Published in final edited form as:

Anesthesiology. 2015 November ; 123(5): 1105–1112. doi:10.1097/ALN.0000000000000821.

Risk of a Diagnosis of Dementia for Elderly Medicare Beneficiaries after Intensive Care

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Abstract

BACKGROUND—Critical illness is likely associated with an increased risk of dementia, but the magnitude remains uncertain.

METHODS—2.5% sample of Medicare beneficiaries who received intensive care in 2005 and survived to hospital discharge. Patients were matched with general population controls (age, sex & race) with 3 years follow-up. We used an extended Cox model to assess the risk of a diagnosis of dementia, adjusting for known risk factors for dementia and the competing risk of death.

RESULTS—Among 10,348 intensive care patients who survived to hospital discharge, dementia was newly diagnosed in 1,648 (15.0%) over the three years of follow-up vs. 12.2% in controls (incidence per 1,000 person-yr: 73.6; 95%CI 70.0–77.1 vs. 45.8; 95%CI 43.2–48.3; Hazard Ratio (HR) 1.61; 95%CI 1.50–1.74; $P<0.001$). After accounting for known risk factors in the year before the index hospitalization, the risk of receiving a diagnosis of dementia remained increased in patients who received intensive care (adjusted HR 1.43; 95%CI 1.32–1.54; $P<0.001$). Inclusion of identifiable risk factors accrued during the quarter of critical illness accounted for almost all of the increased risk (adjusted HR 1.09; 95%CI 1.00–1.20; $P=0.06$).

CONCLUSIONS—Elderly critical care survivors have a 60% increased relative risk, but only 3% increased absolute risk, of receiving a diagnosis of dementia in the subsequent three years compared with the general population. This increased risk is not accounted for by risk factors pre-

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This study was performed in the Department of Anesthesiology, Columbia University

Competing Interests: The authors declare no competing interests

Conflicts: None

existing the critical illness. Surveillance bias, which increases the likelihood of receiving a diagnosis of dementia, could account for some or all of this additional risk.

Keywords

Rates of Incident Dementia; Critical Care; Intensive Care Units

Elderly patients (over the age of 65) comprise approximately half of intensive care unit (ICU) admissions.¹ In addition, mortality rates from critical illnesses such as severe sepsis are decreasing, leading to a large population of elderly survivors.² Declining cognitive function and diagnoses of dementia increase both in severity and incidence after an acute illness among the elderly,^{3–6} and there is a mounting body of evidence suggesting potentially severe decrements follow a critical illness.^{5,6} Long-term cognitive impairment after critical illness may cause substantial disability and distress for individuals and their families. Older people fear developing dementia and experience anxiety regarding loss of self-identity and long-term care.⁷ Also, individuals may make different care choices, as they are less willing to endure burdensome treatments when faced with the possibility of severe functional or cognitive impairment.⁸

Although it has been demonstrated that cognitive impairment increases after critical illness, the magnitude of the effect at the population level has not been adequately estimated, as prior studies have had small sample sizes,^{4,5} or have made comparisons to population norms rather than matched controls.⁶ Furthermore, the issue of whether or not critically ill patients are “sicker”, and thus predisposed to developing dementia has not been elucidated. Thus, the aim of this study was to use a nationally representative Medicare population to calculate the incidence of new diagnoses of dementia for all patients who received critical care compared with matched general population controls. We also sought to determine whether patients who develop critical illness represent a high-risk population due to pre-existing conditions that might predispose this group towards an increased risk of a diagnosis of dementia.

MATERIALS AND METHODS

Design Overview

This was a retrospective study using the Medicare Standard Analytic Files (SAF) from the Centers for Medicare and Medicaid Services (CMS). This dataset contains all fee-for-service claims, including hospital inpatient, hospital outpatient, skilled nursing facility, and “carrier” claims (physician supplier part B files which includes all office visits), home health agency, hospice and durable medical equipment for a random, longitudinal 5% sample of beneficiaries. We linked data from years 2004 through 2008 and derived the inception cohort from the 2005 sample with a follow-up period of 3 years.

Setting and Participants

To generate the cohort for this study, we used the 5% sample of all beneficiaries with fee-for-service Medicare coverage for all years. We first randomly split the sample into two equal parts. From one half we selected all Medicare beneficiaries 66 years who received intensive care during their hospitalization in 2005 (n=23,732). Patients were 66 years or

older to ensure at least a year of Medicare eligibility and availability of medical records prior to intensive care. We used International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes from data for all health care encounters in the year prior and during the index quarter to identify and exclude patients with any diagnosis for dementia (290.x, 294.x, 331.x, 797.x),⁹ and patient with any diagnosis of mild cognitive impairment (331.83) or general symptom mental loss (780.93). We also excluded patients who either died or were sent to hospice at hospitalization discharge or in the same quarter (3 months) of their discharge date. Because cardiac surgery is generally associated with only a transient need for critical care, and also may distinctly alter a patient's risk for a diagnosis of dementia,^{10,11} we omitted anyone who had cardiac surgery (ICD-9-CM codes 35.x, 36.x, 39.61) in the quarter of hospitalization or the prior year (see Figure 1).

We used the other half of the 5% sample to select population controls, matched 1:1 with the cohort of individuals who received intensive care based on age, gender, and race. We categorized age into 5-year intervals, and grouped race as non-Hispanic White, non-Hispanic black, and 'other' (Hispanic and other) for the matching. We used the same exclusion criteria as for the group that received critical care: no diagnosis of dementia/mild cognitive impairment/general symptom mental loss, and no cardiac surgery in the previous year or during the index quarter (quarter of intensive care use in the matched critical care survivor), and no death (or hospice admission) in the index quarter. Additionally, eligible controls may have been hospitalized but *did not receive intensive care during hospitalizations* in the index quarter. We used a completely separate half of the patients to allow controls to be as representative as possible of the general population; in particular, this meant that they could have been hospitalized and received intensive care at times other than the index quarter.

Outcomes and Follow-up

The primary outcome for this study was incidence of new diagnoses of dementia, which was defined using ICD-9-CM codes (290.0–290.4, 294.0, 294.1, 294.8, 331.0, 331.1, 331.2, 331.7, 797.X)^{12,13} recorded from fee-for-service claims in the subsequent three years of follow-up. Because of privacy restrictions, exact dates of hospital discharge and doctor visits were not available in the SAF – only the quarter (3 month period) of the year. We calculated time to diagnosis of dementia and death as the number of quarters (3 month intervals) after the discharge quarter. The quarter in which the first diagnosis of dementia occurred was used as the incident quarter to mark the diagnostic onset for that individual. For person-years at risk each death and incident diagnosis of dementia was marked as occurring at the end of the quarter. The majority of patients who received a diagnosis of dementia during the follow-up had more than one dementia diagnosis in their records (see Supplementary Digital Content 1, Table 5 for number of diagnoses).

STATISTICS

We used ICD-9-CM codes from all healthcare encounters in the year prior to the index quarter to identify specific diseases and conditions known or suspected to be related to dementia.¹² We calculated summary statistics for demographic, clinical characteristics, and pre-existing conditions using percentages, means ($\pm$ standard deviations, SD), and medians

(with inter-quartile ranges, IQR) as appropriate for the entire sample. Follow-up began with the quarter after the index hospitalization quarter and continued until the first diagnoses of dementia, death, or end-of follow-up (3 years).

We calculated the incidence rates for a diagnosis of dementia during the follow-up for the cohort that received intensive care and the control group stratified by 5-year age categories and also stratified by gender. Crude time to incidence of a diagnosis of dementia was examined with a cumulative incidence competing risks (CICR) method using Kaplan-Meier curves accounting for the competing risk of death. Using an extended Cox model, we estimated hazard ratios (HRs) for diagnoses of dementia. We created four models to examine the relative incidence of diagnoses of dementia. First, we generated unadjusted HRs to determine the overall increase in risk for the intensive care cohort. Second was a model adjusting for pre-existing conditions that are known to be associated with an increased risk of dementia to determine whether intensive care patients were at an increased risk of diagnoses of dementia due to prior known disease. As a third model, we included diagnoses accrued by the intensive care cohort during the index hospitalization. A final, fourth model, included all potential diagnoses viewed as risk factors for dementia accrued during the quarter of critical illness for both the intensive care cohort and controls. Because of date restrictions within the data, we could not determine whether or not the diagnoses that occurred during the index quarter outside of the index hospitalization occurred before or after the hospitalization. Thus, we refer to diagnoses as “accrued during the index quarter”. We used a stepwise selection to create parsimonious multivariable models for dementia. These models also accounted for matched characteristics. Covariates that were statistically significant ($P < 0.05$) were kept in the model. We assessed the Cox proportionality assumption graphically and added time-dependent covariates where the effect of a covariate varied during follow-up. This meant that for some diagnoses, the effect was not constant over time. However, as the emphasis of this study was on the risk of dementia, we do not provide a detailed breakdown of these effects of other variables, but note them in the tables.

For our supplementary analysis, we replicated the models splitting the patients as medical or surgical, and then stratified by whether or not they had a documented infection with or without severe sepsis because this is a group of patients well established to be at increased risk of subsequent cognitive impairment and dementia.^{4,12} We identified the subsample of the intensive care cohort with any infection (with and without severe sepsis) using an established definition,¹⁴ and compared these patients with their matched controls.

Based on our prior work,¹² we estimated a sample size ($n=12,000$ for the 2.5% sample, with approximately 17% with dementia in 3 years). We calculated that we had greater than 90% power to show a difference of 2% in the rates of diagnosis of dementia over three years. Findings were considered statistically significant with a P value of < 0.05 . Database management and statistical analyses were performed using Excel (Microsoft, Redmond, WA), and SAS version 9.2 (SAS Institute Inc., Cary, NC) software. For the CICR models we used a SAS macro (comprisk). This research was reviewed and approved by the Columbia University Medical Center Institutional Review Board, New York NY USA (IRB AAAE9908).

Role of the funding Source

This study was funded by K08AG038477 from the National Institute on Aging to Dr. Hannah Wunsch. The funder had no role in the study's design, conduct, or reporting.

RESULTS

Cohort characteristics

After appropriate exclusions, 10,348 Medicare beneficiaries were hospitalized with admission to intensive care and survived to the end of the index hospitalization quarter. The average age of the intensive care cohort was 76.7 years $\pm$ 6.8, with 53.1% female and the majority (88.7%) White, non-Hispanic (see Table 1). Known risk factors for dementia were common, with the majority of both the intensive care cohort and matched controls having at least one risk factor identified. Average follow-up time for the intensive care cohort was 2.3 years $\pm$ 1.0 and for matched controls 2.8 years $\pm$ 0.6. Three-year mortality for the intensive care cohort was 38.3%, more than double that of matched controls (14.7%).

Risk of a diagnosis of dementia in 3 years of follow-up

In the intensive care cohort, 1,648 (15.9%) received a new diagnosis of dementia during the three years of follow-up versus 1,266 (12.2%) of the matched controls (see Table 2). The overall rate of new diagnoses of dementia was 73.6 per 1,000 person-years; 95% CI 70.0–77.1, for the intensive care cohort vs. 45.8 per 1,000 person-years; 95% CI 43.2–48.3, for matched controls, with a hazard ratio of 1.61; 95% CI 1.50–1.74, $P < 0.001$ (see Table 2). Among intensive care survivors, approximately 40% of all new diagnoses of dementia occurred in the first year, but the cumulative incidence of diagnoses of dementia remained larger for the intensive care cohort throughout the entire period of follow-up (see Figure 2). This higher rate was consistent across every age group (see Figure 3), and was also higher in women than in men (data not shown).

Adjusted risk of a diagnosis of dementia

Only a third of the increased risk of a diagnosis of dementia was explained by adjusting for pre-existing conditions that are known to be associated with dementia (adjusted hazard ratio (aHR) for intensive care cohort vs. matched controls: 1.43; 95% CI 1.32–1.54, $P < 0.001$ (see Table 2). Inclusion of diagnoses accrued during the index hospitalization partially attenuated this difference (aHR 1.16; 95% CI 1.05–1.27, $P < 0.001$). Overall, the intensive care cohort received many additional diagnoses during the index quarter that were risk factors for development of dementia (see Supplementary Digital Content 1, Table 1). Inclusion of all additional diagnoses that were risk factors for dementia accrued during the index quarter accounted for most of the difference between groups (aHR 1.09; 95% CI 1.00–1.20, $P = 0.06$). See Supplementary Digital Content 1, Tables 2–4 for the full models).

Among the subgroup of intensive care patients who were medical, the risk of a diagnosis of dementia was higher (HR 1.84; 95% CI 1.69–2.00, $P < 0.001$), and remained elevated even after accounting for all pre-existing diagnoses (aHR 1.56; 95% CI 1.43–1.70, $P < 0.001$), and all new risk factors accrued during the index hospitalization quarter (aHR 1.17; 95% CI 1.06–1.29, $P = 0.002$) (Table 3). There was also an increased risk of a diagnosis of dementia

for patients with infection only or severe sepsis during critical illness, with the higher risk for those with severe sepsis (HR 2.04; 95% CI 1.77–2.34, $P < 0.01$) (Table 3). Adjusting for pre-existing conditions did not explain the increased risk. All diagnoses accrued during the index quarter accounted for most, but not all of the additional risk (aHR 1.24; 95% CI 1.06–1.45, $P = 0.006$).

DISCUSSION

Using population-level data we estimated that elderly survivors of intensive care are diagnosed with dementia at a sixty percent higher rate than matched general population controls, but with only a 3% absolute increase in risk over three years. We demonstrated that the increase in risk of a diagnosis of dementia for patients who required intensive care was not explained by existing conditions that predispose people to dementia. Given the low absolute increased risk, this suggests that the population does not represent an identifiably high-risk group prior to the development of critical illness.

Our findings provide accurate numbers for the absolute increased risk of a diagnosis of dementia in the elderly ICU population relative to the general population; it expands on a study that showed an increase in subsequent dementia after hospitalization but lacked sufficient power to quantify the risk in the critically ill population.³ Our results are also consistent with the findings from a two-center cohort study of patients with respiratory failure or shock that found an increased risk of cognitive impairment for these patients relative to population means,⁶ as well as a study that focused on survivors of severe sepsis from the health and retirement study that found increased rates of cognitive impairment after sepsis⁴. However, it is important to note that our study focuses specifically on dementia, and does not identify subtle changes in cognition or severity of impairment so we cannot compare rates with the previously mentioned studies. We found an increased rate of diagnoses of dementia among all survivors of critical illness, but also confirmed that infection, and severe sepsis in particular, appears to be associated with an even higher risk relative to the general intensive care cohort, and not all of this risk could be explained by accrued diagnosis. The risk of dementia among medical patients also appeared to be higher relative to the general population compared with surgical patients. This may represent a selection bias associated with likelihood of receiving surgery at all, and is an intriguing finding given that none of these patients had a diagnosis of dementia prior to the hospitalization. However, we have previously focused on specific risk factors within an ICU cohort associated with a diagnosis of dementia; thus, we chose not to further assess this question here.¹²

The mechanism for this increased risk is unknown and likely to be complex. As expected for the Medicare population age 65 and over, the majority of our sample had at least one known risk factor for dementia in their prior history. However, our models help to establish that the increased risk for patients who are critically ill seems attributable to the peri-critical illness period, as pre-existing risk factors did not fully account for the increased risk. Several studies hypothesize an event during critical illness that causes or begins long-term neurocognitive damage such as inflammatory response to infection,^{15,16} and the duration of delirium has been associated with an increased risk of cognitive impairment after respiratory

failure or shock.⁶ A bidirectional relationship has also been suggested; a process in which subclinical changes in cognition can increase the risk of an acute illness that then accelerates long-term cognitive decline leading to dementia.¹⁷ We found that patients who received critical care acquired additional identifiable risk factors for dementia during the index hospitalization quarter. Some of these diagnoses may define the critical illness (such as a cerebrovascular accident) and may be seen as “mediators” that could directly impact on cognitive function; others may be unrelated or only partially related to the acute events (such as depression) and have a less clear mechanism of action. Because of restrictions in dates, it was impossible to determine the timing of these additional diagnoses in relation to the hospitalization with critical care.

A key strength to our study was our use of Medicare claims, which remain a vital data source for studies of dementia because beneficiaries are a nationally representative sample of the main at-risk population. The incident rate of dementia across age in our matched controls is typical of other studies of dementia,^{18–20} with an exponential pattern and an approximate doubling of the rate for 5 year increases in age from 70–74 to 75–79.^{20,21} We also found that women were more likely than men to receive a diagnosis of dementia, and that non-Hispanic blacks had a higher rate of diagnoses. This use of population-level data sets our work apart from other studies of critically ill cohorts of patients; we were not limited to a sub-population of critical care survivors and we were able to generate matched controls using the general population and conduct subgroup analyses. Recent studies evaluated potential risk factors and protective factors using similar methods for incident dementia with Medicare data^{22,23}.

A known limitation to the use of administrative data is the accurate assessment of dementia as well as risk factors. Early dementia was found to be under-reported in claims data and the severity of dementia is unknown.^{13,24} Very mild dementia that may be present prior to critical illness, but not identified, could alter conclusions to incorrectly implicate major illness as a risk factor for continued cognitive decline.²⁵ Given this challenge, we used a definition found to capture 82% of dementia cases identified with a neuropsychology battery and also used three years of claims data;¹³ in another study, claims data were found to have a sensitivity of 85% and specificity of 89% when compared to in-home dementia assessment by clinical staff.⁹ Despite our exclusion of diagnosed dementia and cognitive impairment, prevalent cases of undiagnosed mild dementia may have existed in our sample. We were also unable to assess cognitive function prior to critical illness. A previous study found a high prevalence of preexisting cognitive impairment in patients admitted to the medical ICU (42%)^{26,27} and this would suggest that critical care survivors may already have a downward trajectory that we may not have fully captured. We also assessed whether or not patients had at least two diagnoses of dementia, which would provide additional information to suggest that this was not an erroneous diagnosis. Two thirds of the cohort had two or more diagnoses, with the additional caveat of a relatively high death rate during the three years of follow-up (38.3%) which may reduce the likelihood of additional diagnoses.

Finally, a critical illness hospitalization clearly leads to more healthcare encounters after discharge and therefore increases opportunities to diagnose dementia among our intensive care group. Moreover, encounters with specific types of healthcare professionals (such as

neurologists) may increase the likelihood of evaluation and diagnosis of dementia. However, we demonstrate that the increase in rate for incident dementia continued throughout the second and third years of follow-up. We were also careful to describe our finding in terms of receiving a *diagnosis* of dementia. This represents an outcome that is patient (and family) centered, as a new diagnosis represents a large event for many people. A diagnosis of dementia, in particular, comes with huge implications for life trajectory and care planning.^{28,29}

Conclusion

In conclusion, we have determined that the rate of incidence of diagnoses of dementia among elderly survivors of critical illness is 60% higher than in matched general population controls, but translates into only a 3% absolute increase in risk over three years. This increased incidence is not accounted for by risk factors for dementia prior to the critical illness, suggesting that elderly patients who become critically ill do not represent a particularly high risk group for dementia prior to the illness. Our findings are limited by the differential rates of overall diagnoses associated with repeated healthcare encounters, which were more frequent in the intensive care cohort.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding: Funded by K08AG038477 from the National Institute on Aging, (Building 31, Room 5C27, 31 Center Drive, MSC 2292, Bethesda, MD 20892) to Dr. Hannah Wunsch

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Summary Statement: the risk of a diagnosis of dementia is slightly increased in the three years following critical illness relative to general population controls.

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Figure 1.
Flow-chart of exclusions

	3	6	9	12	15	18	21	24	27	30	33	36
Intensive Care Cohort:												
accumulating incidence of diagnosis of dementia	309	525	684	810	959	1077	1167	1276	1380	1463	1558	1648
At risk (alive without diagnosis of dementia)	10348	9309	8660	8170	7755	7359	7007	6733	6443	6162	5933	5717
Control Cohort:												
accumulating incidence of diagnosis of dementia	134	251	357	469	584	685	778	887	980	1069	1167	1266
At risk (alive without diagnosis of dementia)	10348	10119	9913	9700	9492	9291	9100	8907	8711	8538	8365	8178

Figure 2.
Cumulative incidence of diagnoses of dementia in the three years following hospital discharge for intensive care survivors and matched population controls

Figure 3.
Rate of dementia over three years following hospital discharge for intensive care survivors and matched population controls stratified by age.

Table 1

Characteristics of intensive care cohort and matched general population controls

	Intensive Care Cohort	Matched General Population Controls
Characteristics	N=10,348	N=10,348
Age (years)	n (%)	n (%)
Mean $\pm$ SD	76.7 $\pm$ 6.8	76.7 $\pm$ 6.8
66–69	1920 (18.6)	1920 (18.6)
70–74	2505 (24.2)	2505 (24.2)
75–79	2467 (23.8)	2467 (23.8)
80–84	2044 (19.8)	2044 (19.8)
85	1412 (13.7)	1412 (13.7)
Gender		
Female	5496 (53.1)	5496 (53.1)
Male	4852 (46.9)	4852 (46.9)
Race		
White, non-Hispanic	9182 (88.7)	9182 (88.7)
Black, non-Hispanic	752 (7.3)	752 (7.3)
Other	414 (4.0)	414 (4.0)
Pre-existing risk factor for dementia *		
None	1,155 (11.2)	2,449 (23.7)
Cerebrovascular accident	473 (4.6)	205 (2.0)
Cerebrovascular disease	1,423 (13.8)	830 (8.0)
Myocardial Infarction	1,113 (10.8)	441 (4.3)
Congestive heart failure	2,684 (25.9)	999 (9.7)
Valvular disease	1,901 (18.4)	995 (9.6)
Pulmonary circulation disease	518 (5.0)	178 (1.7)
Peripheral vascular disease	2,316 (22.4)	1,109 (10.7)
Hypertension	7,367 (71.2)	5,956 (57.6)
Depression	857 (8.3)	467 (4.5)

	Intensive Care Cohort	Matched General Population Controls
Diabetes	3,349 (32.4)	2,233 (21.6)
Hypoglycemia	462 (4.5)	172 (1.7)
Chronic renal failure	796 (7.7)	195 (1.9)
Head trauma	102 (1.0)	52 (0.5)
Chronic pulmonary disease	3,269 (31.6)	1,615 (15.6)
Hypothyroidism	1,851 (17.9)	1,606 (15.5)
Obesity	529 (5.1)	266 (2.6)
Weight loss	624 (6.0)	340 (3.3)
Fluid and electrolyte disorders	2,018 (19.5)	777 (7.5)
Deficiency Anemias	2,835 (27.4)	1,573 (15.2)
Alcohol abuse	123 (1.2)	62 (0.6)
Drug abuse	44 (0.4)	-
Epilepsy	82 (0.8)	51 (0.5)
Parkinson's disease	154 (1.5)	137 (1.3)
Rheumatoid arthritis/collagen vascular diseases	558 (5.4)	346 (3.3)
Follow-up time, mean $\pm$ SD (years)	2.3 $\pm$ 1.0	2.8 $\pm$ 0.6
Three-year Mortality	3,963 (38.3)	1,525 (14.7)

Notes:

Follow-up time in quarters (3-month intervals) was converted to years, and includes all observed time in the study up to death.

* Based on International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes from all healthcare encounters during the year prior to the index quarter

Incident risk and hazard ratios for receiving a diagnosis of dementia during three years of follow-up for intensive care cohort versus general population controls

Table 2

	Matched Control Cohort n=10,348	Intensive Care Cohort n=10,348
Cases of Incident Dementia, No. (%)	1,266 (12.2)	1,648 (15.9)
Person-Years, No.	27,666	22,399
Crude Incidence Rate, per 1,000 person-years (95% CI)	45.8 (43.2–48.3)	73.6 (70.0–77.1)
Cox Proportional Hazards Models:		HR (95% CI)
1. Unadjusted	<i>ref</i>	1.61 (1.50–1.74)
2. Adjusted for pre-existing risk factors for dementia*	<i>ref</i>	1.43 (1.32–1.54)
3. Adjusted for pre-existing risk factors for dementia* & diagnoses from the index hospitalization	<i>ref</i>	1.16 (1.05–1.27)
3. Adjusted for pre-existing risk factors for dementia* & potential mediators & other risk factors accrued during the quarter of the index hospitalization	<i>ref</i>	1.09 (1.00–1.20)
		<i>P</i> Value
		<0.001
		<0.001
		<0.001
		0.06

Notes:

Abbreviations: HR=hazard ratio, CI=confidence

Models account for matching variables and a prior year history of conditions/diseases associated with dementia. Covariates: Quarters (3-month intervals) of follow-up time was converted to person-years in order to calculate incidence rate. See Tables S2–4 for the full models with all covariates.

* identified from all Medicare claims in the year prior to the quarter of index hospitalization.

Table 3

Hazard ratios for receiving a diagnosis of dementia during three years of follow-up for intensive care cohort versus general population controls, for specific sub-groups of patients

		Unadjusted			Adjusted for pre-existing risk factors for dementia *			Adjusted for pre-existing risk factors for dementia & other risk factors accrued during the quarter of the index hospitalization		
	N (total)	N (dementia)	HR (95% CI)	P Value	HR (95% CI)	P Value	HR (95% CI)	P Value		
Controls	10,348	1,266	<i>ref</i>							
ICU – surgical	4,596	625	1.30 (1.18–1.43)	<0.001	1.26 (1.15–1.39)	<0.001	0.99 (0.89–1.09)	0.77		
ICU – medical	5,752	1,023	1.84 (1.69–2.00)	<0.001	1.56 (1.43–1.70)	<0.001	1.17 (1.06–1.29)	0.002		
Controls	10,348	1,266	<i>ref</i>							
ICU – no infection	6,658	1,010	1.43 (1.32–1.56)	<0.001	1.33 (1.22–1.44)	<0.001	1.04 (0.95–1.14)	0.45		
ICU – infection only	2,300	400	1.85 (1.66–2.08)	<0.001	1.57 (1.40–1.76)	<0.001	1.19 (1.05–1.35)	0.005		
ICU – severe sepsis	1,390	238	2.04 (1.77–2.34)	<0.001	1.80 (1.56–2.07)	<0.001	1.24 (1.06–1.45)	0.006		

Notes:

Abbreviations: HR=hazard ratio, CI=confidence intervals; ICU = intensive care unit

Models account for matching variables.

* identified from all Medicare claims in the year prior to the quarter of index hospitalization.