Population-Based Study of Medical Comorbidity in Early Dementia and "Cognitive Impairment, No Dementia (CIND)"

Association With Functional and Cognitive Impairment: The Cache County Study

Constantine G. Lyketsos, M.D., M.H.S., Leslie Toone, M.S.
JoAnn Tschanz, Ph.D., Peter V. Rabins, M.D., M.P.H.
Martin Steinberg, M.D., Chiadi U. Onyike, M.D., M.H.S.
Christopher Corcoran, Ph.D., Maria Norton, Ph.D.
Peter Zandi, Ph.D., John C.S. Breitner, M.D., M.P.H.
Kathleen Welsh-Bohmer, Ph.D., and The Cache County Study Group

Objective: *Authors investigated medical comorbidity in persons with dementia and "Cognitive Impairment, No Dementia" (CIND).* **Methods:** *The Cache County Study is an ongoing population-based study of the epidemiology of dementia, the risk factors for conversion from CIND to dementia, and the progression of dementia. As part of the study's first incidence wave, persons with dementia (N=149), CIND (N=225), or without cognitive impairment (N=321) were identified and studied. Participants received comprehensive clinical evaluations and were rated on the General Medical Health Rating (GMHR), a global measure of seriousness of medical comorbidity. Participants and informants also completed the Mini-Mental State Exam and provided self-report information about comorbid medical conditions and functioning in activities of daily living.* **Results:** *There were few differences in number or type of comorbid medical conditions between persons with CIND and dementia, but persons with dementia were prescribed more medications. Stroke was more common in dementia participants, but other illnesses common in old age were not significantly different across cognitive groups. Medical comorbidity was more serious in both dementia and CIND, such that both groups were less likely to have "little to no" comorbidity. Seriousness of medical comorbidity was significantly associated with worse day-to-day*

Received March 31, 2004; revised June 28, September 9, 2004; accepted September 16, 2004. From the Division of Geriatric Psychiatry and Neuropsychiatry, Dept. of Psychiatry and Behavioral Sciences, School of Medicine, The Johns Hopkins University (CGL,PVR,MS,CUO), the Center for Epidemiologic Studies, Utah State University (LT,JT,CC,MN), the Dept. of Psychology, Utah State University (JT,MN), the Dept. of Mental Health, Bloomberg School of Public Health, Johns Hopkins University (PZ), the Division of Geriatric Psychiatry, Dept. of Psychiatry, The University of Washington (JCSB), and the Dept. of Psychiatry, School of Medicine, Duke University (KWB). Send correspondence and reprint requests to Constantine G. Lyketsos, M.D., M.H.S., Professor of Psychiatry, Osler 320, Johns Hopkins Hospital, Baltimore, MD 21287. e-mail: kostas@jhmi.edu

functioning and cognition. **Conclusions:** *Persons with CIND and dementia have more serious medical comorbidity than comparable persons without cognitive impairment. This comorbidity may play a role in the progression of CIND and dementia. Future studies should investigate the role of medical comorbidity and its treatment on dementia onset or progression, as well as the mechanisms mediating its neuropathologic effects.* (Am J Geriatr Psychiatry 2005; 13:656–664)

Patients with cognitive disorders, especially dementia, frequently suffer from a range of comorbid medical conditions. These conditions may contribute to the progression of their cognitive and functional decline.[1] Accelerated declines in cognition or functioning are reported after episodes of medical illness, such as urinary tract infection, or surgery.[1] Also, illnesses leading to hospitalization may be a significant factor in the progression of preclinical Alzheimer disease (AD) to frank dementia.[2] The mechanisms involved have not been explored or elucidated.

At the same time, medical comorbidity may be underdiagnosed and undertreated in patients with cognitive disorders.[3,4] Once admitted to the hospital, they have longer stays on medical or surgical units, regardless of admitting diagnosis.[4] This may lead to worse healthcare outcomes, which may further worsen cognition, resulting in a vicious cycle of decline. It may also explain the higher costs of care for medical comorbidities in persons with dementia.[5]

Despite its importance, little is known about medical comorbidity in dementia. There have been very few estimates of the prevalence of medical comorbidity in dementia or of its effects on cognition and day-to-day functioning. One study reported that patients with dementia and milder cognitive impairments have similar rates of comorbid conditions as cognitively intact persons.[3] Another study reported that persons with dementia have different profiles of medical comorbidity than persons without dementia.[6] A study from Alzheimer Disease Centers reported a high prevalence of medical comorbidities, which increased with increasing severity of dementia.[7]

Even less is known about medical comorbidity in persons with other forms of cognitive disorders in later life, referred to here as "cognitive impairment, no dementia" (CIND).[8] CIND-spectrum conditions are highly prevalent after age 60 and confer a substantially increased risk for later conversion to dementia. Given the effects medical comorbidity may have on the progression of dementia, it may also play a role in the progression of CIND to dementia.[2]

We report here findings from The Cache County Study. The study has followed a large cohort of well-characterized persons ≥65 years old for several years. The design of the study allows us too estimate in great detail the medical comorbidity of a large population-based sample of people with dementia and CIND and to assess the effects of this comorbidity on functioning and cognition. Previous studies have not provided estimates from a population-based study or from persons with CIND and have not systematically assessed the effects of comorbidity on cognition and functioning. In this first report, regarding medical comorbidity, we describe the prevalence of a wide range of medical conditions, seriousness of comorbidity, and medication use in participants with dementia, CIND, or without cognitive impairment. We also report on cross-sectional associations between seriousness of comorbidity and cognitive performance or functioning in daily activities.

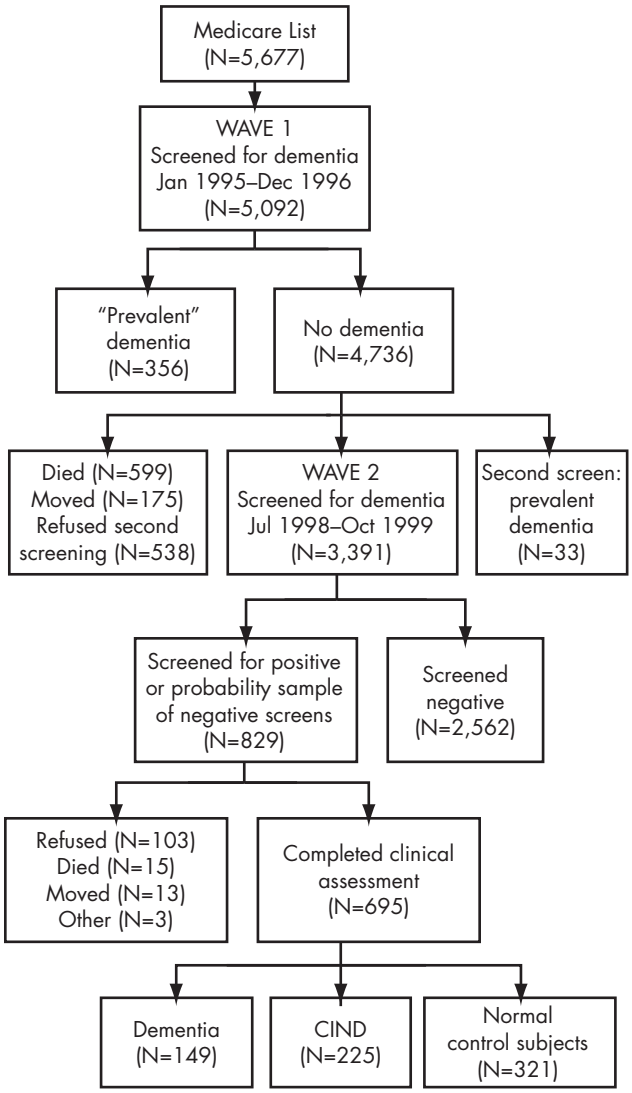
METHODS

Design Overview, Participant Sampling, and Procedures

This was a nested, case–control study of persons with dementia or CIND and cognitively unimpaired control subjects derived from the first-incidence wave of The Cache County Study. The design of the study has been reported in detail previously.[9,10] Institutional Review Boards at Duke University Medical Center, Johns Hopkins University, and Utah State University approved the study. All study participants or next-of-kin signed an informed consent document

for each stage of assessment. Figure 1 contains a flow chart of the selection process for participants included in the analyses reported here. The study approached all permanent residents of Cache County, Utah, who were 65 years of age or older in January of 1995 (N = 5,677). The study enrolled 5,092 individuals (90%), who were all screened for dementia with the Modified Mini-Mental State Exam (3MS),[11] further modified for epidemiological studies,[12] or, if subjects were unable, the Informant Questionnaire for Cognitive Decline in Elderly (IQCODE).[13] Screen-positive individuals on the 3MS (86/87) and a designated subsample were sent to the second screening stage, the Dementia Questionnaire (DQ).[14] The designated subsample was randomly selected in an iterative process according to age, gender, and apolipoprotein-E (APOE) genotype such that, with the completion of the stages of screening and assessment, there would be no fewer than two "clean" control subjects per AD case. The subsample and all other participants with suspected dementia underwent a comprehensive clinical assessment for dementia in their place of residence by a research nurse, a psychometric technician, and a geriatric psychiatrist. Data from these evaluations were used to classify participants at consensus conferences that included two geriatric psychiatrists, a board-certified neurologist, a senior neuropsychologist, and a cognitive neuroscientist.[15] In this way, a total of 356 individuals with dementia were detected at the first study wave, and an additional 33 persons with dementia were identified after Wave 1 but before Wave 2.

FIGURE 1. Flow Chart of Selection Process for Participants



Note: CIND: Cognitive Impairment, No Dementia.

Those without dementia at baseline (N = 4,703) were followed up to be screened again for cognitive impairment 3 years later, in the second wave of the study.[10] A total of 3,391 individuals were screened in Wave 2. Between Waves 1 and 2, 599 had died, 175 had moved out of the area or were lost to follow-up, and 538 refused follow-up. The screening, evaluation, and case-detection methods were identical to those used in the first wave. Again, those in the designated subsample (assigned at Wave 1) completed all stages of dementia screening and assessment. Dementia was defined by DSM-IV criteria,[15] and a group with Cognitive Impairment, No Dementia (CIND) was identified as having a mild cognitive syndrome, consistent with the Canadian Study of Health and Aging approach.[8] Control subjects consisted of all individuals from the incidence wave who, on the basis of the clinical assessment, were considered to be without cognitive impairment.

In this way, we established a population-based panel consisting of two incidence case groups and one control group, defined by cognitive status. The two case groups were defined by the presence of dementia (N = 149) or CIND (N = 225), and the control group consisted of cognitively unimpaired persons (N = 321).

Quantification of Medical Comorbidity

Medical comorbidity was assessed in three ways: 1) by self-report of participants and informants re-

garding current or recent medical conditions; 2) by self-report about participants' and informants' current prescribed non-psychotropic/dementia medications and concurrent review of medicine chests; and 3) by rating participants on the General Medical Health Rating (GMHR) (see below). Whenever possible, information from both participants and informants was used in the quantification of comorbidity. Informants were selected on the basis of their knowledge of the study participants; these were typically spouses, siblings, or adult children. In rare cases, such relatives were not available to serve as informants, in which case, close friends or neighbors were involved. Virtually all informants were closely involved in the lives of the participant and, therefore, are believed to have provided reliable information. There was good-to-excellent agreement between participant and informant reports of medical comorbidity: kappa estimates ranged between 0.49 and 0.94 (Hayden KM, dissertation for the Johns Hopkins School of Public Health; personal communication, 2003).

A detailed review of systems was used to identify each participant's medical illnesses, with follow-up questions to clarify diagnoses and treatments. We specifically asked about arthritis, headaches, other chronic pain, ulcers, constipation, asthma, emphysema/bronchitis, pneumonia, Parkinson disease, stroke, transient ischemic attack (TIA), head injury, brain injury, epileptic seizures, chest pain, angina, hypertension, coronary artery bypass surgery (CABG), angioplasty, heart attack, diabetes, thyroid problems, cholesterol, and cancer.

The GMHR,[16] developed at Johns Hopkins, is a 4-point global rating of seriousness of non-cognitive medical comorbidity in persons with cognitive disorders. It was developed as a clinician rating, based on review of medical history and medications and brief observation and interaction with the subject. Ratings of 4 indicate little-to-no comorbidity; 3: mild-to-moderate comorbidity; 2: moderate-to-severe comorbidity; and 1: serious comorbidity. It is a highly reliable measure, and its validity has also been established.[16]

In this study, GMHR ratings were assigned by a geriatric psychiatrist on the basis of direct and proxy interviews by the nurse, as well as a brief physical and neurological exam. To assess the reliability of these ratings, we calculated the agreement between two raters in a random sample of 150 ratings and found it to be high (Pearson correlation coefficient: 0.704; $p < 0.0001$).

Quantification of Day-to-Day Functioning

A knowledgeable informant rated each participant on the Dementia Severity Rating Scale (DSRS),[17] an 11-item scale of signs and symptoms associated with dementia. Six of the 11 items refer to daily activities (ADLs), including: engagement in social activities, household responsibilities, personal care, meals/feeding, incontinence, and mobility. The other items refer to memory and other cognitive symptoms. Each ADL is assessed on a scale from 0 to 4 (except mobility, which is assessed on a scale from 0 to 6). A rating of "0" indicates that there is no impairment, and the highest rating, of "4" (or "6") indicates complete dependency or loss of ability to perform the ADL. The sum of the six ADL ratings (DSRS-ADL) was used as an indicator of cumulative ADL impairment and was a dependent variable in analyses assessing the association between medical comorbidity and functional impairment.

Quantification of Cognitive Impairment

Participants were also assessed on the Mini-Mental State Exam (MMSE). The total MMSE score was the indicator of cognitive impairment and was a dependent variable in analyses assessing the association between medical comorbidity and cognitive impairment. Because some participants had sensory impairments, analyses involving MMSE were repeated twice, the first using a sensory-adjusted MMSE score [(number of points earned/number of points attempted) $\times$ 30] and the second excluding participants with sensory impairments. Study findings were similar for both methods of MMSE scoring. For simplicity, we report only the results using the sensory-adjusted MMSE score.

Covariates

Other covariates used in the analyses to adjust for their effects on cognitive or functional variables included age, gender, depression, and education. Adjustment for cognitive group was also included in modeling ADL impairment.

Statistical Analysis

First, we present descriptive data comparing cases and control subjects. We used analysis of variance to compare number of medications and number of medical conditions across groups. We conducted tests for independence between each of the most prevalent medical conditions and cognitive classification by use of Pearson χ^2 tests, and we corrected for multiple comparisons. We tested for independence between GMHR rating and cognitive classification with Pearson χ^2 tests. We assessed the nature of significant dependent associations by use of adjusted standardized residuals (ASR)[18] for the two-way contingency tables. Since these residuals have a large-sample standard normal distribution, a negative residual larger than –2 or –3 indicates fewer subjects in a cell than one would expect, given no association between row and column variable. A positive ASR greater than 2 or 3 indicates more subjects in a cell than expected, given that there is no association between the row and column variable. We next used analysis of covariance (ANCOVA) to assess the independent association between GMHR rating and total ADL impairment, controlling for age, gender, depression, education, and cognitive classification, all of which were likely to have independent effects on ADLs. ANCOVA was also applied to examine the independent association between GMHR rating and MMSE score, controlling for age, gender, depression, and education. To reduce the negatively-skewed distribution of MMSE, we used a cubed transformation.

RESULTS

Table 1 contains a comparison of the three study groups on demographic indicators. Participants with dementia and CIND were older than control subjects. Individuals with dementia were less likely to be married (ASR: –3.5; observed count: 64, expected count: 83) and more likely to be living in a nursing home (ASR: 8.4; observed count: 35, expected count: 11) than what would be expected if marital status and nursing home residence were independent of cognitive status.

Table 2 compares the study groups on medical comorbidity variables. When compared on mean number of medical conditions, the three groups did not differ significantly ($F_{[2,\ 692]} = 2.49$; $p = 0.084$). Participants with dementia reported a higher mean number of prescribed medications than non-cases ($F_{[2,\ 674]} = 8.19$; $p < 0.001$; Tukey HSD mean difference = 1.64; $p < 0.001$). With regard to specific comorbidities, few differences were evident between the three cognitive groups, except that serious medical illness, including active severe infection, congestive heart failure, severe pulmonary disease, or cancer (Pearson $\chi^2_{[2]} = 8.48$; $p = 0.014$), stroke (Pearson $\chi^2_{[2]} = 31.74$; $p < 0.001$), or heart attack (Pearson $\chi^2_{[2]} = 8.28$; $p = 0.016$) were more prevalent. However, because we tested 12 different medical conditions, we calculated a Bonferroni adjustment on the α level in order to preserve a Type I error rate of 5%. This adjustment lowered the α level to 0.05/12 (0.0042), which means that only stroke was significantly different across cognitive group, with fewer strokes among the cognitively intact group (ASR: –3.3; observed count suppressed to comply with CMS privacy policy; expected count: 20.5) and more strokes in those with dementia (ASR: 5.6; observed count: 24, expected count: 9.3).

Table 2 also shows GMHR ratings by cognitive group. The low number of participants with "severe" comorbidity likely reflects a much greater likelihood of refusal to participate in the study among persons with currently active, severe health conditions. Differences in frequency of individual GMHR ratings were noted across the cognitive groups (Pearson $\chi^2_{[6]} = 57.22$; $p < 0.001$). Participants with dementia were much less likely to have "little-to-no" comorbidity (ASR: –2.2; observed count: 17, expected count: –2.2), and much more likely to have "moderate-to-severe" comorbidity (ASR: 5.6; observed count: 56, expected count: 31.3). Participants with CIND were much less likely to have "little-to-no" comorbidity (ASR: –2.2; observed count: 29, expected count: 39.2).

Table 3 and Figure 2 contain findings regarding the relationship between GMHR ratings and day-to-day functioning as rated on the DSRS-ADL, and cognition as rated on the MMSE. Figure 2 displays mean scores on the DSRS-ADL or MMSE by GMHR rating. Less serious comorbidity (higher ratings on GMHR) was associated with less impairment (lower mean DSRS-ADL and higher 3MS scores) on both scales (Figure 2 [A, B]). In the CIND group, "severe" GMHR ratings were associated with lower ("better") scores on DSRS-ADL than a rating of "moderate-to-severe" or "mild-to-moderate" (average DSRS-ADL score for

TABLE 1. Comparison of Cognitively Normal Participants With Those With Dementia or Cognitive Impairment, No Dementia (CIND)

	Dementia (N = 149)	CIND (N = 225)	Cognitively Normal (N = 321)	Statistical Comparison
Age, years	83.89 [a] (6.29)	82.38 [a] (7.50)	79.93 [b] (6.73)	$F_{[2, 690]} = 18.90$ p <0.001
Education, years	12.95 [ab] (3.13)	12.95 [a] (2.97)	13.58 [b] (2.90)	$F_{[2, 691]} = 3.84$ p = 0.022
Mini-Mental State Exam[†]	20.47[a] (5.92)	25.82[b] (3.63)	28.30[c] (1.86)	$F_{[2, 689]} = 231.45$ p <0.001
Gender (N, % female, expected count, ASR)	96 (64.4) 84; 2.2	121 (53.8) 127; –1.0	176 (54.8) 182; –0.8	$\chi^2_{[2]} = 4.86$ p = 0.088
Race (N, % white, expected count, ASR)	144 (99.3) 144; –0.5	224 (100) 223; 1.2	318 (99.4) 319; –0.7	$\chi^2_{[2]} = 1.46$ p = 0.482
Marital status (N, % married, expected count, ASR)	64 (43.0) 83; –3.5	119 (52.9) 125; –1.0	203 (63.2) 178; 3.8	$\chi^2_{[2]} = 17.91$ p <0.001
Residence (N, % in nursing home, expected count; ASR)	35 (23.5) 11; 8.4	11 (4.9) 17; –1.8	[‡] ([‡]) 24; –5.2	$\chi^2_{[2]} = 71.95$ p <0.001

Note: Values are mean (standard deviation), unless otherwise indicated. Superscript letters that differ represent significant differences (p <0.05); superscript letters that are the same do not show significantly different. ASR: adjusted standardized residuals.

[†] Adjusting for sensory impairments. Results only slightly affected when participants with sensory impairments were dropped.

[‡] Numbers were suppressed to comply with CMS privacy policy.

TABLE 2. Comparison of the Dementia, CIND, and Cognitively Normal Participants and Subgroups on Number and Type of Medical Conditions, Number of Medications, and GMHR

	Dementia	CIND	Cognitively Normal	Statistical Comparison
Total number of medical conditions	4.1 (2.5)	4.1 (2.4)	3.7 (2.3)	$F_{[2, 692]} = 2.49$ p = 0.084
Total number of prescribed medications	6.2 (4.7)	5.2 (4.4)	4.5 (3.4)	$F_{[2, 674]} = 8.19$ p <0.001
Any gastrointestinal disease (N, %)	100 (69.4)	161 (71.9)	218 (67.9)	$\chi^2_{[2]} = 0.98$ p = 0.613
Hypertension (N, %)	53 (37.1)	93 (41.7)	131 (40.9)	$\chi^2_{[2]} = 0.86$ p = 0.651
Arthritis (N, %)	75 (50.3)	118 (52.4)	180 (56.1)	$\chi^2_{[2]} = 1.55$ p = 0.461
Serious physical illness (N, %)	51 (34.5)	65 (28.9)	71 (22.1)	$\chi^2_{[2]} = 8.48$ p = 0.014
Headaches (N, %)	33 (22.8)	52 (23.2)	68 (21.2)	$\chi^2_{[2]} = 0.35$ p = 0.839
Thyroid disease (N, %)	32 (21.8)	51 (22.8)	69 (21.5)	$\chi^2_{[2]} = 0.13$ p = 0.938
Chronic pain (N, %)	23 (15.9)	52 (23.2)	63 (19.6)	$\chi^2_{[2]} = 3.03$ p = 0.220
Diabetes mellitus (N, %)	29 (19.6)	41 (18.2)	43 (13.4)	$\chi^2_{[2]} = 3.78$ p = 0.151
History of stroke (N, %)	24 (16.4)	[a] ([a])	[a] ([a])	$\chi^2_{[2]} = 31.74$ p <0.001
History of heart attack (N, %)	[a] ([a])	21 (9.3)	11 (3.4)	$\chi^2_{[2]} = 8.28$ p = 0.016
High cholesterol (N, %)	17 (12.4)	31 (14.0)	55 (17.3)	$\chi^2_{[2]} = 2.14$ p = 0.343
GMHR	2.71 (0.68)	2.88 (0.61)	3.12 (0.57)	$F_{[2, 692]} = 26.13$ p <0.001
4: little–none (N, %)	[a, a]	[a, a]	75 (23.4)	$\chi^2_{[6]} = 57.22$ p <0.001
3: mild–moderate (N, %)	74 (49.7)	140 (62.2)	211 (65.7)	
2: moderate–severe (N, %)	56 (37.6)	55 (24.4)	35 (10.9)	
1: severe (N, %)	[a, a]	[a, a]	0, 0.0	

Note: Values are mean (standard deviation), unless otherwise indicated.

CIND: Cognitive Impairment, No Dementia; GMHR: General Medical Health Rating.

[a] Numbers were suppressed to comply with CMS privacy policy.

TABLE 3. Relationship Between GMHR and Activities of Daily Living (ADL), Functioning, and Cognition, as Reported by Informants on the DSRS (Adjusting 3MS Scores for Subjects With Sensory Impairments)

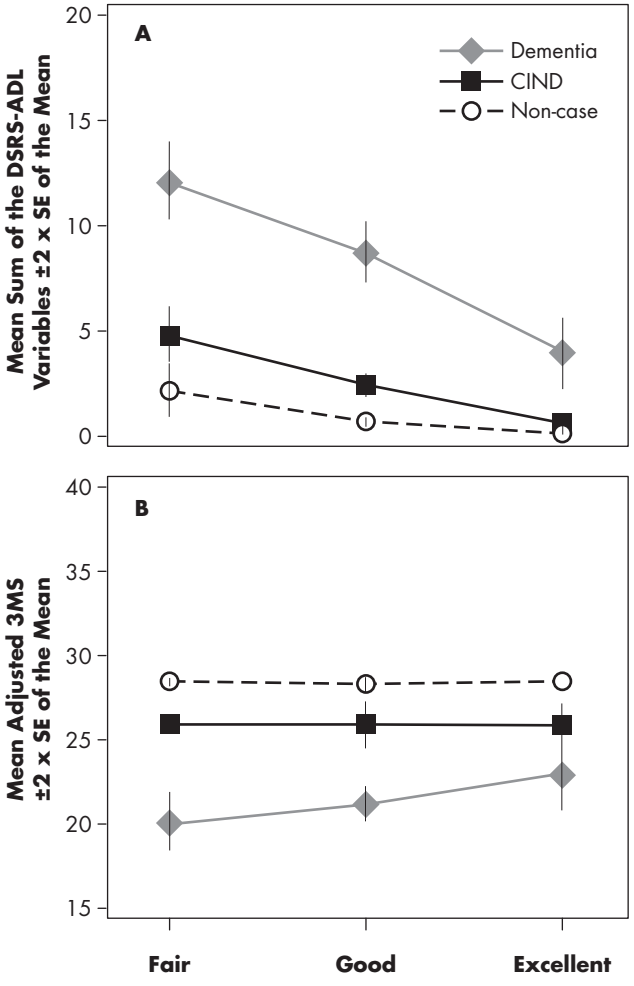
	Unadjusted Model ($F_{[df]}$, p)	Adjusted Model[a] ($F_{[df]}$, p)	
		Main GMHR Effect	GMHR × Cognitive Classification Interaction
Total DSRS-ADL (N = 643)	$65.06_{[2, 640]}$, <0.001	$47.993_{[2, 629]}$, <0.001	$7.019_{[4, 629]}$, <0.001
Modified Mini-Mental State Exam (3MS) Score[b] (n = 688)	$13.11_{[2, 685]}$, <0.001	$6.94_{[2, 672]}$, 0.001	NA

Note: DSRS: Dementia Severity Rating Scale.

[a] Adjusted for age, gender, education, cognitive classification, and cognitive classification × GMHR interaction if significant at p = 0.05. Depression was dropped from the adjusted model because of non-significance (p = 0.268); all other covariates were significant at p = 0.05.

[b] Modified Mini-Mental State Examination (3MS) score was cubed to adjust for a negatively skewed distribution. Adjusted model is adjusted for age, gender, depression, and education; all covariates were significant at p = 0.05. Conclusions do change when subjects with sensory impairment are dropped; GMHR is no longer significant ($F_{[2, 521]} = 2.54$; p = 0.08).

FIGURE 2. Means on DSRS-ADL [A] and 3MS [B], by GMHR, in Participants With Dementia, CIND, or No Cognitive Impairment



Note: DSRS-ADL: sum of the six ADL ratings; 3MS: Modified Mini-Mental State Exam; GMHR: General Medical Health Rating.

"severe" GMHR rating: 2.0; for "moderate-to-severe" GMHR, average DSRS-ADL rating: 4.9; for "mild-to-moderate" GMHR, average DSRS-ADL rating: 2.5; for "little-to-no" illness, average DSRS-ADL rating: 0.6), most likely because only one participant was classified with severe comorbidity on the GMHR.

These relationships are quantified in greater detail in Table 3. This table displays results of ANCOVA with total DSRS-ADL score or MMSE as the dependent variable and GMHR rating as the primary independent variable (simple models). ANCOVA was rerun to adjust for the effects of age, gender, depression, education, and also cognitive classification. Depression was dropped from the DSRS-ADL model because it was not significant at a 0.05 level of significance. Lower GMHR was significantly associated with worse overall ADL functioning (GMHR main effect $F_{[2, 629]} = 47.993$; p <0.001; GMHR moderate-to-severe versus mild-to-moderate: $\beta = 8.17$; $t = 8.09$; p <0.001; GMHR moderate-to-severe versus little-to-none: $\beta = 4.924$; $t = 4.99$; p <0.001). The significant interaction between cognitive classification and GMHR (cognitive group × GMHR interaction: $F_{[4, 629]} = 7.019$; p <0.001) indicates that comorbidity differentially affects functioning among the three cognitive groups. This interaction is graphically depicted in Figure 1 [a]. Pairwise comparisons, using a Bonferroni adjustment for multiple comparisons, revealed that, for the cognitively intact participants, ADL functioning was significantly worse for those with a moderate-to-severe GMHR rating than those with a little-or-no GMHR rating (mean difference = 1.8; p = 0.029). For the CIND and dementia participants, ADL functioning significantly improved for

each level of increase in GMHR (CIND: GMHR "moderate-to-severe" versus "little-or-none:" mean difference = 2.3; $p < 0.001$; for GMHR "mild-to-moderate" versus "little-or-none," mean difference = 1.8; in the dementia group: GMHR "moderate-to-severe" versus "mild-to-moderate," mean difference = 3.3; $p < 0.001$; for GMHR "mild-to-moderate" versus "little-or-none, mean difference = 4.9). For descriptive purposes, Figure 1 [b] shows the interaction between cognitive group and GMHR on cognitive functioning cubed. This interaction and the main effect of cognitive group was not formally tested in the ANCOVA analyses of MMSE, since cognitive classification was based on MMSE. The significant main effect of GMHR on MMSE cubed($F_{[2, 672]} = 6.94$; $p < 0.001$) indicates that comorbidity affects cognition regardless of cognitive group (GMHR for "moderate-to-severe" versus "mild-to-moderate:" $\beta = -2{,}710.7$; $t = -3.52$; $p < 0.001$; GMHR "moderate-to-severe" versus "little-or-none:" $\beta = -849.6$; $t = -1.35$; $p = 0.178$; these parameter estimates are for MMSE cubed).

DISCUSSION

We report on the prevalence and cross-sectional impact of medical comorbidity in persons with CIND and dementia from a population study. Persons with dementia and CIND had slightly higher numbers of comorbid medical conditions and were taking more medications than the cognitively normal subjects. With regard to specific comorbidities, stroke was more common in dementia participants, but other illnesses were not. The more striking finding was that medical comorbidity, when rated globally on the GMHR, was more serious in both dementia and CIND. Thus, persons with CIND and dementia have a greater burden of medical comorbidity than comparable persons without cognitive impairment. It is worth emphasizing that this finding holds true in CIND, a state intermediate between normal cognition and dementia.

Seriousness of medical comorbidity was also significantly associated with worse day-to-day functioning and worse cognition across all levels of cognitive functioning. The former finding, which is not surprising, suggests that functional impairment is probably the additive result of the total number of medical conditions, cognitive or otherwise, from which the person suffers. It is notable that, even in CIND, medical comorbidity affects functioning. The latter finding confirms the association between medical comorbidity and worse cognitive functioning reported by others[7] and extends it to individuals with CIND or no cognitive impairment. The difference between the self-report of medical comorbidity and the GMHR findings is likely reflective of the fact that the latter is intended to assess globally the seriousness of comorbidity by use of a clinical judgment, as opposed to being a count of medical conditions and medications. It appears that the seriousness of current comorbidity primarily drives the association between comorbidity and functional or cognitive impairment.

These findings have important implications. First, cognitive impairment in old age rarely occurs in isolation and is often associated with a range of medical comorbidities. In fact, older persons with clinically significant cognitive impairments have at least as many, if not more, medical problems and take as many medications as their unimpaired counterparts. Furthermore, they are more likely to suffer from cerebrovascular disease. This is consistent with recent findings that both dementia and milder cognitive impairments are associated with cerebrovascular disease[19] and contrasts with what has been reported from a hospitalized patient sample.[5] On the basis of these observations, it is reasonable to ask to what degree these conditions produce cognitive impairment. Although it is clear that several medical conditions can produce cognitive impairment, it is also interesting to speculate as to whether "primary" dementias are themselves "final pathway" products of medical comorbidity. These are questions that cannot be addressed in the present study.

Second, older persons with dementia and CIND have more serious medical comorbidity than their unimpaired counter parts, and this comorbidity affects their day-to-day functioning. This lends further credence to the hypothesis that a vicious cycle may be in place, at least for many persons with dementia and CIND, in which medical comorbidity goes undetected and undertreated because of the effects of the cognitive disorder, and that medical comorbidity, in turn, worsens functioning, further escalating the problem. Because the associations reported here are cross-sectional, the direction of causality cannot be determined.

The study's strengths include its population base,

the inclusion of persons with CIND and dementia, and the relatively large sample size. Limitations include the population's predominantly Caucasian make-up, a possible rating bias because GMHR raters were aware of the cognitive status of participants, and the lack of longitudinal follow-up.

We conclude that medical comorbidity is a significant aspect of CIND and dementia that requires attention because of its seriousness and its effects on cognition and functioning. Given that flare-ups of medical comorbidity may be associated with acute declines of functioning in persons with dementia[1,2] and may be more likely to lead to delirium, with its attendant effects on morbidity and mortality,[20] this vicious cycle may play an important role in the progression of dementia. Also, by extension of this logic, medical comorbidity may play a role in the progression of CIND to dementia, as has already been suggested in one report.[2] Both of the latter points are hypotheses that should be tested in future research. Since attenuating the progression of CIND to dementia and the progression of mild to severe dementia are major public-health priorities, the detection of CIND in primary-care settings, for the purposes of the appropriate and aggressive management of medical comorbidity, may be a critical aspect of the public-health response to dementia.

The Cache County Study group are James Anthony, Ph.D., Truls Østbye, M.D., Ph.D., Erin Bigler, Ph.D., Carl Pieper, Ph.D., James Burke, M.D., Brenda Plassman, Ph.D., Robert C. Green, M.D., M.P.H., David C. Steffens, M.D., Liz Klein, M.P.H., Carol Leslie, M.S., Jeannette J. Townsend, M.D., Bonita W. Wyse, Ph.D., Ronald Munger, Ph.D., M.P.H., and Michael Williams, M.D.

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