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ORIGINAL RESEARCH

Delirium Superimposed on Dementia is Associated With Prolonged Length of Stay and Poor Outcomes in Hospitalized Older Adults

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BACKGROUND: Current literature does not identify the significance of underlying cognitive impairment and delirium in older adults during and 30 days following acute care hospitalization.

OBJECTIVE: Describe the incidence, risk factors, and outcomes associated with incident delirium superimposed on dementia.

DESIGN: A 24-month prospective cohort study.

SETTING: Community hospital.

PATIENTS: A total of 139 older adults (>65 years) with dementia.

METHODS: This prospective study followed patients daily during hospitalization and 1 month posthospital. Main measures included dementia (Modified Blessed Dementia Rating score, Informant Questionnaire on Cognitive Decline in the Elderly), daily mental status change, dementia stage/severity (Clinical Dementia Rating, Global Deterioration Scale), delirium (Confusion Assessment Method), and delirium severity (Delirium Rating Scale-Revised-98). All statistical analysis was performed using SAS 9.3, and significance was an α level of 0.05. Logistic regression, analysis of covariance, or linear regression was performed controlling for age, gender, and dementia stage.

RESULTS: The overall incidence of new delirium was 32% (44/139). Those with delirium had a 25% short-term mortality rate, increased length of stay, and poorer function at discharge. At 1 month follow-up, subjects with delirium had greater functional decline. Males were more likely to develop delirium, and for every 1 unit increase in dementia severity (Global Deterioration Scale), subjects were 1.5 times more likely to develop delirium.

CONCLUSIONS: Delirium prolongs hospitalization for persons with dementia. Thus, interventions to increase early detection of delirium have the potential to decrease the severity and duration of delirium and to prevent unnecessary suffering and costs from the complications of delirium and unnecessary readmissions to the hospital. *Journal of Hospital Medicine* 2013;8:500–505. © 2013 Society of Hospital Medicine

Much attention has been given recently to hospitalized older adults, the critical 30-day period, and posthospital syndrome.[1] What is missing from this dialogue is the contribution and significance of underlying cognitive impairment. By 2050, 14 million older persons in the United States are expected to have dementia.[2] Increasing numbers of older adults diagnosed with dementia are hospitalized and are at increased risk of developing delirium; in fact, delirium occurs in over half of hospitalized persons with dementia.[3] Further, current evidence suggests that delirium may accelerate the clinical course and trajectory of cognitive decline, and may be associated with considerably worse long-term outcomes, including prolonged hospitalization, rehospitalization within 30 days, nursing home placement, and death.[3–6] However, the problem of delirium superimposed on dementia (DSD) remains a neglected area of investigation in hospitalized patients. Delirium is superimposed on dementia when an acute change in mental status (characterized by a fluctuating course, inattention, and either disorganized thinking or altered level of consciousness) is layered on top of preexisting dementia.[4]

Despite the poor outcomes and high prevalence of DSD, little is known about the natural history in hospitalized older adults with dementia. Delirium studies often exclude persons with dementia, even though the prevalence of DSD is extremely high in both community (13%–19%) and hospital (40%–89%) populations and associated with higher costs and utilization compared to dementia and delirium alone.[4,5,7] In 1 study, annual costs for DSD were $9566 compared to $7557 for dementia alone.[7] The few risk-factor studies of DSD were conducted in intensive care unit (ICU) or long-term care settings.[8,9]

The purpose of this study was to describe the incidence, risk factors, and outcomes associated with incident delirium in a prospective cohort of hospitalized older adults with dementia. The study aims were to:

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(1) estimate the incidence of new delirium in hospitalized persons with dementia, (2) identify the risk factors associated with incident delirium superimposed on dementia in this sample, (3) describe the outcomes associated with development of delirium, and (4) evaluate the contributions of delirium severity and duration to outcomes.

METHODS

This 24-month prospective cohort study recruited and enrolled consecutive hospital admissions with dementia in a 300-bed community hospital in central Pennsylvania from July 2006 through November 2008. Data were collected daily from patients during hospitalization, followed by a 1-month posthospitalization interview with patients and their caregivers in the community setting. Patients were included if they spoke English, had been hospitalized fewer than 24 hours, and met the screening criteria for dementia. Patients were excluded if they had any significant neurological condition associated with cognitive impairment other than dementia (eg, brain tumor), a major acute psychiatric disorder, were unable to communicate, or had no caregiver to interview. The interviewers included experienced research assistants (RAs) who were either registered nurses or trained in a health-related field. All staff training of instruments were done with scripted training manuals and video training using manuals for the Confusion Assessment Method (CAM). After training was completed, final inter-rater reliability assessments were conducted until staff reached 100% agreement. The RAs were blinded to the aims and completed over 10 hours of training. Inter-rater reliability checks were conducted on 10% of the sample in the field with >90% agreement attained on all instruments. This study was reviewed by and approved by The Pennsylvania State University institutional review board, and consent was received from all subjects.

Study Measures

Dementia was defined by meeting all 3 criteria of a Modified Blessed Dementia Rating Score of >3, an Informant Questionnaire on Cognitive Decline in the Elderly of ≥3.3, and documented dementia symptoms of at least 6 months' duration prior to current illness.[10–12] The Mini-Mental State Examination (MMSE), purchased from Psychological Assessment Resources, Inc. (Lutz, FL), was used to measure change from day to day and aid in the measurement of delirium, but was not used to establish the diagnosis of dementia. Both the Clinical Dementia Rating Scale[13] and the Global Deterioration Scale (GDS)[14] were used to measure dementia stage and severity.

Delirium and delirium severity were defined according to the validated CAM algorithm;[15] the Delirium Rating Scale-Revised-98 was used for delirium severity.[16] In a recent review, the CAM showed an overall sensitivity of 94% and specificity of 89%.[17] In the present study, delirium was measured in a comprehensive and structured interview that involved the MMSE and CAM criteria, and was based on a 24-hour period of observations, interviews with nurses and family members, and chart review. The CAM was completed daily during patient hospitalization and the follow-up interviews. The CAM assesses 4 criteria including acute and fluctuating nature, inattention, disorganized thought, and altered level of consciousness. Delirium was recorded by the research staff as present or absent each day based on full CAM criteria. Because the goal of the present study focused on full CAM delirium, subsyndromal delirium was not presented in this article.

Delirium duration was defined as the number of days with a positive rating. Data were collected daily from patients during hospitalization, followed by a single interview at 1-month posthospitalization with patients and their caregivers. Most interviews were in person.

Delirium Risk Factors

Central nervous system-active drug use was defined by 2005 American Hospital Formulary Services classification.[18] The Beers criteria were used to define potentially inappropriate medication use.[19] The Cornell scale for depression in persons with dementia was used, with a cut point of 12 indicating depression.[20] Functional status change was measured via the Katz Index of Activities of Daily Living (ADLs) and Lawton Instrumental Activities Of Daily Living (IADLs) change scores.[21] Comorbid conditions were classified with a weighted index that took into account both the number and seriousness of different comorbid diseases.[22] Pain was measured using the Pain Assessment in Advanced Dementia (PAINAD) scale.[23] Dehydration was defined using the blood urea nitrogen (BUN)/creatinine ratio and/or any chart diagnosis of dehydration. Admission lab values (BUN/creatinine) were abstracted from the medical records.

Primary Outcomes

The primary outcomes measured were full CAM delirium, index hospitalization length of stay, cognitive decline (change in MMSE and GDS scores), death, and functional status change (change from baseline to discharge score). One-month mortality was measured by chart review and follow-up family interviews performed at 1 month via telephone or in-person interviews. Mortality was not verified by additional methods.

Statistical Analysis

All statistical analysis was performed using SAS 9.3 (SAS Institute Inc., Cary, NC), and statistical significance was assessed using an α level of 0.05 unless otherwise noted. Descriptive statistics were calculated on all characteristics by incident delirium status.

TABLE 1. Characteristics (With Relative Risk Estimates) and Outcomes of Patients With and Without Delirium (N = 139)

Factor	Delirium, N = 44, 31.7%	No Delirium, N = 95, 68.3%	Relative Risk	95% CI	*P* Value
Demographic covariates					
Age, y, mean (SD)	85.9 (5.9)	82.4 (7.0)	1.07	1.02–1.12	0.0051
Male gender, n (%)	23 (52.3)	33 (34.7)	1.83	1.01–3.31	0.0456
Single/divorced/widowed, n (%)	23 (52.3)	56 (60.2)	0.81	0.45–1.47	0.4882
Education, y, mean (SD)	12.6 (3.2)	12.1 (3.0)	1.06	0.95–1.17	0.3146
Clinical covariates					
Dehydration, n (%)	12 (30.8)	30 (33.7)	0.88	0.45–1.74	0.7152
Fall in last 2 weeks, n (%)	14 (41.2)	21 (29.6)	1.73	0.87–3.43	0.1186
Infection, n (%)	13 (40.6)	21 (30.9)	1.42	0.70–2.88	0.3328
Sensory impairment, n (%)	16 (36.4)	33 (34.7)	1.04	0.56–1.91	0.9132
Lawton score, mean (SD)	1.6 (1.3)	2.3 (2.0)	0.84	0.70–1.01	0.0592
Katz impaired score, mean (SD)	2.3 (2.0)	3.4 (2.1)	0.82	0.71–0.95	0.0072
Charlson score, mean (SD)	2.5 (1.8)	2.3 (1.4)	1.06	0.86–1.30	0.6013
BUN, mean (SD)	28.2 (17.6)	25.6 (15.3)	1.01	0.99–1.03	0.4175
Creatinine, mean (SD)	1.6 (1.3)	2.4 (6.8)	0.99	0.90–1.08	0.7356
Cornell Depression score, mean (SD)	1.6 (0.8)	1.2 (0.9)	1.35	0.99–1.83	0.0553
Global Deterioration score, mean (SD)	4.7 (1.2)	3.9 (1.3)	1.45	1.14–1.86	0.0027
PAINAD score, mean (SD)	2.1 (3.0)	2.0 (2.9)	1.01	0.91–1.12	0.8540
Total number of regular medications, mean (SD)	11.5 (4.6)	11.0 (5.0)	1.00	0.94–1.67	0.9771
Total number of Beers medications, mean (SD)	0.3 (0.7)	0.4 (0.7)	0.76	0.46–1.27	0.2933
Cognitive impairment covariates					
MMSE score, mean (SD)	12.7 (6.8)	17.1 (6.6)	0.94	0.90–0.98	0.0019
Blessed score, mean (SD)	9.5 (3.5)	7.7 (2.9)	1.14	1.04–1.24	0.0038
Measures of delirium—covariates for follow-up outcomes					
Maximum incident delirium severity, mean (SD)	15.4 (5.6)	8.7 (6.1)			<0.0001
Inpatient days with positive CAM, mean (SD)	2.0 (1.1)	0.2 (1.4)			<0.0001
Follow-up outcomes					
Mortality, n (%)	11 (25.0)	9 (9.5)			0.0153
Length of stay, mean (SD)	9.1 (4.4)	5.7 (4.1)			<0.0001
Change in Lawton IADLs from admission to follow-up, mean (SD)	0.4 (1.5)	0.2 (1.8)			0.5094
Change in Katz impaired ADLs from admission to follow-up, mean (SD)	0.3 (1.7)	0.4 (1.6)			0.6919

NOTE: **Abbreviations:** ADLs, Activities of Daily Living; BUN, blood urea nitrogen; CAM, Confusion Assessment Method; CI, confidence interval; IADLs, Instrumental Activities of Daily Living; MMSE, Mini-Mental State Examination; PAINAD, Pain Assessment in Advanced Dementia; SD, standard deviation.

Potential risk factors for incident delirium were examined using χ^2 and *t* tests, where appropriate. Simple proportional hazards models were used to estimate the relative risk (RR) and 95% confidence interval (CI) for incident delirium. A stepwise model-building procedure under a proportional hazards model was used to build a final model for incident delirium that contained all variables that were statistically significant at the 0.05 α level or that had an RR of 1.5 or greater. Adjusted RR and corresponding 95% CI were determined. The outcome in each model was the number of days from admission to an incident delirium diagnosis. Subjects without incident delirium were censored using their length of stay as the total number of days they were at risk for developing delirium.

Finally, to examine the relationships between incident delirium, maximum incident delirium severity and the number of inpatient days positive for delirium with the outcomes of death, impaired in 2 or more IADLs at follow-up, impaired in 2 or more ADLs at follow-up, length of stay, change in IADLs from admission to follow-up, and change in ADLs from admission to follow-up, logistic regression (for the dichotomous outcome of mortality), analysis of covariance or linear regression (depending on the whether the independent variable was categorical or continuous) was performed controlling for age, gender, and GDS score.

RESULTS

Of 256 eligible patients, dual consent was obtained from 154 patient and 154 family research subjects (308 consents). The refusal rate was 39% (n = 102). Fourteen subjects were consented and enrolled but later dropped out due to family/proxy concerns regarding the patient's ability to participate in interviews. Thus, the final sample included 139 patients.

Descriptive statistics for baseline measures are given in Table 1. Briefly, the average age of subjects was 83 years (standard deviation [SD] = 7); 41% were male; 57% were single, divorced, or widowed; and the average number of years of education was 12 years (SD = 3). Thirty-three percent were dehydrated on admission, and 33% had fallen within 2 weeks prior to admission. Thirty-four percent had an infection at baseline, and 36% had some sensory impairment.

The overall incidence of delirium was 32% (44/139) and the range of days to incident delirium was 1

TABLE 2. Logistic, Analysis of Covariance, or Linear Regression Models of Incident Delirium Measures on Mortality, Length of Stay, Change in IADLs Score, and Change in ADLs Score

Variable Outcome mortality	Level	Adjusted Estimate of Association*	*P* Value
Incident delirium, OR (95% CI)†	Yes	2.33 (0.82-6.61)	0.1130
	No	1.00	
Maximum incident delirium severity, OR (95% CI)†		1.05 (0.96–1.14)	0.2719
Number of inpatient days with positive delirium, OR (95% CI)†		1.15 (0.89–1.49)	0.2871
Outcome LOS			
Incident delirium, mean (SE)‡	Yes	9.2 (0.7)	<0.0001
	No	5.6 (0.5)	
Maximum incident delirium severity, slope (SE)§		0.43 (0.06)	<0.0001
Number of inpatient days with positive delirium, slope (SE)§		1.80 (0.21)	<0.0001
Outcome—change in Lawton IADLs from admission to follow-up			
Incident delirium, mean (SE)‡	Yes	0.51 (0.33)	0.3787
	No	0.15 (0.20)	
Maximum incident delirium severity, slope (SE)§		−0.003 (0.03)	0.9260
Number of inpatient days with positive delirium, slope (SE)§		0.16 (0.11)	0.1497
Outcome—change in Katz impaired ADLs from admission to follow-up			
Incident delirium, mean (SE)‡	Yes	0.19 (0.26)	0.5086
	No	0.40 (0.17)	
Maximum incident delirium severity, slope (SE)§		0.05 (0.03)	0.0437
Number of inpatient days with positive delirium, slope (SE)§		0.13 (0.09)	0.1717

NOTE: **Abbreviations:** ADLs, activities of daily living; CI, confidence interval; IADLs, instrumental activities of daily living; LOS, length of stay; OR, odds ratio; SE, standard error of the mean.

*Adjusted for age, gender, and Global Deterioration Scale score.

†Logistic regression.

‡One-way analysis of variance.

§Simple linear regression.

to 8 days. During the baseline period (Table 1), subjects with delirium were older, more likely to be male, had lower Katz impairment scores, higher GDS score, lower MMSE scores on admission, and higher Blessed scores than subjects without delirium. Slightly more persons with delirium had a prior fall, although the RR was not statistically significant. Length of stay measured at discharge was significantly higher for those with delirium (mean = 9.1) than those without delirium (mean = 5.7) ($P < 0.0001$). Subjects with delirium were more likely to have died at 1 month than those without delirium ($P = 0.0153$).

In addition, we analyzed the adjusted relative risk estimates for the final model of incident delirium. Significant risk factors or risk factors with RR estimates at least 1.5 (or <0.66 if protective [Table 1]) that were examined in a more comprehensive multiple proportional hazards model included age, gender, having had a fall in the last 2 weeks, number of impaired ADLs (based on Katz), GDS scores, MMSE scores at baseline, and Blessed scores at baseline. The final proportional hazards included gender and GDS score. Males were nearly 1.8 times as likely to develop delirium than females, and for every 1 unit increase in the GDS, subjects were 1.5 times more likely to develop delirium.

Finally, Table 2 gives the results of examining outcomes related to incident delirium measures. For mortality, there were no statistically significant predictors of death after controlling for age, gender, or GDS. For length of stay, subjects with incident delirium had significantly longer lengths of stay, as incident delirium severity increased by 1 unit the length of stay increased by 0.4 days, and as the number of inpatient days with delirium increased by 1 day the length of stay increased by 1.8 days. For change in the impaired Katz ADLs from admission to follow-up, as incident delirium severity increased by 1 unit the change in impaired Katz ADLs increased by 0.05 units.

DISCUSSION

The most compelling finding from this study is the high incidence of delirium in hospitalized older adults with dementia and the association with poor clinical outcomes in those who develop delirium superimposed on dementia. DSD is difficult to detect and prevent; persons with DSD are at risk for poor quality of life. Those with delirium had a 25% short-term mortality rate ($P = 0.0153$), substantially increased length of stay (9.1 vs 5.1 days with an odds ratio of 1.8) and poorer physical function at discharge and follow-up. At 1 month follow-up, subjects with delirium had greater functional decline and lower GDS scores than those without delirium.

The incidence of delirium in this study was high (32%). Being delirious any time was associated with death and poor function. Delirium was also associated with the stage of the persons' baseline dementia,

advanced age, lower MMSE scores, and falling before admission.

Previous studies have found delirium associated with increased mortality. Three studies found that within 1 year of a delirium episode, a significant number of persons died or were institutionalized.[24–26] Other research has reported death within 1 year of documented delirium episodes, and a 3-fold increased rate of death in the ICU.[24,27–32] This study is 1 of only a few to focus on increased mortality with DSD and to focus uniquely on hospitalized patients with delirium and dementia.

The main risk factors for delirium in this study were male sex and severity of dementia. Our results, combined with those from other recent studies by Voyer and colleagues,[8,33,34] point to the critical importance of screening for dementia in hospitalized older adults as dementia severity is a significant indicator of delirium severity. For instance, Voyer and colleagues[34] reported that persons with mild dementia were likely to experience a mild delirium, whereas those with a more severe level of dementia were more likely to experience moderate to severe delirium. Our findings show that those who experienced episodes of delirium represented a highly vulnerable population with advanced dementia, sensory impairment, more falls and dehydration at admission, and higher Blessed scores. A recent study by Saczynski and colleagues[35] found 40% of patients who had experienced postoperative delirium did not return to their baseline at 6 months. Clearly, preventing delirium should be a critical priority to prevent such deterioration in the highly vulnerable population of hospitalized patients with dementia.

Patients in this study were on a mean of over 11 medications. One-third of dementia patients in our study had also experienced a fall and dehydration at baseline. Other studies have found a relationship between cognitive decline, falling, and medications.[36] Many of these patients came into the hospital with potentially modifiable and preventable community or ambulatory care conditions of polypharmacy, falling, sensory impairment, and dehydration.

Importantly, in our study, length of stay was significantly higher (9.1 vs 5.7) for those with delirium compared to those without delirium. This finding is alarming when examining the economic impact of preventing delirium. Previous studies have found the cost of delirious episodes rivals those for diabetes and heart disease, and that decreasing length of stay by just 1 day would save over $20 million dollars per year.[4,37]

In summary, this study is 1 of the first to report a high incidence of DSD and poorer outcomes for persons who experience delirium compared to those with dementia alone. This is 1 of only a few studies examining unique risk factors and delirium severity for DSD in the acute care setting. Findings from the current study report potential risk factors for development of incident delirium and highlight the challenge of preventing DSD before and during hospitalization. The generalizability of this study may be limited by the use of a nondiverse study population drawn from a single hospital in the northeast United States, though the use of a community hospital increases the relevance to real-world practice settings. Determination of baseline cognitive status and the differentiation of delirium and dementia are difficult, but validated, state-of-the-art methods were used that have been applied in previous studies.

This study provides fundamental methodological improvements over previous work, and advances the science by providing valuable data on the natural history, correlates, and outcomes of DSD. The strengths of this study include the prospective cohort design, the daily assessment for delirium based on a 24-hour period, methods for determining cognitive status at baseline in this difficult population, and utilizing strict blinding of the well-trained outcome assessors.

This study lays the groundwork for future studies to improve care for persons with dementia who present to acute care and to plan prevention programs for delirium before *t*hey are admitted to the hospital. We must be able to translate best practice for DSD into the acute care and community settings to prevent or minimize effects of delirium in persons with dementia. Interventions to increase early detection of delirium by hospital staff have the potential to decrease the severity and duration of delirium and prevent unnecessary suffering and costs from the complications of delirium and preventable readmissions to the hospital.

Thus, this study holds substantial clinical and economic implications for this population in the acute care setting, and will direct future studies leading to changes in real-world practice settings for persons with dementia.

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Dr. Inouye holds the Milton and Shirley F. Levy Family Chair.

References

1. Krumholz HM. Post-hospital syndrome—an acquired, transient condition of generalized risk. *N Engl J Med*. 2013;368(2):100–102.
2. Alzheimer's Association. Alzheimer's disease facts and figures. *Alzheimers Dement*. 2012;8(2):131–168.
3. Steis MR, Fick DM. Delirium superimposed on dementia: accuracy of nurse documentation. *J Gerontol Nurs*. 2012;38(1):32–42.
4. Fick D, Agostini JV, Inouye SK. Delirium superimposed on dementia: a systematic review. *J Am Geriatr Soc*. 2002;50(10):1723–1732.
5. Fong TG, Jones RN, Shi P, et al. Delirium accelerates cognitive decline in Alzheimer disease. *Neurology*. 2009;72(18):1570–1575.
6. Fong TG, Jones RN, Marcantonio ER, et al. Adverse outcomes after hospitalization and delirium in persons with Alzheimer disease. *Ann Intern Med*. 2012;156(12):848–856, W296.

7. Fick D, Kolanowski A, Waller JL, Inouye SK. Delirium superimposed on dementia in a community-dwelling managed care population: a 3-year retrospective study of occurrence, costs, and utilization. *J Gerontol*. 2005;60A(6):748–753.
8. Voyer P, Richard S, Doucet L, Carmichael PH. Factors associated with delirium severity among older persons with dementia. *J Neurosci Nurs*. 2011;43(2):62–69.
9. Girard TD, Pandharipande PP, Ely EW. Delirium in the intensive care unit. *Crit Care* 2008;12(suppl 3):S3.
10. Uhlmann RF, Larson EB, Buchner DM. Correlations of Mini-Mental State and Modified Rating Scale to measures of transitional health status in dementia. *J Gerontol*. 1987;42(1):33–36.
11. Crum RM, Anthony JC, Bassett SS, Folstein MF. Population-based norms for the Mini-Mental State Examination by age and educational level. *JAMA*. 1993;269(18):2386–2391.
12. Tombaugh TN, McIntyre NJ. The mini-mental state examination: a comprehensive review. *J Am Geriatr Soc*. 1992;40(9):922–935.
13. Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. *Br J Psychiatry*. 1982;140:566–572.
14. Auer S, Reisberg B. The GDS/FAST staging system. *Int Psychogeriatr*. 1997;9(suppl 1):167–171.
15. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. *A new method for detection of delirium. Ann Intern Med*. 1990;113(12):941–948.
16. Trzepacz PT, Mittal D, Torres R, Kanary K, Norton J, Jimerson N. Validation of the Delirium Rating Scale-Revised-98: comparison with the delirium rating scale and the cognitive test for delirium. *J Neuropsychiatry Clin Neurosci*. 2001;13(2):229–242.
17. Wei LA, Fearing MA, Sternberg EJ, Inouye SK. The confusion assessment method: a systematic review of current usage. *J Am Geriatr Soc*. 2008;56(5):823–830.
18. American Society of Health-System Pharmacists. *AHFS Drug Information*. Bethesda, MD: American Society of Health-System Pharmacists; 2005.
19. Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts [published correction appears in *Arch Intern Med*. 2004;164:298]. *Arch Intern Med* 2003;163(22):2716–2724.
20. Alexopoulos GS, Abrams RC, Young RC, Shamoian CA. Cornell Scale for Depression in Dementia. *Biol Psychiatry*. 1988;23(3):271–284.
21. Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. *J Am Geriatr Soc*. 1983;31(12):721–726.
22. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373–383.
23. Warden V, Hurley AC, Volicer L. Development and psychometric evaluation of the Pain Assessment in Advanced Dementia (PAINAD) scale. *J Am Med Dir Assoc*. 2003;4(1):9–15.
24. Andrew MK, Freter SH, Rockwood K. Prevalence and outcomes of delirium in community and non-acute care settings in people without dementia: a report from the Canadian Study of Health and Aging. *BMC Med*. 2006;4:15.
25. Pitkala KH, Laurila JV, Strandberg TE, Tilvis RS. Prognostic significance of delirium in frail older people. *Dementia*. 2005;19(2-3):158–163.
26. Witlox J, Eurelings LS, de Jonghe JF, Kalisvaart KJ, Eikelenboom P, van Gool WA. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis. *JAMA*. 2010;304(4):443–451.
27. Ely EW, Shintani A, Truman B, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA*. 2004;291(14):1753–1762.
28. Bellelli G, Speciale S, Barisione E, Trabucchi M. Delirium subtypes and 1-year mortality among elderly patients discharged from a post-acute rehabilitation facility. *J Gerontol*. 2007;62A(10):1182–1183.
29. Edlund A, Lundstrom M, Karlsson S, Brannstrom B, Bucht G, Gustafson Y. Delirium in older patients admitted to general internal medicine. *J Geriatr Psychiatry Neurol*. 2006;19(2):83–90.
30. Kiely DK, Jones RN, Bergmann MA, Marcantonio ER. Association between psychomotor activity delirium subtypes and mortality among newly admitted postacute facility patients. *J Gerontol*. 2007;62A(2):174–179.
31. Leslie DL, Zhang Y, Holford TR, Bogardus ST, Leo-Summers LS, Inouye SK. Premature death associated with delirium at 1-year follow-up. *Arch Intern Med*. 2005;165:1657–1662.
32. McAvay GJ, Van Ness PH, Bogardus ST, et al. Older adults discharged from the hospital with delirium: 1-year outcomes. *J Am Geriatr Soc*. 2006;54(8):1245–1250.
33. Voyer P, McCusker J, Cole MG, Khomenko L. Influence of prior cognitive impairment on the severity of delirium symptoms among older patients. *J Neurosci Nurs*. 2006;38(2):90–101.
34. Voyer P, McCusker J, Cole MG, St. Jacques S, Khomenko L. Factors associated with delirium severity among older patients. *J Clin Nurs*. 2007;16:819–831.
35. Saczynski JS, Marcantonio ER, Quach L, et al. Cognitive trajectories after postoperative delirium. *N Engl J Med*. 2012;367(1):30–39.
36. Wright RM, Roumani YF, Boudreau R, et al. Effect of central nervous system medication use on decline in cognition in community-dwelling older adults: findings from the Health, Aging and Body Composition Study. *J Am Geriatr Soc*. 2009;57(2):243–250.
37. Leslie DL, Marcantonio ER, Zhang Y, Leo-Summers L, Inouye SK. One-year health care costs associated with delirium in the elderly population. *Arch Intern Med*. 2008;168(1):27.