	.215 (.045)	61% (6.6%), P<.001	.089 (.069)	77% (11.1%), P<.001
COPD + ATS dyspnea + FEV1 + covariates#	.176 (.042)	68% (6.1%), P<.001	.016 (.066)	96% (10.6%), P<.001
No. BADL-IADLs not performed or performed with difficulty				
COPD alone	.411 (.046), P<.001	---	.651 (.115), P<.001	---
COPD + ATS dyspnea scale	.119 (.045)	71% (7.2%), P<.001	.320 (.115)	51% (16.0%), P=.001
COPD + FEV1	.283 (.047)	31% (7.6%), P<.001	.601(.117)	8% (17.3%), P=.64
COPD + ATS dyspnea+ FEV1	.065 (.045)	84% (7.2%), P<.001	.328(.117)	50% (16.3%), P=.002
COPD + ATS dyspnea + FEV1 + covariates	.084 (.043)	80% (6.8%), P<.001	.190 (.117)	71% (16.0%), P<.001
Death over two years**	HR (95% Cl)			
COPD alone	3.1 (2.2, 4.2), P<.001	---	2.2 (1.4, 3.6), P=.001	---
COPD + ATS dyspnea scale	2.0 (1.5, 2.9)	33% (19.2%), P=.09	1.8 (1.1, 3.0)	19% (34.9%), P=.59
COPD + FEV1	2.4 (1.8, 3.4)	21% (20.8%), P=.31	1.8 (1.1, 2.9)	20% (34.3%), P=.56
COPD + ATS dyspnea + FEV1	1.8 (1.3, 2.6)	40% (18.7%), P=.03	1.5 (0.9, 2.6)	30% (34.5%), P=.38
COPD + ATS dyspnea + FEV1 + covariates	1.6 (1.1, 2.3)	48% (17.8%), P=.007	(0.6, 1.9)	52% (35.0%), P=.14

Abbreviations: SE, Standard Error; CI, confidence intervals; ATS, American Thoracic Society; BADL-IADL, basic and instrumental activities of daily living; CHS, Cardiovascular Health Study; COPD, chronic obstructive pulmonary disease; FEV1, Forced expiratory volume in one second; HR, hazard ratio; UO, Universal health outcome.

*Two year death estimates are from Cox models; other estimates are from cross sectional regression models. Self-rated health ranged from 1 = excellent to 5 = poor. BADL-IADL functioning was the number of basic and instrumental activities of daily living that participants reported having difficulty with or were unable to perform (range, 0 to 12 in CHS and 0 to 9 in Health ABC).

†The initial Beta (β) coefficient for each universal health outcome can be interpreted as the difference for those with vs. without COPD. For example, the β coefficient for BADL-IADL functioning in CHS is 0.411 meaning that persons with COPD do not do, or perform with difficulty, almost one half more ADL than those without COPD.

‡This is the percent change in the regression coefficient for COPD when the disease-related symptoms/impairments and the covariates are added to the model. The percentage change can be interpreted as the amount of the effect of COPD on the universal outcome that is contributed by the COPD-related symptoms/impairment(s).

[§] ATS dyspnea scale used in CHS (0 = no dyspnea to 5 = too breathless to leave the house or breathless on dressing). A modified 0–3 dyspnea scale was used for Health ABC.

[¶] FEV1 was correlated (>.50) with forced vital capacity (FVC) and FEV1/FVC ratio. FEV1 was chosen as the spirometry measure because it is less dependent on effort and cognition than FVC.

[#] Covariates included age, gender, race, social support, education, smoking, depressive symptoms, and comorbidity index with pulmonary diseases removed.

[**] Hazard ratios and 95% confidence intervals for death over two years

Table 4

Amount of Association between Osteoarthritis and Universal Health Outcomes Accounted for by Disease-related Symptoms in Older Adults

	Cardiovascular Health Study		Health ABC	
Universal health outcome models*	**Effect of Osteoarthritis on UO**	**% of Osteoarthritis effect on UO attributed to symptoms**	**Effect of Osteoarthritis on UO**	**% of Osteoarthritis effect on UO attributed to symptoms**
	β (SE), P-Value†	**(SE)‡, P-Value**	**β (SE), P-Value**	**(SE), P-Value**
Self-rated health (excellent to poor)				
Osteoarthritis alone	.376 (.025), P<.001	---	.249 (.041), P<.001	---
Osteoarthritis + pain§	.264 (.026)	30% (4.3%), P<.001	.103 (.042)	59% (7.4%), P<.001
Osteoarthritis + pain + covariates¶	.157 (.024)	58% (3.9%), P<.001	.115 (.039)	54% (6.8%), P<.001
No. BADL-IADLs not performed or performed with difficulty				
Osteoarthritis alone	.483 (.035), P<.001	---	.345 (.072), P<.001	---
Osteoarthritis + pain	.275 (.037)	43% (5.7%), P<.001	.134 (.074)	61% (12.3%), P<.001
Osteoarthritis + pain + covariates	.137 (.036)	72% (5.5%), P<.001	.135 (.072)	61% (12.0%), P<.001
Death over two years #,**	HR (95% CI)			
Osteoarthritis alone	0.9 (0.7,1.2), P=.41	---	0.5 (0.3, 1.0), P=.04	---

Abbreviations: SE, standard error; HR, hazard ratio; CI, confidence intervals; BADL-IADL, basic and instrumental activities of daily living; CHS, Cardiovascular Health Study; UO, universal health outcome

*Two year death estimates are from Cox models; other estimates are from cross sectional regression models. Self-rated health ranged from 1 = excellent to 5 = poor. BADL-IADL functioning was the number of basic and instrumental activities of daily living that participants reported having difficulty with or were unable to perform (range, 0 to 12 in CHS and 0–9 in Health ABC).

†The initial Beta (β) coefficient for each universal health outcome can be interpreted as the difference for those with vs. without osteoarthritis. For example, the β coefficient for BADL-IADL functioning in CHS is .483 meaning that persons with osteoarthritis do not do, or perform with difficulty, almost one half more BADL-IADL than those without osteoarthritis.

‡This is the percent change in the regression coefficient for osteoarthritis when the disease-related symptoms and the covariates are added to the model. The percentage change can be interpreted as the amount of the effect of osteoarthritis on the universal health outcome that is accounted for by the number of joint sites affected by pain.

§Number of joint sites with self-reported pain (0–8 in CHS and 0–7 in Health ABC). The correlation between the total number of pain sites and localized pain sites (i.e. upper extremity, lower extremity, back) was ≥ 0.50 in CHS and ≥ 0.30 in Health ABC. The percent change in coefficient was similar for the total pain site score as for the three categories of pain site scores.

¶Covariates included age, gender, race, social support, education, smoking, depressive symptoms, and comorbidity index with osteoarthritis removed.

#Hazard ratios and 95% confidence intervals for death over two years.

**Osteoarthritis was not associated with increased risk of death in either cohort so disease-related symptom models were not applicable.

Table 5

Amount of Association between Cognitive Impairment and Universal Health Outcomes Accounted for by Disease-related Impairments in Two Cohorts of Older Adults

	Cardiovascular Health Study		Health ABC	
Universal health outcome models*	**Effect of cognitive impairment on UO**	**% of cognitive impairment effect on UO contributed by impairment(s)**	**Effect of cognitive impairment on UO**	**% of cognitive impairment effect on UO contributed by impairment(s)**
	β (SE) P-Value†	**(SE)‡**	**β (SE), P-Value**	**(SE), P-Value**
Self-rated health (excellent to poor)				
Cognitive impairment alone§	.308 (.050), P<.001	---	.095 (.089), P=.28	---
Cognitive impairment + DSST¶	.016 (.050)	95% (8.5%), P<.001	Not applicable	
Cognitive impairment + DSST + covariates#	.078 (.047)	75% (8.0%), P<.001	Not applicable	
No. BADL-IADLs not performed or performed with difficulty				
Cognitive impairment alone	.488 (.065), P<.001	---	P=.02.357 (.149),	---
Cognitive impairment + DSST	.267 (.067)	45% (10.3%), P<.001	.032 (.150)	91%(24.8%), P<.001
Cognitive impairment + DSST+ covariates	.188 (.063)	61% (9.6%), P<.001	.040 (.147)	89% (24.3%), P<.001
Death over two years **	HR (95% CI)			
Cognitive impairment alone	3.5 (2.5,5.0), P<.001	---	3.2 (2.0, 5.0), P<.001	---
Cognitive impairment + DSST	1.9 (1.3, 2.8)	46% (18.3%), P=.01	1.8 (1.1, 2.8)	44% (24.5%), P=.07
Cognitive impairment + DSST + covariates	1.5 (1.0, 2.2)	58% (16.8%), P<.001	1.5 (0.9, 2.5)	52% (23.8%), P=.03

Abbreviations: SE, standard error; HR, hazard ratio; CI, confidence intervals; CHS, Cardiovascular Health Study; BADL-IADL, basic and instrumental activities of daily living; DSST, Digit Symbol Substitution Test; UO, universal health outcome.

*Two year death estimates are from Cox models; other estimates are from cross sectional regression models. Self-rated health ranged from 1 = excellent to 5 = poor. BADL-IADL functioning was the number of basic and instrumental activities of daily living that participants reported having difficulty with or were unable to perform (range, 0 to 12 in CHS and 0–9 in Health ABC).

†The initial Beta (β) coefficient for each universal health outcome can be interpreted as the difference for those with vs. without cognitive impairment. For example, the β coefficient for BADL-IADL functioning in CHS is 0.488 meaning that persons with cognitive impairment do not perform, or perform with difficulty, one half more BADL-IADL than those without cognitive impairment.

‡This is the percent change in the regression coefficient for cognitive impairment when the disease-related impairment and the covariates are added to the model. The percentage change can be interpreted as the amount of the effect of cognitive impairment on the universal health outcomes that is accounted for by the disease-specific impairment.

§Cognitive impairment not associated with self-rated health in Health ABC so disease-related impairment models not applicable.

¶Assessed by Digit Symbol Substitution Test, a measure of psychomotor speed and executive function; scores range from 0–90.

#Covariates included age, gender, race, social support, education, smoking, depressive symptoms, and comorbidity index with cognitive impairment removed.

**Hazard ratios and 95% confidence intervals for death over two years.