



Published in final edited form as:

*J Am Geriatr Soc.* 2011 September ; 59(9): 1686–1691. doi:10.1111/j.1532-5415.2011.03573.x.

## Contribution of Multiple Chronic Conditions to Universal Health Outcomes

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### Abstract

**OBJECTIVES**—To determine the relative effect of five chronic conditions on four representative universal health outcomes.

**DESIGN**—Cross-sectional.

**SETTING**—Cardiovascular Health Study.

**PARTICIPANTS**—Five thousand two hundred and ninety-eight community-living participants aged 65 and older.

**MEASUREMENTS**—Multiple regression and Cox models were used to determine the effect of heart failure (HF), chronic obstructive pulmonary disease (COPD), osteoarthritis, depression, and cognitive impairment on self-rated health, 12 basic and instrumental activities of daily living (ADLs and IADLs), six-item symptom burden scale, and death.

**RESULTS**—Each condition adversely affected self-rated health ( $P < .001$ ) and ADLs and IADLs ( $P < .001$ ). For example, persons with HF performed  $0.70 \pm 0.08$  fewer ADLs and IADLs than those without; persons with depression and persons with cognitive impairment performed  $0.59 \pm 0.04$  and  $0.58 \pm 0.06$  fewer activities, respectively, than those without these conditions. Depression, HF, COPD, and osteoarthritis were associated with  $1.18 \pm 0.04$ ,  $0.40 \pm 0.08$ ,  $0.40 \pm 0.05$ , and  $0.57 \pm 0.03$  more symptoms, respectively, in individuals with these conditions than in those without. HF (hazard ratio (HR) = 2.84, 95% confidence interval (CI) = 1.97–4.10), COPD (2.62, 95% CI = 1.94–3.53), cognitive impairment (2.05, 95% CI = 1.47–2.85), and depression (1.47, 95% CI = 1.08–2.01) were each associated with death within 2 years. Several paired combinations of conditions had synergistic effects on ADLs and IADLs. For example, individuals with HF plus depression performed 2.0 fewer activities than persons with neither condition, versus the 1.3 fewer activities expected from adding the effects of the two conditions together.

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**Author Contributions:** All authors contributed to the conceptualization of the study; interpretation of the data; and preparation, review, and approval of the manuscript.

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

**CONCLUSION**—Universal health outcomes may provide a common metric for measuring the effects of multiple conditions and their treatments. The varying effects of the conditions across universal outcomes could inform care priorities.

### Keywords

multiple chronic conditions; patient-reported outcomes; universal health outcomes

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Managing multiple conditions separately can be burdensome, even harmful.<sup>1–5</sup> This concern is particularly relevant for older adults. Multiple chronic conditions co-occur in almost 50% of persons aged 60 and older.<sup>6,7</sup> Older adults vary in which conditions or health outcomes are most important to them personally,<sup>8,9</sup> suggesting that there is no inherent hierarchy of conditions or outcomes to help simplify clinical decision-making.

Many changes will be needed to make the care of individuals with multiple chronic conditions more effective and efficient. From a practical standpoint, treatment decisions predicated on optimizing a few cross-disease outcomes may be less complex and burdensome than addressing multiple diseases and disease-specific outcomes separately. Cross-disease or universal health outcomes that reflect the important clinical effects of chronic conditions and their treatments could serve as a common metric across conditions upon which to base clinical decisions. Self-reported and universal health outcomes such as health-related quality of life and daily functioning are well established in clinical research<sup>10,11</sup> although not widely incorporated into clinical practice. Universal health outcomes such as symptom burden, functional capacity, self-rated health, and survival are among the domains included in health status measures and are outcomes that older adults deem important. Research supports the association between individual chronic conditions and these representative universal health outcomes,<sup>12–17</sup> but less is known about the relative effect of chronic conditions on these outcomes when multiple conditions are considered together, as is relevant to older adults with multiple chronic conditions. The aim of the current study was to determine the relative effect of five common chronic conditions on four representative universal health outcomes.

## METHODS

### Study Population

The Cardiovascular Health Study (CHS) cohort, a sex- and age-stratified random sample of Medicare-eligible individuals from four geographically dispersed counties, was studied.<sup>18</sup> Eligibility criteria included aged 65 and older; not living in an institution; capable of giving informed consent; not using a wheelchair; and not receiving hospice care, radiation treatment, or chemotherapy. The initial sample of 5,201 participants was recruited from 1989 to 1990; an additional 687 African Americans who met the same eligibility criteria were recruited from 1992 to 1993. Of the 5,680 participants who were alive at the first follow-up and agreed to include their data in the public data set, the 5,298 (93.3%) who had available data for chronic conditions and universal health outcomes were studied. Participants provided informed consent. Institutional review board approval was received.

### Data

Sociodemographic and health data were obtained from person-level interviews. Data on chronic conditions were collected using self-report, medical record abstraction, and Medicare claims data. The data were from CHS publicly released files.

The five chronic conditions, selected because of prevalence and morbidity in older adults, were heart failure (HF), chronic obstructive pulmonary disease (COPD), osteoarthritis,

depression, and cognitive impairment. CHS investigator-developed algorithms were used to define HF. The combination of self-report according to physician diagnosis and claims data was used for COPD. Self-report of physician-based diagnosis was used for osteoarthritis. Depression was defined as a score of 10 or higher on the Center for Epidemiologic Studies Depression Scale (CES-D) (range 0–30).<sup>19</sup> Cognitive impairment was defined using claims data for dementia or a modified Mini-Mental State Examination (3MS) score that was more than 1.5 standard deviations below the strata mean for education (<high school; high school) and race (black, other), which are criteria with a high specificity for dementia.<sup>20</sup> The five chronic conditions were categorized as present or absent.

The four representative universal health outcomes were self-rated health, basic and instrumental activity of daily living (ADL and IADL) functioning, symptom burden, and death. Self-reported health ranged from excellent (1) to poor (5). ADL and IADL score was the number of ADLs and IADLs that the participant reported difficulty performing (range 0–12; walking, transferring (out of bed), eating, toileting, dressing, bathing, light and heavy housework, shopping, preparing meals, paying bills, and using the phone). The six-item symptom burden scale, based on validated scales,<sup>16,21</sup> was created from questions throughout the interviews. Death was ascertained from medical records, obituaries, death certificates, and next-of-kin interviews.

Covariates included age, sex, race, education, smoking status, and comorbidity. Comorbidity was measured using a modified Functional Comorbidity Index score with the five conditions removed.<sup>22</sup>

### Statistical Analysis

Analyses were performed using the first follow-up because it had the best ascertainment of the five conditions and four universal health outcomes. Death was ascertained in the 2 years after the first follow-up; the other analyses were cross-sectional.

Multiple linear regression including all five chronic conditions and the covariates in the models were used to evaluate the effects of the five conditions on each of self-rated health, ADLs and IADLs, and symptom burden. Cox models were used to examine the relationship between the conditions and death. Correlations between the chronic conditions were all less than 0.10. Variance inflation factors for all variables included in the models were less than 5, suggesting that multicollinearity was not a problem.

Models were fit with the five chronic conditions and interaction terms composed of two conditions, adjusting for relevant covariates, to determine whether the effects of any paired combinations were greater than additive for any outcome. A global test of whether the interactions were collectively different from 0, suggesting the presence of significant interactions, was conducted by comparing the adjusted model with the five chronic conditions and these interactions with the adjusted model including only the chronic conditions. The *F*-test was used for the multiple linear regression models and the likelihood ratio test for the Cox models. If the global test was significant at  $P < .05$ , the significance of the separate interactions was tested at the .01 level.

Standard regression diagnostics were used to assess model fit. The proportional hazards assumption was examined in the Cox models by including time-by-covariate interaction terms.

## RESULTS

Characteristics of the cohort are presented in Table 1. The mean age was  $72.6 \pm 5.4$ ; 57.5% were female, and 14.4% were black.

The effects of the five chronic conditions on the universal health outcomes are displayed in Table 2. All five conditions were adversely associated with self-rated health ( $P < .001$ ) and ADLs and IADLs ( $P < .001$ ). Accounting for the other conditions and covariates, persons with HF performed  $0.70 \pm 0.08$  fewer activities without difficulty than persons without HF. Individuals with depression and individuals with cognitive impairment performed  $0.59 \pm 0.04$  and  $0.58 \pm 0.06$  fewer activities, respectively, than persons without these conditions. Persons with depression had  $1.18 \pm 0.04$  more symptoms than those without. Persons with HF, COPD, and osteoarthritis experienced  $0.40 \pm 0.08$ ,  $0.40 \pm 0.05$ , and  $0.57 \pm 0.03$  more symptoms, respectively, than those without each of these conditions. HF (adjusted hazard ratio (AHR) = 2.84, 95% confidence interval (CI) = 1.97–4.10), COPD (AHR = 2.62, 95% CI = 1.94–3.53), cognitive impairment (AHR = 2.05, 95% CI = 1.47–2.85), and to a lesser extent, depression (AHR = 1.47, 95% CI = 1.08–2.01) increased the risk of death.

ADL and IADL functioning was the only universal health outcome in which interactions (synergies) between two conditions demonstrated significant effects (Figure 1). HF showed a significant interaction with COPD and depression, suggesting that the combination of HF with either of these conditions was associated with a greater than additive effect on ADL and IADL performance. Depression interacted with HF, osteoarthritis, and cognitive impairment. The paired combinations of conditions with the greatest effect on function were HF with depression and cognitive impairment with depression. Individuals with HF and depression performed 2.0 fewer activities without difficulty than persons with neither condition, versus the 1.3 fewer activities expected from adding the effects of the two conditions together. Individuals with cognitive impairment and depression performed 2.1 fewer ADLs and IADLs without difficulty than persons without these two conditions, versus the 1.2 fewer activities expected from adding the effects of the two conditions together.

## DISCUSSION

The five chronic conditions contributed significantly to each universal health outcome, except osteoarthritis to death and cognitive impairment to symptom burden. These findings expand current understanding of the relationships between the individual chronic conditions and the universal health outcomes by ascertaining the relative contributions of the conditions. Although there were similarities in the contribution of the conditions across outcomes, there were differences as well.

Death and disability are health outcomes commonly used to measure chronic disease burden.<sup>23</sup> HF was the most potent determinant of death. COPD and cognitive impairment were also associated with greater risk of death, consistent with Centers for Disease Control and Prevention reports.<sup>24</sup> Depression also remained a significant contributor to death within 2 years after accounting for the other conditions and relevant covariates.

Avoidance of disability is of high priority to older adults.<sup>8</sup> Although it is likely that different conditions affect different ADLs,<sup>13</sup> chronic disease burden also appears to affect overall functioning.<sup>14</sup> The reliability of self-reported ADLs and IADLs in cognitively impaired participants cannot be verified. Cognitively impaired individuals tend to overestimate their functioning relative to proxy reports, although agreement is good.<sup>25</sup> Several disease combinations contributed to greater disability than would be expected according to the additive effects of the individual conditions. Corroborating previous work,<sup>26</sup> depression was

a particularly potent co-occurring condition, synergistically worsening the individual effects of HF, osteoarthritis, and cognitive impairment on functional level.

Symptom relief is a treatment goal for most chronic conditions. The symptom burden from individual chronic conditions is well chronicled. The current study determined the relative contribution of multiple chronic conditions. Depression had the largest symptom burden.

Although not assessed routinely in clinical practice, self-perceptions of older adults predict the course of their health.<sup>27</sup> HF and depression were the two conditions most strongly affecting self-rated health. The potent contribution of depression to ADL and IADL performance, symptom burden, self-rated health, and death supports the importance of effectively treating depression in individuals with multiple conditions.

Some of the methods used deserve comment. The study population was a community-based cohort with excellent chronic condition and universal health outcome data. The wealth of demographic, behavioral, and comorbidity factors allowed their known effects on the universal outcomes to be accounted for. Many other chronic conditions in addition to the five included also affect universal health outcomes. Similarly, many other universal health outcomes warrant investigation.

With the exception of death, the chronic conditions and universal health outcomes were assessed cross-sectionally because the associations between the conditions and symptom burden, function, and self-rated health are likely to be at their strongest contemporaneously. Although temporal precedence could not be determined, previous studies have established longitudinal relationships between the individual conditions and the universal health outcomes.

Although it is biologically plausible that the conditions caused the outcomes, it cannot be determined whether this was the case or whether they were merely associated with them. It is probable that condition-specific impairments, such as forced expiratory volume and dyspnea for COPD, explain at least some of these effects.<sup>17</sup> This possibility is important to investigate because these condition-related impairments are often the targets of intervention. Knowing which impairments account for the effect of specific conditions on different universal health outcomes could help establish treatment priorities in the face of multiple chronic conditions.<sup>17</sup>

Other than functional disability, it was not found that any combination of conditions had a greater-than-additive on the universal health outcomes. Lack of power may have precluded identification of additional interactions. This topic is ripe for investigation. If a few disease combinations account for an outsized proportion of universal health outcomes, treatment could focus on important disease combinations.

These findings suggest potential approaches to caring for persons with multiple chronic conditions. For example, the variability in the extent to which each chronic condition affected the various universal health outcomes, combined with the variability in health outcome priorities in older adults,<sup>8</sup> suggests that clinical decision-making could begin with eliciting priorities. If maximum survival is a person's priority, for example, care might focus on treatments with the greatest likelihood of increasing survival with HF or COPD. For individuals in whom symptom burden is most important, the treatment priority might be managing symptoms associated with depression, HF, COPD, and osteoarthritis.

A compelling reason for basing treatment effectiveness on universal, rather than solely disease-specific, outcomes is that treatments have beneficial and harmful effects across conditions and health outcomes. A medication, for example, may reduce risk of death from

myocardial infarction but increase symptoms such as fatigue or muscle weakness, in turn adversely affecting function. Determining the effect of treatments on universal health outcomes, not merely disease-specific outcomes, could inform clinical decision-making for individuals with multiple chronic conditions by measuring overall treatment benefit or harm. Consensus on a set of reliable, reproducible outcomes that are feasible in clinical practice will be needed if we are to move to treatment evaluation and clinical decision-making based on universal health outcomes.

Universal health outcomes show promise as common metrics for measuring the effect of multiple chronic conditions and their treatments. The varying effects of the conditions across the universal outcomes could inform priorities and decision-making for older adults with multiple chronic conditions.

## 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.

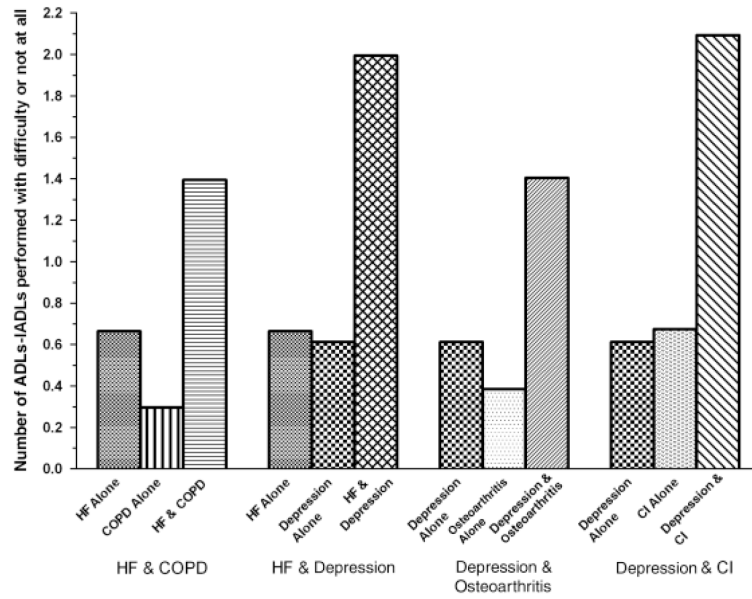
This research was supported by R21 AG033244 and the Yale Pepper Center (P30 AG021342), both from the National Institute on Aging. CHS was supported by Contracts N01-HC-85079 through N01-HC-85086, N01-HC-35129, N01 HC-15103, N01 HC-55222, N01-HC-75150, and N01-HC-45133 and Grant U01 HL080295 from the National Heart, Lung, and Blood Institute, with additional contribution from the National Institute of Neurological Disorders and Stroke.

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**Figure 1.** Effect of interactions between paired conditions on activities of daily living (ADLs) and instrumental activities of daily living (IADLs). The figure displays the four two-condition interactions that were significant. The model was adjusted for the five conditions, age, sex, race, education, smoking, and the Functional Comorbidity Index score with the five conditions removed. The *F*-test that the interactions between conditions were all equal to 0 was rejected ( $F = 15.9$ ;  $P < 0.001$ ) ( $P < .001$ ), suggesting that there were significant two-condition interactions. Individuals with the combinations of heart failure (HF) and chronic obstructive pulmonary disease (COPD), HF and depression, depression and osteoarthritis, and depression and cognitive impairment (CI) were able to perform fewer ADLs and IADLs without difficulty than would be expected from adding the effect of each paired condition together.



**Table 1**

Characteristics of the Cardiovascular Health Study Cohort\* (N = 5,298)

Characteristic	Value
Age, mean $\pm$ SD	72.6 $\pm$ 5.4
Female, n (%)	3,044 (57.5)
Black, n (%)	760 (14.4)
<High school education, n (%)	1,471 (27.8)
Married, n (%)	3,550 (67.1)
Current smoker, n (%)	617 (11.6)
Self-reported health, mean $\pm$ SD	2.8 $\pm$ 0.9
Number of activities of daily living and instrumental activities of daily living performed with difficulty, mean $\pm$ SD	0.6 $\pm$ 1.3
Number of symptoms, mean $\pm$ SD	1.9 $\pm$ 1.3
Died over 2 years of follow-up, n (%)	232 (4.4)
Heart failure, n (%)	216 (4.1)
Chronic obstructive pulmonary disease, n (%)	584 (11.0)
Osteoarthritis, n (%)	3,070 (58.0)
Depression (Center for Epidemiologic, n (%) Studies Depression Scale score $\geq$ 10)	863 (16.3)
Cognitive impairment, n (%)	410 (7.7)
Number of the 5 diseases possessed, n (%)	
0	1,648 (31.1)
1	2,450 (46.2)
2	1,200 (22.6)

\* Includes the original and the African-American samples as described in Methods. N reflects the number of participants included in at least one model. SD = standard deviation.

**Table 2**

Effect of Five Chronic Conditions on Four Universal Outcomes in the Cardiovascular Health Study Cohort (N = 5,298)

Chronic Condition	Universal Health Outcome			Death, Hazard Ratio (95% Confidence Interval) <sup>§</sup>
	Self-Rated Health	ADL and IADL Functioning <sup>*</sup>	Symptom Burden <sup>†</sup>	
	$\beta$ (Standard Error) P-Value <sup>‡§</sup>			
HF	0.51 (0.06) <.001	0.70 (0.08) <.001	0.40 (0.08) <.001	2.84 (1.97–4.10)
Chronic obstructive pulmonary disease	0.27 (0.04) <.001	0.28 (0.05) <.001	0.40 (0.05) <.001	2.62 (1.94–3.53)
Osteoarthritis	0.24 (0.02) <.001	0.27 (0.03) <.001	0.57 (0.03) <.001	0.85 (0.65–1.11)
Depression	0.43 (0.03) <.001	0.59 (0.04) <.001	1.18 (0.04) <.001	1.47 (1.08–2.01)
Cognitive impairment	0.21 (0.04) <.001	0.58 (0.06) <.001	–0.08 (0.06)	.18 2.05 (1.47–2.85)

Two-year death estimates are from Cox models; other estimates are from cross-sectional multiple regression models. All models included all five chronic conditions. Self-rated health ranged from excellent (1) to poor (5).

<sup>\*</sup> Activity of daily living (ADL) and instrumental activity of daily living (IADL) functioning was the number of ADLs and IADLs that participants reported having difficulty performing: walking, transferring, eating, toileting, dressing, bathing, light and heavy housework, shopping, preparing meals, paying bills, and using the phone (range 0–12).

<sup>†</sup> Symptom burden scale (range 0–6) was the number of the following symptoms reported: pain, fatigue, dizziness or imbalance, weakness, gastrointestinal symptoms, and shortness of breath or dyspnea.

<sup>‡</sup> The beta coefficient ( $\beta$ ) for each universal health outcome can be interpreted as the effect of the condition on the universal health outcome (e.g., the difference in the universal health outcome between those with and without heart failure (HF), independent of the other four conditions and covariates in the model). For example,  $\beta$  for ADL and IADL functioning for HF is 0.70, meaning that, adjusting for the other conditions and covariates, persons with HF performed approximately 0.70 fewer ADLs and IADLs without difficulty than those without HF. The covariates included age, sex, race, education, smoking, and the Functional Comorbidity Index score with the five conditions removed.

<sup>§</sup> The covariates for all models included age, sex, race, education, smoking, and the Functional Comorbidity Index score with the five conditions removed. The comorbidities included in this index score were osteoporosis, neurological disease, stroke, diabetes mellitus, upper gastrointestinal disease, visual impairment, hearing impairment, degenerative disc disease, and obesity.