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Effects of alternative interventions among hospitalized, cognitively impaired older adults

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Aim: Compare within site effects of three interventions designed to enhance outcomes of hospitalized cognitively impaired elders. **Methods:** Prospective, nonrandomized, confirmatory phased study. In Phase I, 183 patients received one of three interventions: augmented standard care (ASC), resource nurse care (RNC) or Transitional Care Model (TCM). In Phase II, 205 patients received the TCM. **Results:** Time to first rehospitalization or death was longer for the TCM versus ASC group ($p = 0.017$). Rates for total all-cause rehospitalizations and days were significantly reduced in the TCM versus ASC group ($p < 0.001$, both). No differences were observed between RNC versus TCM. **Conclusion:** Findings suggest the TCM is more effective than ASC. However, potential effects of the RNC relative to the TCM warrant further study.

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Cognitive impairment (CI) has been reported to add to the complex care needs of an average of 43% of hospitalized older adults in USA, negatively affecting patients' health and quality of life and unnecessarily increasing healthcare costs [1–6]. CI also increases an older adult's risk for rehospitalization [7]. While often CI is associated with neurodegenerative diseases including Alzheimer's disease [8], it can result from a variety of medical problems such as heart failure [9], delirium due to infections and other physical risks [3]. Many patients with CI have no prior history of Alzheimer's disease or other dementias [10]. The collective impact of the disturbances to memory, orientation, executive function and behavior common among this population result in unique set of patient and family caregiver needs, which are especially challenging throughout patients' vulnerable transitions in health and healthcare [1].

All too often, unrecognized or poorly managed cognitive deficits among hospital-

ized older adults lead to a cascade of costly and often avoidable adverse clinical events (e.g., falls, functional decline, incontinence, malnutrition) that span the entire episode of care and contribute to avoidable rehospitalizations, nursing home placements or death [2–4,10–18]. Advancing knowledge is critically important to address the distinct needs of this growing patient population but, until recently, has not been a major focus of rigorous research. However, findings from a few areas of inquiry related to care management of this patient group during and following hospitalizations suggest potential solutions.

Systematic assessment and communication of older adults' cognitive findings to relevant health team members, for example, has contributed to improved care outcomes [19]. The use of hospital resource nurses with special preparation in the clinical management of this high-risk group also has been shown to improve functional status of patients during hospitalizations and significantly decrease the

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frequency and length of delirium in hospitalized older adults [20]. The Transitional Care Model (TCM), an approach that spans hospital to home, has consistently demonstrated enhanced care experiences and health outcomes for cognitively intact older adults, while reducing rehospitalizations and costs; however, studies of this care management model have excluded cognitively impaired older adults [21–23]. Additionally, examination of each of these interventions has been limited to comparisons between intervention and standard care groups. Comparisons of the relative effects of evidence-based care management interventions are essential to enhance posthospital outcomes of this vulnerable population.

An earlier comparison of the effects of the aforementioned interventions across sites and at same time period (Phase I; 2006–2008) using propensity score weighted groups revealed that hospitalized cognitively impaired older adults who received the TCM intervention had a longer time to first rehospitalization or death [24]. In addition, when compared with older adults receiving lower dose interventions, the TCM intervention group had fewer rehospitalizations and days, with the greatest impact in the first month following hospital discharge. This current paper reports the effects of these alternative interventions within sites and over time (Phase I vs Phase II; 2008–2010). The study team hypothesized that cognitively impaired hospitalized older adults who received the TCM, a hospital to home intervention would, relative to other lower dose interventions which are limited to hospital care only, would demonstrate increased time to first rehospitalization or death and fewer total all-cause rehospitalizations and days.

Methods

Design

A nonrandomized, confirmatory phased design was used to compare the effects of alternative interventions implemented during two different time periods (Phase I; 2006–2008 and Phase II; 2008–2010) (Table 1). This study design was chosen due to the nature of the interventions, and the inability to randomize subjects at the patient level. Randomization at the patient level was not feasible due to the potential for within site cross-contamination of the interventions at the site level. To control for observable differences in patient characteristics across sites in Phase I analyses, propensity score matching was used. Phase II allowed for confirmation of intervention differences, where comparisons are carried out within sites over time and account for both observed and unobserved patient and site characteristics. No propensity score matching was used in the Phase I to II modeling. Overall, the two-phase approach minimized threats to the internal valid-

ity of the study. This study was reviewed and approved by the University of Pennsylvania Institutional Review Board.

Settings

Three hospitals in the Philadelphia area (one academic medical center and two community hospitals) affiliated with one health system participated in this study. Throughout the study period, participating hospitals did not routinely screen patients for CI; all sites applied a consistent set of hospital care and discharge planning procedures.

Interventions

The intervention protocols tested in this study are summarized below and detailed protocols are published elsewhere [25].

Augmented standard care

All patients at all participating sites and in both phases were assessed for cognitive deficits by trained research assistants (RAs) via chart reviews for documented diagnoses of dementia or screening using a standardized assessment tools [19]. This assessment was comprised of valid and reliable measures of orientation, recall and executive function [26,27]. The cognitive screen was completed within 24 h of patients' hospital admissions, with findings documented in patients' medical records and verbally communicated to the primary nurse, physician and social worker assigned to each patient within one hour of completion (average 22 min/per patient). The augmented standard care (ASC) was included as part of the other two interventions.

Resource nurse care

The resource nurse care (RNC) intervention [28,29] was implemented by hospital employed registered nurses (RNs) who had completed web-based modules focused on managing and transitioning hospitalized older adults with cognitive deficits. The study team, in consultation with clinical experts, developed the modules [25]. The RNC extended from patient enrollment to index hospital discharge. Each RN who completed the training had to achieve an 80% or higher on the module post-test to be considered a 'resource nurse' (59 out of 69 RNs completed the modules). Nurses completed the training as part of an in-service. Average time to complete all resource nurse training modules was 6 h. Resource nurses were assigned to a patient after the patient-family caregiver dyad was enrolled. Resource nurses either provided direct care and/or coached other nonresource trained staff nurses involved in the care of enrolled patients from enrollment to hospital discharge [29].

Table 1. Intervention by site by phase.

Hospital sites	Phase I (February 2006–March 2008)	Phase II (April 2008–March 2010)
A	Augmented standard care	TCM
B	Resource nurse care	TCM
C	TCM	TCM

TCM: Transitional Care Model.

Transitional Care Model

The TCM intervention [21–23] was implemented by master's prepared advanced practice nurses (APNs) and extended from patient enrollment through an average of 2 months postindex hospital discharge [25]. APNs completed TCM-specific web-based modules and a 1 month clinical experience individualized to each APN's needs. In addition, the APNs completed the RNC training modules. The TCM intervention combined hospital and home visits, at least one in person visit with the patient to their physician(s) office with an average of 11 visits in total and ten telephone calls per patient. APNs were available 7 days a week for visits and calls. The TCM intervention substituted for traditional home care by skilled nurses.

Screening & recruitment

Weekday review of medical records of all hospitalized patients 65 years and older was completed at the three participating hospitals by RAs with at least bachelor's degrees and special role preparation in screening for CI. Inclusion criteria at the time of enrollment included all of the following: 65 years of age or older adult; screened as having cognitive deficits; hospitalized at one of three hospital sites, lived within a 30-mile radius of admitting hospital, spoke English, was expected to return home following hospital discharge and had a family caregiver also willing to enroll. Exclusion criteria included any of the following: undergoing active treatment for cancer, stroke or end-stage renal disease, enrollment in hospice; or untreated substance abuse or psychiatric condition (all documented in medical records).

Patients met the cognitive impairment screening threshold if they had a documented diagnosis of dementia or were assessed by RAs as having cognitive deficits that may impact transition in care [1,30]. Specifically, deficits in orientation and recall were assessed using the Six Item Screener (SIS) [26]. Scores of four or less on the SIS indicated deficits in orientation and recall. Patients who passed the SIS (SIS >4) were further evaluated for deficits in executive function using a clock drawing task (CLOX1) [27]. Patients with five or more errors on this 15-point assessment scale were considered to have deficits in executive function (defined as decision making ability, memory, attention, focus) which is required

for an individual to be able to organize, plan and complete everyday tasks [27]. Eligible patients and their family caregivers were approached by RAs; interested patients provided assent and family caregivers provided informed consent for the patient and themselves.

In total, 52% (1884/3635) of patients assessed for cognitive impairment during the two phases of this study were identified as having cognitive deficits (Table 2). Among those identified with CI, 66.1% (1246/1884) met all other inclusion and exclusion criteria. Among eligible patients, 536 patient-family caregiver dyads (43.0%) enrolled in the study; lack of interest in research on part of patients or family caregivers was the primary reason for deciding not to enroll (details published elsewhere [25]). In total, 40 (7.5%; 40/536) patient-family caregiver dyads were identified as ineligible after enrollment and excluded from the analyses. Of the remaining 496 patient-family caregiver dyads, the primary reasons for attrition were: withdraw (7.1%; 35/496), lost to follow-up (4.2%; 21/496), death (before discharge from hospital or immediately after discharge with no follow-up data, 3.6%; 18/496) and inability to complete the TCM intervention (3.0%; 15/496; e.g., patient moved, enrolled caregiver died, unable to complete home visits). There were no significant differences in baseline characteristics between the final sample and those lost to attrition. The attrition rate was consistent with rates reported in other clinical trials having a similar patient population [22,23]. Finally, at one hospital (site B) 19 patients received the ASC only intervention prior to the roll out of the RNC. Because the aim of the study was to make within site comparisons by intervention, and was powered such that each site would receive a single intervention in Phase I, these 19 patients were not included in this set of analyses.

Outcome variables

Time to first rehospitalization or death, total number of all-cause rehospitalizations and days rehospitalized over time (Phase I vs Phase II) were the primary outcomes.

Time to first rehospitalization or death

Time was measured from date of the index hospital discharge to the time of an event (e.g., first rehospitalization or death).

Table 2. Enrollment and attrition by site, phase and intervention group (2006–2010), n = 388.						
Enrollment summary	Phase I (February 2006–March 2008)			Phase II (April 2008–March 2010)		
	Site A	Site B [†]	Site C	Site A	Site B	Site C
Intervention	ASC	RNC	TCM	TCM	TCM	TCM
Enrolled in study	61	94	96	88	85	88
Determined ineligible [‡]	3	3	12	8	5	8
Attrition:						
– Withdrew	4	6	5	6	8	5
– Lost to follow-up	6	9	1	0	2	4
– Died before first follow-up/in hospital	2	5	2	3	2	0
– Incomplete intervention	0	0	9	0	0	2
– Other (e.g., moved out of state, caregiver died)	0	0	1	2	0	1
Final sample by site and intervention	46	71	66	69	68	68
Total final sample by phase	183			205		
[†] In total, 19 additional patients were enrolled at this site that received the ASC intervention only. Because the aim of the study was to make within site comparisons by intervention, and was powered such that each site would receive a single intervention in Phase I, these 19 patients were not included in this set of analyses.						
[‡] Patients' eligibility changed for two reasons: new ineligible diagnosis identified during index hospitalization or discharge from index hospitalization changed to long-term placement in a nursing home.						
ASC: Augmented standard care; RNC: Resource nurse care; TCM: Transitional Care Model.						

talization or death) or last interview for censored patients. Data on all rehospitalizations were collected from patients and family caregivers and independently confirmed through medical records' review. Reported deaths were confirmed in the Social Security Death Index online. A total of 23 patients died during the study period (eight in Phase I and 15 in Phase II). Among the 23 patients that died, 12 were rehospitalized at least once prior to death. Among the remaining 11 patients, eight were enrolled in hospice at the time of death and three died during a rehospitalization. There were no differences in the analyses with or without these deaths, therefore all data are included as an event for these analyses.

Total number of rehospitalizations & days rehospitalized

The number of all-cause rehospitalizations and days rehospitalized per patient were assessed in 30-day increments through 6 months postindex hospital discharge.

Independent variables

Baseline sociodemographic patient characteristics (e.g., age, sex, race, living situation) and family caregivers characteristics (e.g., relationship to patient), as well as patient clinical data were collected via in-person interviews by RAs and supplemented by chart abstractions (Table 3). Cognitive status was assessed using

the Mini Mental State Examination (MMSE) [31] and Confusion Assessment Method (CAM) [32] for delirium. The presence of depressive symptoms was assessed using the Geriatric Depression Scale [33] if MMSE ≥16 or the Cornell Scale for Depression in Dementia [34] if MMSE <16. Time burden associated with caregiving was assessed using a subscale of Caregiver Burden Inventory [35]. All assessment tools were selected on the basis of use of the scale with a similar population in the USA and evidence in the literature for its use with individuals with CI (e.g., Geriatric Depression Scale [36–38]; CAM [3,20,32,39]; Cornell Scale for Depression in Dementia [34,40]; Caregiver Burden Inventory [35]).

Statistical analyses

Descriptive statistics regarding patients' and family caregivers' baseline characteristics, including frequencies and percentages for categorical variables, and means, standard deviations and ranges for continuous variables are presented in Table 3. Comparisons between Phase I and Phase II groups at each hospital site were conducted using chi-square tests, Fisher's exact tests and two sample t-tests, as appropriate. All variables with a p-value 0.10 or less were included in subsequent modeling [41,42].

A multivariable analysis of time to first rehospitalization or death using accelerated failure time (AFT) modeling with a loglogistic distribution was used to examine differences between alternative interven-

tions over time for each of three hospital sites (A, B or C) [43]. This parametric approach was chosen over the commonly used Cox proportional hazards model because the underlying assumption of proportional hazards was not met [44]. Patients alive and remaining free from hospitalization were censored at study completion. The association of primary interest is represented by ($\exp[-\beta]$) and estimates the acceleration in time to first rehospitalization or death for patients in Phase II compared with Phase I [43]. Individual Kaplan–Meier curves [45] of the time to first rehospitalization or death were generated for each site comparing Phase I to II by intervention type. Log rank tests [46] were used to compare the survival curve distributions by intervention and the Wilcoxon (Breslow) test was used to test for statistical differences early in the survival curves [47]. Poisson generalized estimating equations (log link) and linear mixed models relying on an exchangeable covariance matrix were used to model the number of rehospitalizations per patient as well as log transformed rehospitalization days per patient through 6 months [48,49]. Poisson modeling controlled for varying days at risk for rehospitalization over time and accounted for correlation between observations for the same person. Estimates of phase by intervention group effects, along with their interaction with time, are presented for each phase by site. The association of primary interest for all-cause rehospitalizations is represented by ($\exp[\beta]$) and expresses the relative rate in hospitalizations in Phase II relative to Phase I. The association of primary interest for all-cause rehospitalization days is also represented by ($\exp[\beta]$) and estimates the ratio of geometric means for days hospitalized for Phase II compared with Phase I. Predicted model estimates were used to graphically describe longitudinal changes.

Results

The final sample included 388 patients, each with an enrolled family caregiver. At enrollment, 18.0% (70/388) had a documented diagnosis of dementia, 43.6% (169/388) had deficits in orientation and recall and 38.4% (149/388) had deficits in executive function. In total, 24% of the final sample also screened positive for delirium (92/388) during the index hospitalization. Overall, 5.7% (22/388) of the sample died within 180 days of index hospital discharge

Time to first rehospitalization or death

Figure 1 provide visual comparisons of Kaplan–Meier estimates for time to first rehospitalization or death within each site. Overall, statistically significant differences are observed when comparing ASC versus TCM groups but not for the RNC versus TCM on the basis

of the Wilcoxon (Breslow) test. The largest difference between the groups on time to first rehospitalization or death is observed early in the Kaplan–Meier curve (at 30 days Phase I vs II - site A: ASC: 24% vs TCM: 4%; site B: RNC: 18% vs TCM: 9%; site C: TCM: 8% vs TCM: 10%). Based on nonoverlapping 95% CIs from the Kaplan–Meier estimates, the difference in time to first rehospitalization or death at 30 and 60 days is statistically significant at the 0.05 level for the ASC versus TCM groups. No statistically significant differences are observed in sites B and C.

Although, not statistically significant, time to first rehospitalization or death is longer for the TCM patients than the non-TCM patients. For site A, 25% of the sample had a rehospitalization or died by day 33 in the ASC group versus day 90 for the TCM group. For site B, 25% of the RNC group was rehospitalized or died by day 58 versus day 81 for the TCM group. Notably, at site C, where the TCM was provided in both phases, 25% of the patients were rehospitalized or died by day 88 (Phase I) versus day 66 (Phase II).

The loglogistic AFT model (Table 4) estimate of progression to rehospitalization or death is significantly slower for the TCM group versus the ASC group at site A (acceleration factor: 0.35; $p = 0.02$). While not statistically significant, the progression to rehospitalization or death is slower for the TCM group versus RNC group at site B (acceleration factor: 0.56; $p = 0.17$). For site C, the AFT model demonstrated an accelerated progression to rehospitalization or death by a factor of 1.28 for Phase II, though not statistically significant.

Total all-cause rehospitalizations

The predicted estimates for total all-cause rehospitalizations over time, based on multivariable generalized linear modeling, are provided by site and phase in Table 5. Mean all-cause rehospitalization estimates for ASC versus TCM are 0.12 versus 0.06, respectively. Over time, the ASC has a significantly steeper slope than the TCM group in site A ($p = 0.03$). Mean all-cause rehospitalization estimates for RNC versus TCM are 0.12 versus 0.11, respectively. Mean all-cause rehospitalization estimates for TCM versus TCM are 0.10 versus 0.10, Phase I versus Phase II, respectively.

The relative rate for total all-cause rehospitalizations is significantly less for the TCM group (Phase II) as compared with the ASC group (Phase I) at site A ($\exp[-2.00] = 0.14$; $p < 0.001$; Table 5). However, there are no statistically significant differences observed between Phase I versus II in sites B or C (Table 5). The relative rate for total all-cause rehospitalizations decreases significantly over time at site A for the ASC group ($\exp[-0.085] = 0.92$; $p < 0.001$), while remaining consistently low over time for the TCM group

Table 3. Clinical and nonclinical patient and family caregiver characteristics by hospital, phase and intervention group (n = 388).

Variables	Site A			Site B			Site C		
	Phase I	Phase II	p-value	Phase I	Phase II	p-value	Phase I	Phase II	p-value
Intervention type	ASC	TCM		RNC	TCM		TCM	TCM	
Total (n)	46	69		71	68		66	68	
Male, n (%)	18 (39.1)	20 (29.0)	0.31	24 (33.8)	18 (26.5)	0.37	26 (39.4)	24 (35.3)	0.72
Age, mean $\pm$ SD (range); years [†]	80.5 $\pm$ 6.1 (70–96)	82.9 $\pm$ 8.52 (65–102)	0.09	80.9 $\pm$ 6.4 (65–98)	80.7 $\pm$ 7.7 (65–96)	0.90	79.4 $\pm$ 6.6 (68–96)	79.6 $\pm$ 7.3 (66–98)	0.85
White, n (%) [†]	17 (37.0)	23 (33.3)	0.69	56 (78.9)	64 (94.1)	0.02	33 (50.0)	46 (67.7)	0.05
Patient lives alone, n (%)	34 (73.9)	42 (60.9)	0.16	54 (76.1)	45 (66.2)	0.45	8 (72.7)	14 (69.1)	0.71
Dementia diagnosis, n (%) [†]	6 (13.0)	14 (20.3)	0.45	20 (28.2)	8 (11.8)	0.01	8 (12.1)	14 (20.6)	0.25
Number of coexisting conditions, mean $\pm$ SD (range)	5.2 $\pm$ 2.4 (1–11)	4.9 $\pm$ 2.4 (0–10)	0.57	4.5 $\pm$ 2.6 (0–11)	4.3 $\pm$ 2.3 (0–12)	0.91	5.7 $\pm$ 2.5 (1–12)	5.7 $\pm$ 2.5 (1–13)	0.93
Number of hospitalizations in prior 6-months, mean $\pm$ SD (range)	0.9 $\pm$ 1.1 (0–5)	0.8 $\pm$ 1.3 (0–9)	0.67	0.99 $\pm$ 1.3 (0–5)	0.8 $\pm$ 0.9 (0–3)	0.39	1.3 $\pm$ 2.4 (0–11)	1.0 $\pm$ 1.7 (0–8)	0.33
Delirium present, n (%) [†]	6 (13.6)	20 (29.0)	0.07	21 (30.9)	23 (33.8)	0.97	10 (17.2)	12 (17.7)	1.00
Not assessed, n (%)	2 (4.3)	0 (0.0)		3 (4.4)	0 (0.0)		8 (12.1)	0 (0.0)	
MMSE, mean $\pm$ SD (range)	24.0 $\pm$ 4.2 (15–30)	22.6 $\pm$ 5.9 (7–30)	0.17	20.9 $\pm$ 7.0 (4–30)	21.2 $\pm$ 4.9 (6–30)	0.83	21.7 $\pm$ 5.9 (2–30)	21.8 $\pm$ 5.1 (6–30)	0.99
Unable to complete, n (%)	1 (2.2)	0 (0)		5 (7.0)	2 (2.9)		0 (0)	1 (1.5)	
Basic activities of daily living, mean $\pm$ SD (range) [†]	4.5 $\pm$ 1.9 (0–6)	5.0 $\pm$ 1.5 (1–6)	0.20	4.3 $\pm$ 2.1 (0–6)	5.3 $\pm$ 1.4 (0–6)	<0.001	4.4 $\pm$ 1.9 (0–6)	5.5 $\pm$ 1.0 (1–6)	<0.001
Instrumental activities of daily living, mean $\pm$ SD (range)	5.06 $\pm$ 2.1 (1–8)	4.69 $\pm$ 2.7 (0–8)	0.44	4.2 $\pm$ 2.8 (0–8)	5.0 $\pm$ 2.7 (0–8)	0.18	5.3 $\pm$ 2.5 (0–8)	5.7 $\pm$ 2.6 (0–8)	0.36
Missing, n (%)	2 (4.4)	1 (1.4)		4 (5.6)	0 (0)		5 (7.6)	0 (0.0)	
Depressive symptoms present, n (%)	9 (19.6)	23 (33.3)	0.14	16 (22.5)	15 (22.1)	0.40	8 (12.1)	16 (23.5)	0.11
Index hospitalization diagnosis, n (%):									
– Cardiac/pulmonary [†]	9 (19.6)	32 (46.4)	0.01	25 (35.2)	29 (42.0)	0.63	35 (53.0)	38 (55.9)	0.86
– Orthopedic/mechanical fall [†]	17 (37.0)	7 (10.1)	<0.001	14 (19.7)	9 (13.2)	0.30	4 (6.1)	6 (8.8)	0.74
– Neurologic	4 (8.7)	8 (11.6)	0.76	10 (14.1)	13 (19.1)	0.72	10 (15.2)	9 (13.2)	0.81
– GI/GU	9 (19.6)	13 (18.8)	1.00	11 (15.5)	16 (23.5)	0.47	7 (10.6)	6 (8.8)	0.78
– Endocrine/metabolic [†]	7 (15.2)	9 (13.0)	0.79	11 (15.5)	1 (1.5)	<0.001	10 (15.2)	9 (13.2)	0.81

Percentages may not add to 100 due to rounding.

[†]All multivariable models were adjusted for covariates demonstrating significance (p-values of 0.10 or less).

ASC: Augmented standard care; GI/GU: Gastrointestinal/genitourinary; MMSE: Mini mental state examination; RNC: Resource nurse care; SD: Standard deviation; TCM: Transitional Care Model.

Table 3. Clinical and nonclinical patient and family caregiver characteristics by hospital, phase and intervention group (n = 388) (cont.).

Variables	Site A			Site B			Site C		
	Phase I	Phase II	p-value	Phase I	Phase II	p-value	Phase I	Phase II	p-value
Caregiver variables:									
– Male, n (%)	10 (21.7)	20 (29.0)	0.52	14 (19.7)	13 (19.1)	0.76	17 (25.8)	20 (29.4)	0.70
– Age, mean $\pm$ SD (range); years	60.2 $\pm$ 13.2 (34–82)	59.7 $\pm$ 12.2 (35–93)	0.83	60.9 $\pm$ 13.7 (36–93)	57.7 $\pm$ 15.2 (18–90)	0.37	60.4 $\pm$ 12.1 (34–85)	56.8 $\pm$ 14.8 (23–87)	0.12
– Caregiver burden inventory – time subscale, mean $\pm$ SD (range) [†]	7.2 $\pm$ 6.0 (0–20)	7.7 $\pm$ 6.4 (0–20)	0.69	7.3 $\pm$ 6.7 (0–20)	5.8 $\pm$ 6.8 (0–20)	0.06	7.1 $\pm$ 5.1 (0–19)	5.2 $\pm$ 5.0 (0–20)	0.03
– Missing, n (%)	2 (4.4)	0 (0.0)		4 (5.6)	0 (0)		10 (15.2)	0 (0)	
Relationship to patient, n (%): [†]			0.36			0.05			0.24
– Spouse	15 (32.6)	14 (20.3)		19 (26.8)	6 (8.8)		20 (30.3)	12 (17.7)	
– Adult child	25 (54.4)	44 (63.8)		35 (49.3)	38 (55.9)		33 (50.0)	40 (58.8)	
– Other relative/friend/other (e.g., Godchild)	6 (13.04)	11 (15.9)		17 (23.9)	24 (35.3)		13 (19.7)	16 (23.5)	

Percentages may not add to 100 due to rounding.

[†]All multivariable models were adjusted for covariates demonstrating significance (p-values of 0.10 or less).

ASC: Augmented standard care; GI/GU: Gastrointestinal/genitourinary; MMSE: Mini mental state examination; RNC: Resource nurse care; SD: Standard deviation; TCM: Transitional Care Model.

Figure 1. Kaplan–Meier curve of sites A, B and C.
ASC: Augmented standard care; RNC: Resource nurse care; TCM: Transitional Care Model.

Table 4. Individual multivariable accelerated failure time models for time to first rehospitalization or death comparing Phase I to Phase II by intervention within each site

Site	Phase I vs II	Acceleration factor (exp[-β])	95% CI: (exp[-β])		p-value
			Lower limit	Upper limit	
A	ASC (ref) vs TCM	0.354	0.151	0.833	0.017
B	RNC (ref) vs TCM	0.556	0.239	1.297	0.174
C	TCM (ref) vs TCM	1.186	0.570	2.468	0.648

Recruitment into Phase I: February 2006–March 2008; Phase II: April 2008–December 2009. TCM all multivariable models were adjusted for covariates demonstrating significance (p-values of 0.10 or less) in [Table 1](#). Exp(-β) represents the acceleration factor. Interpretation example: the time to first rehospitalization among those in the TCM group is accelerated by a factor of 0.354 times that of the ASC group. ASC: Augmented standard care (lower); ref: Reference group; RNC: Resource nurse care (medium); TCM: Transitional Care Model (higher).

([Figure 2A](#)). At site B, the relative rate for total all-cause rehospitalizations decreases significantly over time for both intervention groups (RNC: exp[-0.042] = 0.96; p = 0.03); TCM: (exp[-0.05] = 0.95; p = 0.04) ([Table 5](#)). Finally, at site C the relative rate for total all-cause rehospitalizations is flat for the Phase I TCM group but has a steeper slope (e.g., decreases significantly over time) for Phase II TCM intervention group (exp[-0.05] = 0.95; p = 0.04).

Total all-cause rehospitalization days

The predicted estimates for total all-cause rehospitalization days based on multivariable Poisson generalized estimating equation modeling over time by site and phase are provided in [Table 6](#). Mean outcome estimates for all-cause rehospitalization days for ASC versus TCM are 0.72 versus 0.33, respectively. Over time, the ASC has a significantly steeper slope than the TCM group in site A (p = 0.01). Mean outcome estimates for all-cause rehospitalization days appear similar for RNC versus TCM, 0.63 versus 0.70, respec-

tively. At site C, mean outcome estimates for all-cause rehospitalization days differ from Phase I to II for the TCM groups (0.43 vs 0.49, respectively). Over time, the TCM Phase II has a significantly steeper slope than the TCM Phase I group (p = 0.02).

In multivariable modeling presented in [Table 6](#), the estimated geometric mean for all-cause rehospitalization days in Phase II (TCM) is 0.26-fold that of Phase I (ASC) (exp[-1.34] = 0.26; p = 0.007). The estimated geometric mean for all-cause rehospitalization days decreases significantly over time for the ASC group at site A (exp[-0.06] = 0.94; p = 0.002) while the TCM group (site A, Phase II) remains consistently low and does not change over time (exp[-0.004] = 1.00; p = 0.76). There are no statistically significant differences observed between Phase I versus II in sites B or C, see [Table 6](#). The estimated geometric mean for all-cause rehospitalization days for the RNC group decreases over time (exp[-0.04] = 0.96; p = 0.05), while the TCM group (site B, Phase II) does not change significantly over time (exp[-0.03] = 0.97; p = 0.15). Finally, at site C

Table 5. Multivariable general linear modeling of all-cause rehospitalizations.

Site	Predictor variables Phase I vs II	Relative rate (exp[β])	95% CI:		p-value
			Lower limit (exp[β])	Upper limit (exp[β])	
A	ASC (ref) vs TCM	0.135	0.045	0.412	<0.001
B	RNC (ref) vs TCM	1.122	0.446	2.819	0.807
C	TCM (ref) vs TCM	1.688	0.647	4.404	0.285
A	Time × Phase I – ASC	0.919	0.875	0.965	0.001
	Time × Phase II – TCM	1.000	0.944	1.059	0.992
B	Time × Phase I – RNC	0.959	0.922	0.997	0.034
	Time × Phase II – TCM	0.950	0.903	0.998	0.041
C	Time × Phase I – TCM	0.985	0.951	1.021	0.412
	Time × Phase II – TCM	0.947	0.899	0.996	0.035

Recruitment into Phase I: February 2006–March 2008; Phase II: April 2008–December 2009. TCM all multivariable models were adjusted for covariates demonstrating significance (p-values of 0.10 or less) in [Table 1](#). Exp(-β) represents the relative risk for all-cause rehospitalizations and ratio of geometric means for rehospitalization days. Interpretation example: the rate of all-cause rehospitalization among those in the TCM group is 0.135 that of those in the ASC group. For the interpretation of the site A time x Phase I interaction: for each unit increase in time, the rate of all-cause rehospitalization is reduced by ~8% (1–0.919 = 0.081).

ASC: Augmented standard care (lower); ref: Reference group; RNC: Resource nurse care (medium); TCM: Transitional Care Model (higher).

Figure 2. Rehospitalizations and days rehospitalized over time by phase and site. (A) Rehospitalizations over time by phase by site. **(B)** Total days rehospitalized over time by phase by site.

ASC: Augmented standard care; Ph: Phase; RNC: Resource nurse care; S: Site; TCM: Transitional Care Model.

the estimated geometric mean of all-cause rehospitalization days remains flat in Phase I ($\exp[0.002] = 1.00$; $p = 0.78$) but has a steeper slope (e.g., drops significantly over time) for Phase II patients who received the TCM intervention ($\exp[-0.05] = 0.95$; $p = 0.02$).

Discussion

Overall study findings of a hospital to home (TCM) intervention relative to a hospital only intervention (ASC) for cognitively impaired hospitalized older adults support that the more intensive cross-setting intervention (TCM) had a greater effect on time to first rehospitalization or death and all-cause rehospitalizations and days than augmenting standard care. While not statistically significant, differences between the TCM in comparison to a hospital-based RNC intervention in time to first event were observed. However, no differences in total rehospitalization rates and days through 6 months between RNC and TCM were identified. These findings have several important implications for healthcare delivery and future research.

The study's focus on care management of older adults with CI during vulnerable transitions from hos-

pital to home is especially noteworthy, with 10–20% of adults 65 years and older having mild CI (often unrecognized) [50] and the projected growth of older adults with Alzheimer's disease and other dementias expected to reach approximately 14 million people by 2050 [8]. This growing patient population is at high risk for cognitive decline, increased use of costly healthcare resources and other poor outcome [51,52]. Unfortunately, research efforts designed to enhance care management have traditionally excluded older adults with cognitive deficits [53].

While this paper reports findings from confirmatory analyses of a comparative effectiveness study of promising care strategies, rehospitalization outcomes achieved using current care approaches provides important contextual information. Available Medicare 30-day rehospitalization rates for common diagnoses at the three hospitals that participated in this study allowed for comparisons between the rehospitalization rates observed among study patients with similar nonstudy patients. Between 2007 and 2011, the mean rehospitalization rate for Medicare beneficiaries admitted to the three hospital sites for major cardiopulmonary diagnoses was

22% at 30 days [54]; this rate is similar to the 30-day rehospitalization rate for the ASC group, slightly higher than the RNC group rate and substantially higher than the TCM group rates at each site in both phases.

Despite earlier reports suggesting improved outcomes for this patient group [19], the lower dose hospital-based intervention designed to provide information regarding cognitive deficits to healthcare professionals directly involved in each patient's care appears to have had little impact on time to first rehospitalization or death and the rehospitalization when compared with the TCM, a more intensive hospital to home intervention. More recent evidence from other clinical trials [21,22,55] reinforce this study finding. Assessment and communication of cognitive findings using standardized tools has demonstrated limited value in enhancing care and outcomes of this patient group. Specifically, researchers have reported that this information without additional reinforcement does not change healthcare professionals' hospital practice behaviors [10]. While assessing for CI is an essential component in designing and implementing plans of care to address the unique needs of cognitively impaired patients transitioning from hospital to home [56], this strategy alone does not appear to have an effect on rehospitalization measures.

Study findings revealed no differences in any of the examined rehospitalization measures between the RNC and TCM interventions, suggesting that the medium dose intervention is just as effective as the higher dose intervention. When compared with the TCM, the RNC appears to offer a more efficient path to improving outcomes for this patient group. The lack of both statistical and clinically meaningful differences in total rehospitalization rates and days rein-

forces this interpretation. The solution suggested by these findings is strengthening the competencies of the hospital workforce in addressing the complex needs of cognitively impaired patients.

These findings are inconsistent with multiple prior studies of the TCM to standard care [21–23], including earlier comparative effectiveness research [57]. Based on earlier findings revealing the capacity of the TCM to address gaps in care throughout transitions from hospitals to home that negatively impacted high risk groups, the study team had hypothesized a greater positive impact for the TCM relative to the RNC in rehospitalization measures between the RNC and TCM groups. Potential reasons for the absence of differences were explored. For example, while group differences in time to event (hospitalization or death) estimated by the Kaplan–Meier curve were not statistically different, differences between the groups are suggested (see Figure 1, site B). *Post hoc* power calculations revealed that the sample size was insufficient to demonstrate statistical significances between the RNC versus TCM groups on time to first event. Indeed, inadequate power to detect statistically significant differences was an issue for all of the rehospitalization outcomes assessed in the RNC versus TCM groups. Thus, while the medium dose intervention may be just as effective as the higher dose intervention in improving posthospitalization outcomes, additional adequately powered studies are needed to confirm these findings.

Limitations

There are a number of limitations to this comparative effectiveness study that may limit the generalizability of the study findings. First, the study, while designed

Table 6. Multivariable general linear modeling of all-cause rehospitalization days.

Site	Predictor variables Phase I vs II	Ratio of geometric means (exp(β))	95% CI:		p-value
			Lower limit (exp(β))	Upper limit (exp(β))	
A	ASC (ref) vs TCM	0.263	0.100	0.690	0.007
B	RNC (ref) vs TCM	1.031	0.314	3.392	0.960
C	TCM (ref) vs TCM	2.338	0.964	5.669	0.060
A	Time $\times$ Phase I – ASC	0.936	0.897	0.976	0.002
	Time $\times$ Phase II – TCM	0.996	0.972	1.021	0.761
B	Time $\times$ Phase I – RNC	0.961	0.924	0.999	0.046
	Time $\times$ Phase II – TCM	0.970	0.931	1.011	0.152
C	Time $\times$ Phase I – TCM	1.002	0.987	1.018	0.784
	Time $\times$ Phase II – TCM	0.953	0.914	0.992	0.020

Recruitment into Phase I: February 2006–March 2008; Phase II: April 2008–December 2009. TCM all multivariable models were adjusted for covariates demonstrating significance (p-values of 0.10 or less) in Table 1. Exp(β) represents the relative risk for all-cause rehospitalizations and ratio of geometric means for rehospitalization days. Interpretation example: the rate of all-cause rehospitalization days among those in the TCM group is 0.100 that of those in the ASC group. For the interpretation of the site A time $\times$ Phase I interaction: for each unit increase in time, the rate of all-cause rehospitalization is reduced by ~6% ($1 - 0.936 = 0.064$).

ASC: Augmented standard care (lower); ref: Reference group; RNC: Resource nurse care (medium); TCM: Transitional Care Model (higher).

to make within site comparisons, was only powered to detect statistically significant differences between ASC and TCM on time to first all-cause rehospitalization or death. *Post hoc* power calculations confirm we had sufficient power to demonstrate observed differences between the ASC versus TCM groups at site A for the three outcomes of interest, but were underpowered to detect differences for RNC versus TCM groups. Second, these within site comparisons were necessary due to the inability to randomize at the patient level. The goal of the within site comparisons was to account for the unique characteristics at each site. Finally, for the reason noted earlier in the 'Methods' section, 19 patients were not included in the final analyses. To address this limitation, a sensitivity analysis of the outcomes at site B with the three groups (Phase I ASC and RNC vs Phase II TCM) that included these 19 patients was conducted. Results were similar to the data presented here.

Conclusion

In comparison to the lowest intensity hospital only intervention (ASC), study findings suggest the TCM has the potential to improve costly resource use outcomes for this vulnerable group of patients and reduce their use of costly health services. Findings also suggest that the medium dose intervention (RNC) may be as effective as the higher dose intervention (TCM) in subsequent resource use. However, further study is

warranted to examine the effects of the RNC medium dose intervention compared with the higher dose TCM intervention with a larger sample. Additionally, future research needs to focus on care management strategies designed to enhance the outcomes of cognitively impaired older adults throughout vulnerable hospital to home transitions to determine which interventions are more patient- and family caregiver-centered, effective and efficient among specific subgroups of patients.

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

Executive summary

- The primary study aim was to compare over time the effects of alternative evidence-based interventions of varying intensities delivered within the same sites, with each designed to enhance postdischarge outcomes of hospitalized cognitively impaired older adults.
- A prospective, nonrandomized, confirmatory phased study was conducted over two time periods and included a total of 388 cognitively impaired older adults admitted to one of three hospitals.
- Between 2006 and 2008 (Phase I), 183 patients received one of three different evidence-based protocols: a lower dose intervention (augmented standard care [ASC]); a medium dose intervention (resource nurse care [RNC]) and a higher dose intervention (Transitional Care Model [TCM]).
- Between 2008 and 2010 (Phase II), 205 patients received the higher dose TCM protocol.
- Primary outcome variables were: time to first rehospitalization or death (analyzed via Kaplan–Meier estimates and accelerated failure time models) and total number of all-cause rehospitalizations and days (analyzed via Poisson generalized estimating equations and linear mixed models) assessed through 6 months postindex hospitalization.
- In total, 25% of patients enrolled in the ASC and RNC groups were rehospitalized or died between day 33 and day 58 compared with days 66–90 for the TCM groups. The largest differences between the groups on this outcome were observed within 30 days of the index hospital discharge. Time to first rehospitalization or death was significantly longer only for the TCM group versus the ASC group ($p = 0.017$).
- The relative rates for total all-cause rehospitalizations and all-cause rehospitalization days were significantly less between the ASC versus TCM groups ($p < 0.001$, both) but not significantly different between the RNC versus TCM groups due to sample size constraints.
- Site comparisons suggest that the TCM, compared with a low dose intervention (ASC) of assessing cognition and communicating data regarding cognitive deficits, is more effective in decreasing rehospitalizations.
- There were no differences on the number of rehospitalizations or days rehospitalized at the site with the medium dose (RNC) versus higher dose (TCM) interventions. Due to inadequate sample size, the effects of the RNC relative to the TCM on rehospitalizations warrant further study.

References

Papers of special note have been highlighted as:

• of interest; •• of considerable interest

- 1 Boustani M, Baker MS, Campbell N *et al.* Impact and recognition of cognitive impairment among hospitalized elders. *J. Hosp. Med.* 5(2), 69–75 (2010).
- **Provides background on cognitive impairment among hospitalized older adults in the USA.**
- 2 Boyd CM, Landefeld CS, Counsell SR *et al.* Recovery of activities of daily living in older adults after hospitalization for acute medical illness. *J. Am. Geriatr. Soc.* 56(12), 2171–2179 (2008).
- 3 Inouye SK. Delirium in older persons. *N. Engl. J. Med.* 354(11), 1157–1165 (2006).
- 4 Sands LP, Yaffe K, Covinsky K *et al.* Cognitive screening predicts magnitude of functional recovery from admission to 3 months after discharge in hospitalized elders. *J. Gerontol. A Biol. Sci. Med. Sci.* 58(1), 37–45 (2003).
- 5 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.* 168(1), 27–32 (2008).
- 6 Wilson RS, Hebert LE, Scherr PA, Dong X, Leurgens SE, Evans DA. Cognitive decline after hospitalization in a community population of older persons. *Neurology* 78(13), 950–956 (2012).
- 7 Phelan EA, Borson S, Grothaus L, Balch S, Larson EB. Association of incident dementia with hospitalizations. *JAMA* 307(2), 165–172 (2012).
- 8 Alzheimer's Association. 2015 Alzheimer's disease facts and figures. *Alzheimers Dement.* 11(3), 332–384 (2015).
- **Provides background on Alzheimer's disease and other dementia in the USA.**
- 9 Heckman GA, Patterson CJ, Demers C, St Onge J, Turpie ID, McKelvie RS. Heart failure and cognitive impairment: challenges and opportunities. *Clin. Interv. Aging* 2(2), 209–218 (2007).
- 10 Boustani MA, Campbell NL, Khan BA *et al.* Enhancing Care for hospitalized older adults with cognitive impairment: a randomized controlled trial. *J. Gen. Intern. Med.* 27(5), 561–567 (2012).
- 11 Mitchell SL, Teno JM, Kiely DK *et al.* The clinical course of advanced dementia. *N. Engl. J. Med.* 361(16), 1529–1538 (2009).
- 12 Bynum JP, Rabins PV, Weller W, Niefeld M, Anderson GF, Wu AW. The relationship between a dementia diagnosis, chronic illness, medicare expenditures, and hospital use. *J. Am. Geriatr. Soc.* 52(2), 187–194 (2004).
- 13 Rudolph JL, Zanin NM, Jones RN *et al.* Hospitalization in community-dwelling persons with Alzheimer's disease: frequency and causes. *J. Am. Geriatr. Soc.* 58(8), 1542–1548 (2010).
- 14 Mecocci P, Von Strauss E, Cherubini A *et al.* Cognitive impairment is the major risk factor for development of geriatric syndromes during hospitalization: results from the GIFA study. *Dement. Geriatr. Cogn. Disord.* 20(4), 262–269 (2005).
- 15 Hitcho EB, Krauss MJ, Birge S *et al.* Characteristics and circumstances of falls in a hospital setting: a prospective analysis. *J. Gen. Intern. Med.* 19(7), 732–739 (2004).
- 16 Pedone C, Ercolani S, Catani M *et al.* Elderly patients with cognitive impairment have a high risk for functional decline during hospitalization: the GIFA study. *J. Gerontol. A Biol. Sci. Med. Sci.* 60(12), 1576–1580 (2005).
- 17 Krauss MJ, Evanoff B, Hitcho E *et al.* A case–control study of patient, medication, and care-related risk factors for inpatient falls. *J. Gen. Intern. Med.* 20(2), 116–122 (2005).
- 18 Thornlow DK, Anderson R, Oddone E. Cascade iatrogenesis: factors leading to the development of adverse events in hospitalized older adults. *Int. J. Nurs. Stud.* 46(11), 1528–1535 (2009).
- 19 Cole MG. Delirium in elderly patients. *Am. J. Geriatr. Psychiatry* 12(1), 7–21 (2004).
- 20 Inouye SK, Bogardus ST Jr, Charpentier PA *et al.* A multicomponent intervention to prevent delirium in hospitalized older patients. *N. Engl. J. Med.* 340(9), 669–676 (1999).
- 21 Naylor M, Brooten D, Jones R, Lavizzo-Mourey R, Mezey M, Pauly M. Comprehensive discharge planning for the hospitalized elderly. A randomized clinical trial. *Ann. Intern. Med.* 120(12), 999–1006 (1994).
- **Provides background on the Transitional Care Model (TCM) randomized control trials.**
- 22 Naylor MD, Brooten D, Campbell R *et al.* Comprehensive discharge planning and home follow-up of hospitalized elders: a randomized clinical trial. *JAMA* 281(7), 613–620 (1999).
- **Provides background on the TCM randomized control trials.**
- 23 Naylor MD, Brooten DA, Campbell RL, Maislin G, McCauley KM, Schwartz JS. Transitional care of older adults hospitalized with heart failure: a randomized, controlled trial. *J. Am. Geriatr. Soc.* 52(5), 675–684 (2004).
- **Provides background on the TCM randomized control trials.**
- 24 Naylor MD, Hirschman KB, Hanlon AL *et al.* Comparison of evidence-based interventions on outcomes of hospitalized, cognitively impaired older adults. *J. Comp. Eff. Res.* 3(3), 245–257 (2014).
- **Provides details on the propensity score matched Phase I of the three group comparative effectiveness study reported here.**
- 25 McCauley K, Bradway C, Hirschman KB, Naylor MD. Studying nursing interventions in acutely ill, cognitively impaired older adults. *Am. J. Nurs.* 114(10), 44–52 (2014).
- **Provides detailed background on the different nursing intervention protocols, including the resource nurse and TCM.**
- 26 Callahan CM, Unverzagt FW, Hui SL, Perkins AJ, Hendrie HC. Six-item screener to identify cognitive impairment among potential subjects for clinical research. *Med. Care* 40(9), 771–781 (2002).
- 27 Royall DR, Cordes JA, Polk M. CLOX: an executive clock drawing task. *J. Neurol. Neurosurg. Psych.* 64(5), 588–594 (1998).

- 28 Fulmer TT. Grow your own experts in hospital elder care. *Geriatr. Nurs.* 12(2), 64–66 (1991).
- 29 Rapp C. Iowa Veterans Affairs Consortium. Evidence-based protocol: acute confusion/delirium. In: *Series on Evidence-Based Practice For Older Adults*. Titler M (Ed.). University of Iowa Gerontological Nursing Interventions Research Center, Research Dissemination Core Iowa City, IA, USA (1998).
- 30 Nazir A, Lamantia M, Chodosh J et al. Interaction between cognitive impairment and discharge destination and its effect on rehospitalization. *J. Am. Geriatr. Soc.* 61(11), 1958–1963 (2013).
- Provides background the impact of cognitive impairment on rehospitalizations in the USA.
- 31 Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”. A practical method for grading the cognitive state of patients for the clinician. *J. Psych. Res.* 12(3), 189–198 (1975).
- 32 Inouye SK, Van Dyck CH, Alessi CA, Balkin S, Siegel AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann. Intern. Med.* 113(12), 941–948 (1990).
- 33 Yesavage JA, Brink TL, Rose TL et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J. Psych. Res.* 17(1), 37–49 (1983).
- 34 Alexopoulos GS, Abrams RC, Young RC, Shamoian CA. Cornell scale for depression in dementia. *Biol. Psychiatry* 23(3), 271–284 (1988).
- 35 Novak M, Guest C. Application of a multidimensional caregiver burden inventory. *Gerontologist* 29(6), 798–803 (1989).
- 36 Yesavage J, Brink T, Tl R et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J. Psych. Res.* 17(1), 37–49 (1983).
- 37 Katz I, Parmalee P. Assessment of depression in patients with dementia. In: *Measurement in Elderly Chronic Care Populations*. Lawton M, Holmes D, Ory M (Eds). Springer New York, NY, USA, 90–103 (1997).
- 38 Conradsson M, Rosendahl E, Littbrand H, Gustafson Y, Olofsson B, Lövhelm H. Usefulness of the geriatric depression scale 15-item version among very old people with and without cognitive impairment. *Aging Ment. Health* 17(5), 638–645 (2013).
- 39 Wei LA, Fearing MA, Sternberg EJ, Inouye SK. The confusion assessment method (CAM): a systematic review of current usage. *J. Am. Geriatr. Soc.* 56(5), 823–830 (2008).
- 40 Caserta M, Lund DA, Wright SD. Exploring the caregiver burden inventory (CBI): further evidence for a multidimensional view of burden. *Int. J. Aging Human Dev.* 43(1), 21–34 (1996).
- 41 Maldonado G, Greenland S. Simulation study of confounder-selection strategies. *Am. J. Epidemiol.* 138(11), 923–936 (1993).
- 42 Vittinghoff E, Glidden D, Shiboski S, McCulloch C. *Regression Methods in Biostatistics: Linear, Logistic, Survival, and Repeated Measures Models*. Springer, NY, USA (2005).
- 43 Landau S. Survival Analysis. In: *Encyclopedia of Quantitative Risk Analysis and Assessment*. Melnick EL, Everitt BS (Eds). Wiley-Blackwell, Hoboken, NJ, USA 1736–1743 (2008).
- 44 Cox DR. Regression models and life tables. *J. Royal Stat. Soc. Series B* 34(2), 187–220 (1972).
- 45 Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J. Am. Statist. Assoc.* 53, 457–481 (1958).
- 46 Peto R, Peto J. Asymptotically efficient rank invariant test procedures. *J. Royal Stat. Soc. Series A (General)* 135(2), 185–207 (1972).
- 47 Kalbfleisch JD, Prentice RL. *Statistical Analysis of Failure Time Data*. Wiley-Blackwell, NY, USA (1980).
- 48 Long JS. *Regression Models for Categorical and Limited Dependent Variables*. Sage Publications, Thousand Oaks, CA, USA (1997).
- 49 Laird NM, Ware JH. Random-effects models for longitudinal data. *Biometrics* 38(4), 963–974 (1982).
- 50 Petersen RC, Caracciolo B, Brayne C, Gauthier S, Jelic V, Fratiglioni L. Mild cognitive impairment: a concept in evolution. *J. Intern. Med.* 275(3), 214–228 (2014).
- 51 Krumholz HM. Post-hospital syndrome - an acquired, transient condition of generalized risk. *N. Engl. J. Med.* 368(2), 100–102 (2013).
- 52 Fong TG, Jones RN, Marcantonio ER et al. Adverse outcomes after hospitalization and delirium in persons with Alzheimer disease. *Ann. Intern. Med.* 156(12), 848–856 (2012).
- 53 Taylor JS, Demers SM, Vig EK, Borson S. The disappearing subject: exclusion of people with cognitive impairment and dementia from geriatrics research. *J. Am. Geriatr. Soc.* 60(3), 413–419 (2012).
- 54 US Department of Health and Human Services. Medicare Hospital Compare (2012). www.hospitalcompare.hhs.gov/
- 55 McCormick WC, Kukull WA, Van Belle G, Bowen JD, Teri L, Larson EB. Symptom patterns and comorbidity in the early stages of Alzheimer’s disease. *J. Am. Geriatr. Soc.* 42(5), 517–521 (1994).
- 56 Covinsky KE, Pierluissi E, Johnston C. Hospitalization-associated disability: “she was probably able to ambulate, but I’m not sure”. *JAMA* 306(16), 1782–1793 (2011).
- 57 Naylor MD, Bowles KH, McCauley KM et al. High-value transitional care: translation of research into practice. *J. Eval. Clin. Prac.* 19(5), 727–733 (2013).