Effect of Chronic Disease–Related Symptoms and Impairments on Universal Health Outcomes in Older Adults

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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: The Cardiovascular Health Study (CHS) and the Health, Aging and Body Composition Study (Health ABC).

PARTICIPANTS: Five thousand six hundred fifty-four CHS members 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 (ADLs and IADLs), and death. Disease-related symptoms and impairments included HF symptoms and ejection fraction (EF) for HF, Dyspnea Scale and forced expiratory volume in 1 second for COPD, joint pain for osteoarthritis, and executive function for cognitive impairment.

RESULTS: The diseases were associated with the universal health outcomes ($P < .001$) except osteoarthritis with death (both cohorts) and cognitive impairment with self-rated health (Health ABC). Symptoms and impairments accounted for 30% or more of each disease's effect on the universal health outcomes. In CHS, for example, HF was associated with one fewer (0.918) ADL and IADL performed without difficulty than no HF; HF symptoms accounted for 27% of this effect and EF for only 5%. The hazard ratio for death with HF was 6.5 (95% confidence interval = 4.7–8.9) with EF accounting for 40% and HF symptoms for only 14%.

CONCLUSION: Disease-related symptoms and impairments accounted for much of the significant associations between the four chronic diseases and the universal health outcomes. Results support considering universal health outcomes as common metrics across diseases in clinical decision-making, perhaps by targeting the disease-related symptoms and impairments that contribute most strongly to the effect of the disease on the universal health outcomes.
J Am Geriatr Soc 59:1618–1627, 2011.

Key words: chronic diseases; universal health outcomes; self-reported outcomes; clinical decision-making

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 end points, increasingly with multiple pharmacological and nonpharmacological 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 individuals 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 most chronic diseases affect. Determining the effect of treatments on these universal health outcomes would facilitate the identification of those treatments with the greatest overall effects on individuals' health.

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DOI: 10.1111/j.1532-5415.2011.03576.x

0002-8614/11/$15.00

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, and other self-reported outcomes. 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 report that they are concerned about specific diseases because of their effect on these cross-disease, universal health outcomes.[22] Although there is no single set of universal health outcomes, activity of daily living (ADL) 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, ADLs, self-rated health, and other self-reported outcomes, 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 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 and impairments, the usual therapeutic targets or measures of disease severity, are the focus of disease-specific decision-making. If disease-related symptoms and impairments account for much of the effect of chronic diseases on universal health outcomes, and individuals endorse the central importance of universal health outcomes, 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, whether and to what extent disease-related symptoms and impairments accounted for significant associations between chronic diseases and universal health outcomes was determined. Four common chronic conditions and three representative universal health outcomes were studied.

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). It was decided to study two cohorts to assess the robustness of results. These two community-based cohorts were chosen because they have a wealth of disease-related symptom and impairment data. The CHS cohort was recruited from a sex- 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 aged 65 and older, not living in an institution, expected to remain in the area for 3 years, and able to provide 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 5,888 participants. The 5,654 cohort members with data for at least one of the 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, aged 70 to 79 who were eligible and consented.[24] Eligible participants reported no life-threatening cancers or difficulty walking one-quarter of a mile, climbing 10 steps, or performing ADLs and instrumental ADLs (IADLs) at baseline. Of 3,075 participants, 2,733 (89%) had a Year 5 (2001/02) assessment; the 2,706 participants with data for at least one of the analytical models were included in the current study. The cohorts were followed every 6 months. All participants provided informed consent; respective institutional review board approvals were received. The Yale School of Medicine's human investigation committee approved the study.

Data

Sociodemographic, functional, and health data were obtained from person-level interviews and clinical examinations. Information on diseases was collected using 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, were heart failure (HF), chronic obstructive pulmonary disease (COPD), osteoarthritis, and cognitive impairment or 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 (SDs) below the strata mean for education (<high school; ≥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 (subjective complaints) and impairments (physiological or other derangements such as ejection fraction (EF)) chosen for study were those considered to result from the disease and represent therapeutic targets or measures of disease severity. For the CHS cohort, disease-related symptoms and impairments for HF included the CHS HF symptom score[29] and EF. HF-related impairments were not available in Health ABC. The candidate COPD-related impairments included the American Thoracic Society (ATS) Dyspnea Scale[30] and spirometry measures, which

included forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and FEV_1/FVC. The candidate osteoarthritis impairments included total number of pain sites and site-specific pain (upper extremity, lower extremity, and back). The cognitive-related impairment was defined according to results on the Digit Symbol Substitution Test (DSST), a measure of processing speed and executive function.[31] 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 were self-rated health, ADL and 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 five-level self-reported health measure ranged from excellent (1) to poor (5) in both cohorts. ADL and IADL functioning, a commonly used measure of disability, was assessed using a scale that ranged from 0 to 12 in CHS and 0 to 9 in Health ABC based on the number of ADLs and IADLs with which the participant reported having difficulty or could not perform.[32,33] The 12 activities included in CHS were walking, transferring (out of bed), eating, toileting, dressing, bathing, light housework, heavy housework, shopping, preparing meals, paying bills, and using the telephone. The activities in Health ABC were similar except eating, toileting, paying bills, and using the telephone were not asked about but any of working, volunteering, or providing care was asked about.

Death was ascertained primarily by interviews with next of kin.

Descriptive and Covariate Data

The covariates were age, sex, race, education, smoking status, social support, depressive symptoms assessed with the Center for Epidemiologic Studies Depression Scale (10 items, range 0–30),[34] and comorbidity. Comorbidity was measured using the Functional Comorbidity Scale, which includes arthritis, osteoporosis, asthma, COPD, angina pectoris, HF, myocardial infarction, neurological disease, stroke, peripheral vascular disease, diabetes mellitus, upper gastrointestinal disease, depression, anxiety, visual impairment, hearing impairment, degenerative disc disease, and obesity.[35] Cardiovascular disease, 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 and 6 had the best available symptom, impairment, and universal outcome data. For both cohorts, death was ascertained over the 2 years after the disease ascertainment.

Multiple linear regression was used 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 FEV_1 and the ATS Dyspnea Scale was 0.22; all other correlations were less than 0.20. Multicollinearity was assessed by calculating variance inflation factors for all variables included in the regression models. Variables with values greater than 5 were excluded from the regression models.

In the multiple regression models, the universal health outcome was the dependent variable. The independent variables were disease status (1 = present, 0 = absent), disease-related impairments, and covariates. Models were fitted hierarchically to the data in the following sequence: disease status alone; disease status adjusted for disease-related impairments, singly and then in combination; and disease status adjusted for disease-related impairments and covariates. To estimate the level of the association between a disease and a universal health outcome that the disease-related impairments accounted for, the percentage change in the regression coefficients for disease status between the models unadjusted for disease-related impairments (β) and the adjusted model (β^*) were calculated. Specifically, percentage change was calculated as $[(\beta - \beta^*)/\beta] \times 100\%$, so that positive values represent the level of a disease effect on the universal health outcome attributed to the impairment. The variance of the percentage change was estimated using the Delta method and was used to assess its significance (percentage change/standard error is approximately normally distributed).[36] Regression diagnostics were used to assess the fit of the multiple regression models.

Time to death was analyzed using the Cox model using the same approach as for the multiple regression models. Percentage 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 using graphical techniques and examination of residuals.

RESULTS

Characteristics of the cohorts are presented in Table 1. The Health ABC cohort was older and had a higher percentage of blacks than the CHS cohort. The mean age of the CHS cohort was 72.8 ± 5.6, 57.5% were female, and 14.4% were black. The mean age of the Health ABC cohort at Year 5 was 77.6 ± 2.9, 53% were female, and 39.8% were black. With the exception of more ADL and IADL difficulties and a lower prevalence of osteoarthritis in Health ABC, the two cohorts were similar in terms of 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 that disease-related symptoms and EF accounted for in CHS varied for the universal health outcomes (Table 2). For example, HF symptoms accounted for 25% of the effect

Table 1. Characteristics of the Two Cohorts*

Characteristic	CHS N = 5,654†	Health 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)
<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
Number of 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
Number of ADLs and instrumental ADLs 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 2 years of follow-up, n (%)	282 (5.1)	217 (8.2)
Heart failure, n (%)	262 (4.6)	141 (5.3)
Chronic obstructive pulmonary disease, 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)

*The Cardiovascular Health Study (CHS) cohort included the original and the African-American cohort as described in Methods. Characteristics are at baseline for the original cohort and the first follow-up for the African-American cohort for CHS and at Year 5 to 6 for the Health, Aging and Body Composition Study (Health ABC) cohort.
†N reflects the number of participants included in at least one analysis model.
‡Range 6–24, with higher scores indicating lower support.
§Range 1 = excellent to 5 = poor.
SD = standard deviation; ADL = activity of daily living.

of HF on self-rated health and 27% on ADL and IADL functioning but did not account for the association with death. Conversely, EF accounted for 40% of the association of HF with death ($P = .08$) but did not contribute to the association with self-rated health or ADL and IADL functioning. The HF-related symptoms and EF were unavailable in Health ABC.

The associations between COPD, osteoarthritis, and cognitive impairment and the universal health outcomes, and the contribution of the disease-related symptoms and impairments to these associations, are displayed in Tables 3 to 5. Dyspnea contributed more than 50% of COPD's effect on self-rated health and ADL and IADL functioning and 33% of COPD's effect on death ($P = .09$) (Table 3). Although not reaching statistical significance, FEV_1 accounted for 20% to 30% of COPD's effect on each universal health outcome except for ADL and IADL functioning in Health ABC. Osteoarthritis was not associated with a greater risk of death (Table 4). Pain accounted for 30% to 70% of the effect of osteoarthritis on self-rated health and ADL and IADL function (Table 4). Cognitive impairment had a strong association with ADL and IADL function and death in both cohorts (Table 5). DSST accounted for 44% to 95% of these effects (Table 5).

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, ADL and IADL functioning, and death confirm previous findings in older adults.[12–18,20–22,37–40] The current study adds to the understanding of the relationship between chronic diseases and universal health outcomes by determining how much of the disease-related symptoms and impairments that constitute therapeutic targets and indicators of disease severity account for the association.

The percentage of disease association with the universal health outcomes attributed to disease-related symptoms and impairments ranged from almost one-third to more than 95% for the four diseases. The amounts that the symptoms and impairments contributed 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 and 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 more or less of the relationship for some universal outcome than for others.

HF symptoms accounted for the largest amount of the effect of HF on self-rated health and ADL and IADL functioning, whereas low 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 EF[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 this possibility in the current study could not be addressed. HF-related symptoms and impairments were not assessed in Health ABC, so the relationships could not be corroborated 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 FEV_1 in Health ABC may reflect the smaller sample size. There is no consensus on the best spirometry measure for airflow limitations. FEV_1, which is highly correlated with FEV_1/FVC, is more reproducible[44] and less affected by effort and cognition than FVC and has been used as a measure of decline in lung function in observational studies.[38,44,45] The current 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. Osteoarthritis-related impairments such as range of motion or radiographic abnormalities cannot be commented on because they were completed on only a small subset of Health ABC members. Although it cannot be ensured that the pain reported was due to osteoarthritis, only joint sites were included. Although it is likely that arthritic involvement of specific joints has unique effects,[46] 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.

Table 2. Level of Association Between Heart Failure and Universal Health Outcomes That Disease-Related Symptoms and Impairments Accounted for in Older Adults

	Cardiovascular Health Study					Health ABC		
	Effect of HF on UO			Effect of HF on UO Contributed by Symptoms and Impairments, %		Effect of HF on UO		
UO Model*	β (SE)†	HR (95% CI)‡	*P*-Value	% (SE)§	*P*-Value	β (SE)†	HR (95% CI)‡	*P*-Value
Self-rated health (excellent to poor)			<.001					
HF alone	0.946 (0.066)			—		0.426 (0.089)		<.001
HF+HF symptoms‖	0.709 (0.066)			25 (8.4)	.003	Not available		
HF+EF#	0.852 (0.069)			10 (9.2)	.28	Not available		
HF+HF symptoms+EF	0.627 (0.068)			34 (8.3)	<.001	Not available		
HF+HF symptoms+EF+covariates**	0.489 (0.063)			48 (7.4)	<.001	Not available		
Number of ADLs and IADLs not performed or performed with difficulty			<.001					
HF alone	0.918 (0.073)			—		0.449 (0.147)		.002
HF+HF symptoms	0.670 (0.073)			27 (9.3)	.004	Not available		
HF+EF	0.869 (0.076)			5 (10.4)	.63	Not available		
HF+HF symptoms+EF	0.631 (0.076)			31 (9.4)	.001	Not available		
HF+HF symptoms+EF+covariates	0.493 (0.071)			46 (8.5)	<.001	Not available		
Death over 2 years**			<.001					
HF alone		6.5 (4.7–8.9)		—			3.0 (1.9–4.7)	<.001
HF+HF symptoms		5.6 (4.0–7.9)		14 (28.7)	.63		Not available	
HF+EF		3.9 (2.7–5.6)		40 (22.8)	.08		Not available	
HF+HF symptoms+EF		3.4 (2.3–5.0)		47 (20.7)	.02		Not available	
HF+HF symptoms+EF+covariates		2.9 (2.0–4.2)		55 (18.1)	.002		Not available	

* Two-year death estimates are from Cox models; other estimates are from cross-sectional regression models. Heart failure (HF)-related symptoms and impairments were not available in the Health, Aging and Body Composition Study (Health ABC). Activity of daily living (ADL) and instrument ADL (IADL) functioning was the number of ADLs and IADLs that participants reported having difficulty with or were unable to perform (range 0–12 in CHS and 0–9 in Health ABC).

† The initial β coefficient for each universal health outcome can be interpreted as the effect of the disease on the universal health outcome (the difference in the universal health outcome between those with and without heart failure. For example, for CHS, β for ADL and IADL functioning was 0.918, meaning that persons with HF do not perform, or perform with difficulty, almost one more ADL and IADL than those without HF.

‡ Hazard ratios (HRs) and 95% confidence intervals (Cis) for death over 2 years.

§ This is the percentage change in the regression coefficient for heart failure when the disease-related symptoms and impairments and the covariates are added to the model. The percentage change can be interpreted as the amount of the effect of HF on the universal health outcomes that the HF-related symptoms and impairments contribute.

‖ CHS heart failure symptom score (0 to 3)—sleeping with pillows, awakening with shortness of breath, and swelling of ankles.

Ejection fraction categorized in CHS as ≥55%, 45-54%, <45%.

** Covariates were age, sex, race, social support, education, smoking, depressive symptoms, and Functional Comorbidity Index score with cardiovascular disease removed.

SE = standard error; EF = ejection fraction; UO = universal health outcome.

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 ADL and IADL functioning outcome. DSST,[31] a measure of executive function and processing speed, contributed much of the effect of cognitive impairment on ADL and IADL functioning and death, as has been shown previously.[47–50] The contribution of other cognitive deficits, including short-term memory, could not be determined in the current study but has been assessed previously, with variable results.[39,51] Reliability of self-reported outcomes such as self-rated health and ADL and IADL functioning may be limited in individuals with cognitive impairment. Previous work has shown that, although there is good agreement, cognitively impaired individuals tend to overestimate their functional abilities relative to proxy reports, suggesting that the contribution of cognitive impairment to ADL and IADL functioning may have been underestimated.[52]

Table 3. Level of Association Between Chronic Obstructive Pulmonary Disease (COPD) and Universal Health Outcomes (UOs) That Disease-Related Symptoms and Impairments in Older Adults Accounted For

	CHS				Health ABC			
	Effect of COPD on UO			COPD Effect on UO That Symptoms and Impairments Contributed[†]	Effect of COPD on UO			COPD Effect on UO That Symptoms and Impairments Contributed[†]
UO Model[*]	β (SE)[†]	HR (95% CI)[§]	*P*-Value	% (SE)[‡] *P*-Value	β (SE)[†]	HR (95% CI)[§]	*P*-Value	% (SE)[‡] *P*-Value
Self-rated health (excellent to poor)			<.001				<.001	
COPD alone	0.556 (0.045)			—	0.393 (0.069)			—
COPD+ATS Dyspnea Scale[‖]	0.258 (0.044)			54 (6.5) <.001	0.142 (0.068)			64 (11.0) <.001
COPD+FEV_1[#]	0.438 (0.046)			21 (6.9) .002	0.274 (0.070)			30 (11.4) .009
COPD+ATS Dyspnea Scale+FEV_1	0.215 (0.045)			61 (6.6) <.001	0.089 (0.069)			77 (11.1) <.001
COPD+ATS Dyspnea Scale+FEV_1+covariates[**]	0.176 (0.042)			68 (6.1) <.001	0.016 (0.066)			96 (10.6) <.001
Number of ADLs and IADLs not performed or performed with difficulty			<.001				<.001	
COPD alone	0.411 (0.046)			—	0.651 (0.115)			—
COPD+ATS Dyspnea Scale	0.119 (0.045)			71 (7.2) <.001	0.320 (0.115)			51 (16.0) .001
COPD+FEV_1	0.283 (0.047)			31 (7.6) <.001	0.601 (0.117)			8 (17.3) .64
COPD+ATS Dyspnea Scale+FEV_1	0.065 (0.045)			84 (7.2) <.001	0.328 (0.117)			50 (16.3) .002
COPD+ATS Dyspnea Scale+FEV_1+covariates	0.084 (0.043)			80 (6.8) <.001	0.190 (0.117)			71 (16.0) <.001
Death over 2 years[§]	HR (95% CI)		<.001				*P*=.001	
COPD alone		3.1 (2.2–4.2)		—		2.2 (1.4–3.6)		—
COPD+ATS Dyspnea Scale		2.0 (1.5–2.9)		33 (19.2) .09		1.8 (1.1–3.0)		19 (34.9) .59
COPD+FEV_1		2.4 (1.8–3.4)		21 (20.8) .31		1.8 (1.1–2.9)		20 (34.3) .56
COPD+ATS Dyspnea Scale+FEV_1		1.8 (1.3–2.6)		40 (18.7) .03		1.5 (0.9–2.6)		30 (34.5) .38
COPD+ATS Dyspnea+FEV_1+covariates		1.6 (1.1–2.3)		48 (17.8) .007		(0.6–1.9)		52 (35.0) .14

[*] Two-year death estimates are from Cox models; other estimates are from cross-sectional regression models. Activity of daily living (ADL) and instrumental ADL (IADL) functioning was the number of ADLs and IADLs that participants reported having difficulty with or were unable to perform (range 0–12 in the Cardiovascular Health Study (CHS) and 0–9 in the Health, Aging and Body Composition Study (Health ABC)).

[†] The initial β coefficient for each UO can be interpreted as the difference between those with and without chronic obstructive pulmonary disease (COPD). For example, the β coefficient for ADL and IADL functioning in CHS is 0.411, meaning that persons with COPD do not perform, or perform with difficulty, almost one-half more ADLs than those without COPD.

[‡] The percentage change in the regression coefficient for COPD when the disease-related symptoms and impairments and the covariates are added to the model. The percentage change can be interpreted as the level of the effect of COPD on the UO that the COPD-related symptoms and impairments contribute.

[§] Hazard ratios (HRs) and 95% confidence intervals (CIs) for death over 2 years.

[‖] American Thoracic Society (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.

[#] Forced expiratory volume in 1 second) FEV_1) was correlated (>.50) with forced vital capacity (FVC) and FEV_1/FVC ratio. FEV_1 was chosen as the spirometry measure because it is less dependent on effort and cognition than FVC.

[**] Covariates were age, sex, race, social support, education, smoking, depressive symptoms, and comorbidity index with pulmonary diseases removed.

SE = standard error.

Other of the methods used require comment. The use of two large community-based cohorts with disease and health outcome data was a strength. Diagnostic accuracy is always a concern in epidemiological studies. It is likely that the combination of medical record or claims data plus self-report enhanced reliability. The similar, albeit not identical, relationships in the two cohorts strengthen confidence in the findings. Although 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

Table 4. Level of Association Between Osteoarthritis and Universal Health Outcomes That Disease-Related Symptoms Accounted for in Older Adults

	Cardiovascular Health Study				Health ABC			
	Effect of Osteoarthritis on UO			Osteoarthritis Effect on UO Attributed to Symptoms[†]	Effect of Osteoarthritis on UO			Osteoarthritis Effect on UO Attributed to Symptoms[†]
Universal Health Outcome Models[*]	β (SE)[†]	HR (95% CI)[#]	*P*-Value	% (SE)[‡] *P*-Value	β (SE)[†]	HR (95% CI)[#]	*P*-Value	% (SE)[‡] *P*-Value
Self-rated health (excellent to poor)			<.001				<.001	
Osteoarthritis alone	0.376 (0.025)			—	0.249 (0.041)			—
Osteoarthritis+pain[§]	0.264 (0.026)			30 (4.3) <.001	0.103 (0.042)			59 (7.4) <.001
Osteoarthritis+pain+covariates[‖]	0.157 (0.024)			58 (3.9) <.001	0.115 (0.039)			54 (6.8) <.001
Number of ADLs and IADLs not performed or performed with difficulty			<.001				<.001	
Osteoarthritis alone	0.483 (0.035)			—	0.345 (0.072)			—
Osteoarthritis+pain	0.275 (0.037)			43 (5.7) <.001	0.134 (0.074)			61 (12.3) <.001
Osteoarthritis+pain+covariates	0.137 (0.036)			72 (5.5) <.001	0.135 (0.072)			61 (12.0) <.001
Death over 2 years[**]								
Osteoarthritis alone		0.9 (0.7–1.2)	.41	—		0.5 (0.3–1.0)	.04	—

[*] Two-year death estimates are from Cox models; other estimates are from cross-sectional regression models. Activity of daily living (ADL) and instrumental ADL (IADL) functioning was the number of ADLs and IADLs that participants reported having difficulty with or were unable to perform (range 0–12 in the Cardiovascular Health Study (CHS) and 0–9 in the Health, Aging and Body Composition Study (Health ABC)).

[†] The initial β coefficient for each universal health outcome (UO) can be interpreted as the difference between those with and without osteoarthritis. For example, the β coefficient for ADL and IADL functioning in CHS is 0.483, meaning that persons with osteoarthritis do not perform, or perform with difficulty, almost one half more ADL and IADLs than those without osteoarthritis.

[‡] Percentage 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 UO that the number of joint sites affected by pain account for.

[§] 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 (upper extremity, lower extremity, back) was ≥0.50 in CHS and ≥0.30 in Health ABC. The percentage change in coefficient was similar for the total pain site score as for the three categories of pain site scores.

[‖] Covariates were age, sex, race, social support, education, smoking, depressive symptoms, and comorbidity index with osteoarthritis removed.

[#] Hazard ratios (HRs) and 95% confidence intervals (CIs) for death over 2 years.

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

SE = standard error.

heart failure symptoms would have had a stronger effect on current ADL and IADL functioning than function ascertained 6 months later when the universal health outcomes were next ascertained in the cohorts. Because temporal sequence and establishment of causality can be determined only longitudinally, the current analyses ascertained only 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]

The percentage effects, based on the regression coefficients, were reported to determine how much of the association between disease and universal health outcome the disease-related symptoms and impairments accounted for.[53,54] This approach is similar to determining the mediating effect of the symptoms and impairments.[53,54] The focus was on the changes that occurred in the association between disease and universal outcome (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, it is likely that there 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. 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 that the symptoms and impairments accounted for cannot be determined from the current analyses, but given the magnitude of the effects, it is unlikely that the relationships would be eliminated by controlling for treatments.

Some of the disease-related impairments such as FEV_1 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. Al-

Table 5. Level of Association Between Cognitive Impairment and Universal Health Outcomes That Disease-Related Impairments Accounted for in Two Cohorts of Older Adults

	Cardiovascular Health Study				Health ABC			
	Effect of Cognitive Impairment on UO			Cognitive Impairment Effect on UO That Impairments Contributed†	Effect of Cognitive Impairment on UO			Cognitive Impairment Effect on UO That Impairments Contributed†
Universal Health Outcome Models*	β (SE)†	HR (95% CI)**	*P*-Value	% (SE) *P*-Value‡	β (SE)†	HR (95% CI)	*P*-Value	% (SE)‡ *P*-Value
Self-rated health (excellent to poor)			<.001				.28	
Cognitive impairment alone§	0.308 (0.050)			—	0.095 (0.089)			—
Cognitive impairment+DSST‖	0.016 (0.050)			95 (8.5) <.001	Not applicable			
Cognitive impairment+DSST+covariates#	0.078 (0.047)			75 (8.0) <.001	Not applicable			
No. BADL-IADLs not performed or performed with difficulty			<.001				.02	
Cognitive impairment alone	0.488 (0.065)			—	0.357 (0.149)			—
Cognitive impairment+DSST	0.267 (0.067)			45 (10.3) <.001	0.032 (0.150)			91 (24.8) <.001
Cognitive impairment+DSST+covariates	0.188 (0.063)			61 (9.6) <.001	0.040 (0.147)			89 (24.3) <.001
Death over 2 years**			<.001				<.001	
Cognitive impairment alone		3.5 (2.5–5.0)		—		3.2 (2.0–5.0)		—
Cognitive impairment+DSST		1.9 (1.3–2.8)		46 (18.3) .01		1.8 (1.1–2.8)		44 (24.5) .07
Cognitive impairment+DSST+covariates		1.5 (1.0–2.2)		58 (16.8) <.001		1.5 (0.9–2.5)		52 (23.8) .03

* Two-year death estimates are from Cox models; other estimates are from cross-sectional regression models. Activity of daily living (ADL) and instrumental ADL (IADL) functioning was the number of ADLs and IADLs that participants reported having difficulty with or were unable to perform (range 0–12 in the Cardiovascular Health Study (CHS) and 0–9 in the Health, Aging and Body Composition Study (Health ABC)).

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

‡ Percentage 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 UOs that the disease-specific impairment accounts for.

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

‖ Assessed according to the Digit Symbol Substitution Test (DSST), a measure of psychomotor speed and executive function (range 0–90).

Covariates were age, sex, race, social support, education, smoking, depressive symptoms, and comorbidity index with cognitive impairment removed.

** Hazard ratios (HRs) and 95% confidence intervals (CIs) for death over 2 years.

SE = standard error.

though perhaps not unique to specific diseases, the symptoms and impairments are those clinically ascribed to the diseases studied.

The current study was limited to four common chronic diseases. It is possible, and even likely, that similar relationships between diseases, disease-related symptoms and impairments, and universal health outcomes exist with most diseases. Only three universal health outcomes were investigated. 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. It is hoped that a set of reliable, valid, reproducible, clinically feasible universal health outcomes will eventually be chosen for use in clinical practice. It was decided to consider symptoms to be disease-related and to include depression as a comorbidity. The fact that symptoms can be viewed as specific to individual diseases and common across diseases and that depression is 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 between the symptoms and impairments and universal health outcomes need to be established.

It will eventually need to be determined which diseases or disease-related symptoms and 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 and impairments and on the universal health outcomes also must be determined. Although 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.[55] 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.[56] The comparative effectiveness of bronchodilators or corticosteroids at improving dyspnea, FEV_1, or function is not yet known. To acquire this evidence, and to ensure that treatment is targeted toward the most important outcome to the individual and to the disease manifestations that affect that outcome, universal health outcome domains and disease-related symptoms and 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 adults. At the population level, the potential effect of recommended treatments on universal health outcomes could be considered in disease management guidelines. At the individual level, clinical decision-making could begin with the individual prioritizing which universal outcomes (e.g., functioning vs prolonged survival) was most important. The clinician would then 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 individuals with HF for whom prolonged survival is most important, whereas 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 between, 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 adults.

ACKNOWLEDGMENTS

Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

The corresponding author had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

This research was supported by R21 AG033244 and the Yale Pepper Center (P30 AG021342), both from the National Institute on Aging, and by a Clinical and Translational Science Award (UL1 RR024139) from the National Institutes of Health. Funding for Health study is from N01AG-6-2101, N01AG-6-2103, and N01AG-6-2106. This research was also supported in part by the Intramural Research Program of the NIH, National Institute on Aging. CHS was supported by Contracts N01-HC-85079 through N01-HC-85086, N01-HC-35129, N01 HC-15103, N01 HC-55222, N01-HC-75150, N01-HC-45133 and Grant U01 HL080295 from the National Heart, Lung, and Blood Institute, with additional contribution from the National Institute of Neurological Disorders and Stroke.

Author Contributions: All authors contributed to the conceptualization of the study; interpretation of the data; and preparation, review, and approval of the manuscript. There are no conflicts of interest, including financial interests and relationships.

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

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