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DELIRIUM AS A PREDICTOR OF MORTALITY IN MEDICARE BENEFICIARIES DISCHARGED FROM THE EMERGENCY DEPARTMENT: A NATIONAL CLAIMS LEVEL ANALYSES UP TO 12 MONTHS

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021258
Article Type:	Research
Date Submitted by the Author:	19-Dec-2017
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Keywords:	GERIATRIC MEDICINE, Delirium, Mortality, Claims Data

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Abstract: 300

Word Count: 3,379

References: 17

Figures: 2

Tables: 2

ABSTRACT

Background: Delirium is common among seniors discharged from the Emergency Department (ED) and associated with increased risk of mortality. Prior research has addressed mortality associated with seniors discharged from the ED with delirium, however has generally relied on data from one or a small number of institutions and at single time points.

Objectives: Analyze mortality rates among seniors discharged from the ED with delirium up to 12 months at the national level.

Design: Retrospective Cohort Study

Setting: Analyzed data from the Center for Medicare & Medicaid Services (CMS) limited datasets for 2012 to 2013.

Participants: Medicare fee-for-service beneficiaries aged 65 years or older discharged from the ED. We focused on new incidence cases of delirium, patients with any prior claims for delirium, hospice claims, or End-Stage Renal Disease (ESRD) were excluded. Sample size included 26,245 delirium claims, and a randomly selected sample of 262,450 controls.

Outcome Measures: Mortality within 12 months after discharge from the ED, excluding patients transferred or admitted as inpatients.

Results: Among all beneficiaries, 46,508 (16.1%) died within 12 months. Of which 39,404 (15.0%) were in the non-delirium (i.e., control group) and 7,104 (27.1%) were in the delirium cohort respectively. Mortality was strongest at 30 days with an adjusted hazard ratio of 4.82 (95%, 4.60-5.04). Over time, delirium was consistently associated with increased mortality risk compared to controls up to 12-months (HR 2.07; 95%, 2.01-2.13). Covariates that affected mortality included older age, comorbidity, and presence of dementia.

Conclusions: Our results demonstrate delirium is a significant marker of mortality among seniors in the ED, and mortality risk is most salient in the first 3 months following an ED visit. Given the significant clinical and financial implications, there is a need to increase delirium screening and management within the ED to help identify and treat this potentially fatal condition.

KEY WORDS: ***Geriatrics, Delirium, Mortality, Claims Data***

Strengths & Limitations of this Study

- Many estimates for the burden of delirium in the ED come from cohort studies and surveys, which are often not population-based. There are very few estimates of incidence of geriatric delirium nationally, we leverage national claims data to analyze mortality rates nationally among seniors discharged from the ED with delirium at multiple time points up to 12 months.
- CMS data is one of the richest sources of utilization information nationally with sizable samples, documented procedures and diagnoses, verified deaths, beneficiary demographic information, and revenue center details
- Highlighting the burden of delirium in the Emergency Department (ED) can lend support to the implementation of screening and treatment recommendations, which in turn may reduce delirium-associated mortality.
- However, claims data lack information on severity and duration of illness prior to the diagnosed event.

INTRODUCTION

The Emergency Department (ED) is often the point of entry for seniors into the healthcare system, and as such plays a unique role in setting the trajectory of care for this rapidly growing and often vulnerable segment of the population. Thus, timely screening of life-threatening conditions such as delirium is critical in the ED.

Delirium is broadly defined as an acute decline in attention and global cognitive functioning,[1] which is not only common, but often fatal in older adults.[2] In the United States alone, of the nearly 20 million older adults seen in the ED each year,[3] approximately 8-17% present to the ED suffering from delirium.[4] Prior research indicates that patients with delirium have a 12-month mortality rate between 10-26%,[5] which is comparable to patients with sepsis or acute myocardial infraction.[6] Additionally, the increased mortality risk for delirium patients in the ED has been identified at multiple time points, specifically at 3, 6, and 12 months. [3 5 7]

Furthermore, delirium is also costly and management can be resource intensive. For example, delirium is often associated with increased length of stay among hospitalized patients, may require use of restraints, sedative medications, or additional staffing (e.g. sitters) and generally linked to greater functional and cognitive decline. [8]

Despite the growing body of research demonstrating delirium is an independent predictor of mortality, as well as increased costs, management of delirium in the ED has not been well studied. In fact, some studies suggest delirium goes undiagnosed by up to 80% of ED physicians [8 9], highlighting the magnitude of the missed opportunity to improve recognition and management of this potentially fatal condition.

While prior research has addressed the mortality risk associated with seniors discharged from the ED with delirium, much of this research has relied on data from a few, if not a single institution. Furthermore, previous research has typically examined mortality at only single points in time. Our work builds off this growing body of literature by leveraging national claims data to analyze mortality rates among seniors discharged from the ED with delirium at multiple time points up to 12 months, with implications for screening and treatment recommendations.

METHODS

Study Design & Data Source

Our study was a retrospective analysis of all available national claims-level data from 2012 to 2013. We analyzed data from the Center for Medicare & Medicaid Services (CMS) Research Data Assistance Center (ResDAC) dataset which includes data for approximately 98 percent of the U.S. population aged 65 years and older. [10] CMS data is one of the richest sources of utilization information nationally with sizable samples, documented procedures and diagnoses, verified deaths, beneficiary demographic information, and revenue center details. For our study, we utilized data for each institutional and non-institutional claim type with each record representing a beneficiary claim.

Inclusion/exclusion criteria

An ED-associated claim qualified as an index encounter if it was the beneficiary's initial ED outpatient-only claim during the study period and if the claim had subsequent claims-level data available for three months before and 12 months after index encounter (15 months of available data in total). The three-month control period prior to index ED encounter was used to exclude beneficiaries with any prior claims for delirium, hospice claims, or End-Stage Renal Disease (ESRD) to reduce the potential confounding nature of these factors and to focus largely on new incident cases of delirium. Index encounters that resulted in observation or an inpatient stay were also excluded due to likelihood of that these cases may represent higher acuity conditions. Once exclusion criteria were applied, we removed a total of 3,808,806 claims (90,758 delirium, 223,292 Hospice, and 3,494,756 ESRD claims) leaving us with a total of 5,477,626 claims for our analyses. See Figure 1 for a flowchart showing application of the inclusion/exclusion criteria

Cohort Selection

Of the 5,477,626 claims, we focused our analyses on two cohorts: A delirium cohort, and a control group of beneficiaries without delirium. The groups were constructed as follows:

Delirium cohort: Of the 5,477,626 eligible claims, delirium was identified based on presence of a qualifying outpatient diagnosis claim that included ICD-9 codes (293.0, 290.41, 293.89, 780.09, 292.81, 300.11, 290.11, 290.3, 293.1, and categories 308, and 584 to 586) (see Appendix 1 for a more detailed description of codes). We limited delirium diagnoses to claims where at least one of these ICD-9 codes was documented at least once within any diagnosis, at which point the claim was flagged as a delirium encounter. We identified a total of 25,980 beneficiaries with qualifying index encounters and a total of 26,245 delirium claims.

Control cohort: The control group consisted of beneficiaries with no delirium diagnosis present. Of the eligible 5,477, 626 claims for our analyses, 5,451,381 qualifying index ED claims were eligible for the control group after selection of the delirium cohort from the eligible claims. Considering the size of our control group, we randomly selected from the 5,451,381 potential control beneficiaries using a 10:1 ratio following prior research on recommended statistical practice based on simulation studies of a minimum of 10 events per variable. [11] Following random selection, our control group included a total of 251,971 beneficiaries and a total of 262,450 claims.

Mortality

Mortality was flagged for all individuals who died within 12-months from index encounter and flagged only if the death date was verified at 30 days, 90 days, 6 months, and 12 months. Total number of deaths recorded for the delirium and control groups at 12 months were 7,104 (27.1) and 39,404 (15.0%) respectively. See Table 1 for mortality rate by death date.

Statistical Analysis

Our analyses focused on two primary areas: (1) the role of delirium as an independent predictor for mortality; and (2) identifying the effect of covariates (age, gender, dementia, & Charlson Comorbidity Index (CCI)) on mortality.

We first compared the two cohorts using independent group t-test and X^2 test for quantitative and categorical variables and found significant differences between the cohorts with respect to demographic and clinical measures. Members of the delirium cohort were more likely than controls to be older (mean age: 79 vs. 77), more likely to have a lower level of illness and severity burden (mean CCI: 4 vs. 6),[12] and more likely to have a primary diagnosis of mental/neurological clinical classification. The cohorts did not differ with respect to gender or ethnicity as both cohort's members were more likely to be Caucasian females (See Table 1).

Time 0 was defined as date of index encounter and days between death date and index encounter was calculated for the model. In addition, beneficiaries were censored at the end of the 12-month follow-up period if death did not occur or loss of follow-up, whichever occurred earlier. We then used the exponential model for the survival time distribution to estimate yearly mortality rates for the delirium and control cohort using an unadjusted Kaplan-Meier survival curve. In addition, a score test (univariate Cox proportional hazards model) was utilized as a comparison to the unadjusted Kaplan-Meier survival curves. [13]

Table 1: Cohort Characteristics

Characteristics	Delirium	Control (No Delirium)
Total	26,245 (100)	262,450 (100)
Age	…	…
65-74	8,723 (33.2)	106,163 (40.4)
75-84	9,500 (36.2)	96,998 (37.0)
≥85	8,022 (30.6)	59,272 (22.6)
Mean Age	79	77
Gender	…	…
Female	16,279 (62.1)	160,421 (61.1)
Male	9,966 (37.9)	102,012 (38.8)
Race	…	…
Caucasian	22,699 (86.5)	222,177 (84.7)
African American	2,243 (8.5)	27,328 (10.4)
Asian	345 (1.3)	3,115 (1.2)
Hispanic	473 (1.8)	4,683 (1.8)
Native American	134 (0.51)	1,389 (0.53)
Other/Unknown	281 (1.1)	2,852 (1.1)
Charlson Comorbidity Scores	…	…
None (0)	12,423 (47.3)	113,743 (43.3)
Low (1-4)	13,182 (50.2)	141,832 (54.0)
Moderate (5-9)	595 (2.3)	6,553 (2.5)
High (10+)	45 (0.17)	305 (0.12)
Mean CCI Score	4	6
Primary Diagnosis (ICD-9 Codes)	…	…
Infectious Diseases (0-139)	252 (1.0)	2,235 (0.9)
Neoplasms (140-239)	93 (0.4)	926 (0.4)
Mental/Neurological (240-289)	4,651 (17.7)	8,547 (3.3)
Cardiovascular (390-429)	1,396 (5.3)	17,038 (6.5)
Cerebrovascular (430-459)	1,117 (4.3)	7,814 (3.0)
Respiratory (460-519)	794 (3.0)	15,802 (6.0)
Digestive (460-519)	312 (1.2)	13,927 (5.3)
Urogenital (580-629)	1,552 (5.9)	14,509 (5.5)
Musculoskeletal (710-739)	412 (1.6)	19,779 (7.5)
Symptoms (782-789)	1,803 (6.9)	60,126 (22.9)
Injuries (790-799)	151 (0.6)	1,593 (0.6)
Ill-defined, Skin, or Missing (680-709)	58 (0.2)	5,299 (2.0)
Endocrine (240-289)	1,463 (5.6)	10,788 (4.1)
Mortality		
30 Days	3,129 (11.9)	7,649 (2.9)
90 Days	4,251 (16.2)	15,267 (5.8)
6 Months	5,364 (20.4)	24,453 (9.3)
12 Months	7,104 (27.1)	39,404 (15.0)

Additionally, to adjust for possible prognostic factors of delirium on mortality, we used a multivariable Cox proportional hazards model with the following covariates: age, gender, dementia, and comorbidity (as defined by CCI). To address the potential interaction of delirium on mortality based on these characteristics, we evaluated all covariates in the multivariable Cox model, and then selected statistically significant interactions for further testing. In addition, to confirm results we re-ran these analyses using multiple randomly selected samples from within the control group and found no statistically significant differences.

RESULTS

During the 12-month study period 288,695 claims were included in our analysis sample, of which 26,245 comprised the delirium cohort and 262,450 control claims. Beneficiaries were largely similar with respect to gender, and primary diagnosis distributions, however when evaluating comorbidity scores, beneficiaries had higher scores in the control group suggesting higher risk of mortality (see Table 1). Among all beneficiaries, 46,508 (16.1%) died within 12 months. Of which 39,404 (15.0%) were in the non-delirium (i.e., control group) and 7,104 (27.1%) were in the delirium cohort respectively. In the delirium cohort, Kaplan-Meier survival decreased rapidly during the first 30 days after the index visit and thereafter continued to decline at a slower pace in comparison to the control group. At 30 days after index visit, the survival rate for beneficiaries with delirium was 88.2%, while the control group had a survival rate of 97.6%.

Results from the univariate and multivariate Cox proportional hazard models for 30 days, 90 days, 6 months, and 12 months are reported in Table 2. Our unadjusted results for delirium and mortality was strongest at 30 days as illustrated in the Kaplan-Meier survival curve (HR, 4.35; 95% CI, 4.17-4.54) (see Figure 2). Even after adjusting for covariates, delirium was still independently associated with approximately a five-fold increase in mortality during the 30-day follow-up period (HR 4.82; 95% CI, 4.60-5.04). Over time from index ED encounter, delirium was still c associated with an increased risk of mortality compared to the control group. However, mortality risk (while still significant) did decrease over time up until 12 months (HR 2.07; 95%, 2.01-2.13).

Table 2: Cox Proportional Hazard Ratios in Intervals to 12-Month Mortality

Mortality Rate	Variable	Univariate	Multivariate
30 Days	Delirium/Control	4.35† (4.17-4.54)	4.82 † (4.60-5.04)
…	Age	1.06† (1.05-1.06)	1.06 † (1.05-1.06)
…	Male/Female	0.72 † (0.69-0.74)	0.70 † (0.67-0.73)
…	CCI	1.29† (0.77-1.28)	1.30 † (1.29-1.31)
…	Dementia	1.84† (1.75-1.94)	1.44 † (1.35-1.53)
…	Delirium*Dementia	…	0.41 † (0.36-0.45)
90 Days	Delirium/Control	3.02 † (2.14-2.30)	3.27 † (3.15-3.40)
…	Age	1.06 † (1.05-1.06)	1.06 † (1.05-1.06)
…	Male/Female	0.74 † (0.72-0.76)	0.72 † (0.70-0.75)
…	CCI	1.32 † (1.31-1.32)	1.32 † (1.31-1.33)
…	Dementia	2.12 † (2.04-2.20)	1.58 † (1.51-1.65)
…	Delirium*Dementia	…	0.48 † (0.44-0.52)
6 months	Delirium/Control	2.42 † (2.35-2.49)	2.55 † (2.47-2.64)
…	Age	1.06 † (1.05-1.06)	1.06 † (1.05-1.06)
…	Male/Female	0.76 † (0.74-0.78)	0.73 † (0.71-0.75)
…	CCI	1.31 † (1.30-1.31)	1.31 † (1.31-1.32)
…	Dementia	2.25 † (2.18-2.31)	1.64 † (1.58-1.70)
…	Delirium*Dementia	…	0.53 † (0.49-0.57)
12 months	Delirium/Control	2.02 † (1.96-2.07)	2.07 † (2.01-2.13)
…	Age	1.06 (1.05-1.06)	1.06 † (1.05-1.06)
…	Male/Female	0.76 † (0.75-0.78)	0.73 † (0.71-0.74)
…	CCI	1.30 † (1.29-1.31)	1.30 † (1.29-1.31)
…	Dementia	2.28 ‡ (2.23-2.34)	1.62 † (1.57-1.66)
…	Delirium*Dementia	…	0.60 † (0.56-0.64)

Data are hazard ratios for univariate & multivariate for time periods to 1-year mortality rate (95% confidence interval). Of 277,951 patients, 46,508 died (16.7%) in both groups. Of which 39,404 (15.0%) were in the control group (no delirium) & 7,104 (27.1%) were in the delirium cohort, respectively.
Note(s): †P-value < 0.001; * indicates interaction

Other covariates that affected mortality rate included older age and higher comorbidity scores. However, women with delirium had a decreased risk of mortality, compared to males with delirium (HR 0.73; 95% CI, 0.71-0.74) at 12 months (see Table 2).

The presence of dementia, on the other hand, had a stronger association in the univariate model, however our adjusted multivariate model indicated dementia was not a significant predictor of mortality and instead associated with a significant protective effect on mortality. This protective effect is demonstrated by the significant statistical interaction between delirium and dementia ($P \geq 0.001$) while adjusting for covariates (HR 0.60; 95% CI, 0.56-0.64).

DISCUSSION

Our study found that delirium is an independent predictor of mortality among ED patients diagnosed with delirium in the ED compared to ED patients without delirium, even after adjusting for confounding factors such as age, gender, comorbidity, and dementia. While delirium had a strong effect on mortality during the entire 12-month follow-up period, the strongest association was at 30 days following index ED visit.

Generally, our findings are consistent with prior research examining delirium and mortality risk. For example, Lewis et al. observed that patients with delirium discharged from the ED had a significantly higher mortality risk at 3 months compared to a comparable control group (14% verses 8%), and we found similar unadjusted results at 3 months (16% verses 6%). Similarly, our findings report a two-fold mortality risk for delirium patients at 12 months following an ED visit (HR 2.07; 95%, 2.01-2.13) in line with McCusker et al (HR 2.11; 95%, 1.18-3.77), after adjusting for covariates. However, our results indicate a higher risk of mortality compared to prior research at 6 months, as Han et al. found seniors to be 1.7 times more likely to be at risk for mortality (HR 1.72; 95% CI, 1.04-2.86), compared to our study which found the risk to be over 2.5 times more likely at 6 months (HR 2.55, 95% CI, 2.47-2.64). In addition, our findings are also consistent with prior research on delirium as an independent indicator for mortality in the inpatient setting.[3] For instance, past studies report a two-fold increase in mortality risk among delirium patients, and our results point to a similar two-fold increase in mortality during 12-month follow-up.

Our findings are also in line with prior research highlighting the role of dementia superimposed on delirium and its protective effect on mortality.[3] Others have theorized as to why this is the case, however further research is needed in distinguishing acute behavioral changes of delirium with the longer-term changes associated with dementia to properly evaluate its impact. One reason may be that delirium may be harder to distinguish in patients with dementia, leading to misclassification in claims data. Further research is needed in distinguishing acute behavioral changes of delirium with the longer-term changes associated with dementia and the proper screening and measurements.

Given the clinical as well as cost implications, our results call for an increase in screening and management of delirium in the ED. A practical first step is through implementation of a validated delirium screening tool into the ED clinical workflow. Since the majority of patients with delirium have a clinically subtle presentation, it is often missed by providers, which is likely to be the case in a busy ED. While multiple resources exist for delirium screening, the most widely used in the inpatient setting is the Confusion Assessment Method (CAM). The brief CAM (b-CAM) is a modified and validated screening tool for delirium and is one of, if not the only instrument validated for use in the ED setting.[14 15] The b-CAM takes less than 2 minutes to perform, is highly reliable, easy to use, and requires minimal training, all of which make it an ideal instrument for an ED.[16] While other validated screening instruments are available such as the Delirium Rating Scale, the Nurses Delirium Screening Checklist, or the 4As test, many of these tools were not designed for use in the ED and either require specialized training or more time to complete than is often available in an ED encounter.[17]

A growing number of EDs specializing in geriatric care (i.e., Geriatric Emergency Departments) are already incorporating delirium protocols and screening instruments into their ED workflow. In fact, the Geriatric Emergency Department Guidelines, endorsed by leading professional societies in Emergency Medicine, Nursing and Geriatrics, identify delirium screening, and specifically the b-CAM as a recommended screening instrument for use in the ED's. The Society for Academic Emergency Medicine has even recommended delirium screening as a key quality indicator for geriatric emergency care underscoring the importance of detection and management of delirium in the ED. [2 14]

While screening for delirium is an important first step, screening alone is insufficient and must be followed by clinical intervention to be effective. Based on screening results, decreased use of psychoactive medication or other non-pharmacologic approaches such as increased mobilization (i.e., reduced of physical restraints, bladder catheters), and re-orienting the patient through cognitive stimulation are examples of interventions used in the inpatient setting that may also be appropriate for the ED. [7] While it remains unclear whether instruments such as the b-CAM or follow-up interventions used in the inpatient setting are associated with reduced mortality risk in the ED, incorporating a delirium instrument into ED workflows represents an important first step to more reliably detect delirium in the ED. Future research will then need to address the most effective screening and treatment protocols.

Limitations

Our study utilized national claims-level data, which poses several limitations. The date of claims submission does not necessarily reflect date of service however these differences are often considered marginal. Additionally, claims data lack information on severity and duration of illness prior to the diagnosed event. While we attempted to address this issue by including a three-month control period prior to qualifying index encounters and focusing on outpatient claims only, this still did not address the severity of delirium, which is likely to impact mortality risk.

Furthermore, we identified 26,245 (0.35%) patients ≥ 65 with delirium which is lower compared to rates of delirium in the ED widely reported in literature, which ranges anywhere from 3.6-35% with a mean of 17.5%. [4 5 9] Our lower incidence of delirium based on available claims may reflect a failure to diagnose, failure to code, or a lower rate of delirium patients in ED's. This potential absence of delirium diagnoses from a national claims database may limit the generalizability of our findings in helping capture the true impact of delirium on mortality.

CONCLUSIONS

Our study of national claims-level data demonstrates that delirium is a significant marker of mortality among seniors visiting the ED, and that mortality risk is most prominent in the first three months following an ED visit. Given the significant clinical as well as financial implications associated with seniors discharged from the ED with delirium, there is a need to increase delirium screening and management within the ED to help identify and treat underlying conditions. Specifically, future research is needed to focus on implementation and dissemination of existing delirium protocols (i.e., screening and follow-up interventions) for the ED and whether doing so helps reduce mortality risk in seniors discharged from the ED with this fatal and potentially avoidable condition.

FOOTNOTES

Figure Legends

Figure 1. Flowchart for inclusion/exclusion criteria

Figure 2. Kaplan-Meier Survival Curves
Assessing changes over time in the unadjusted effect of delirium on mortality in comparison to the control group (no delirium). The dotted line represents patients with delirium and when compared to the control group the survival rate decreased rapidly during the first 30 days after the index visit and continued to decline slowly.

Contributors Statement: JI, TK, AL, and KK contributed to study design. JI and TK performed the data analysis. JI led drafting of the manuscript, with additional manuscript writing performed by AL and KK All authors had full access to all the data including statistical reports and tables in the study and can take full responsibility for the integrity of the data and the accuracy of the data analysis.

Funding: This project received no specific funding.

Competing Interests: All authors declare no financial relationships with any organizations that might have an interest in the submitted work or other relationships or activities that could appear to have influenced the submitted work.

Data Sharing Statement: No additional data available

Transparency: The lead author affirms that the manuscript is an honest, accurate and transparent account of the study analyzed and reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

REFERENCES

1. Albert M, Linda Ashman, Jill Emergency Department Visits by Persons Aged 65 and Over: United States. NCHS Data Brief 2013 (130).

2. Fong T, Tulebaev SI, Sharon Delirium in Elderly Adults: Diagnosis, Prevention, and Treatment Nature Reviews Neurology 2009;**5**:210-20.

3. Kakuma R, Galbaud Du Fort G, Arsenault Lea. Delirium in Older Emergency Department Patients Discharged Home: Effect on Survival Journal of American Geriatics Society 2003;**51**(4):443-50.

4. Inouye SW, Rudi Sacynski, Jane Delirium in Elderly People Lancet 2015 **383**(9920):911-22.

5. McCusker JM, Cole Abrahamowicz, Michal Delirium Predicts 12 Month Mortality JAMA Internal Medicine 2002 **4**(162):457-63.

6. Gower LG, Medley Kang, Christopher Emergency Department Management of Delirium in the Elderly Western Journal of Emergency Medicine 2012 **2**(13):194-201.

7. Han JW, Amanda Ely, Wesley Delirium in the Older Emergency Department Patient - A Quiet Epidemic Emergency Medicine Clinics of North America 2010 **3**(28):611-31.

8. Han J, Zimmerman EC, Nathan, et al. . Delirium in Older Emergency Department Patients: Recognition, Risk Factors, and Psychomotor Subtypes Journal of the Society for Academic Emergency Medicine 2009 **16**:193-200.

9. Han J, Shintani AE, Svetlana, et al. . Delirium in the Emergency Department: an Independent Predictor of Death Within Six Months. Annals of Emergency Medicine 2010 **3**(56):244-52.

10. Tyree PL, Bonnie Lafferty, William Challenges and Advantages of Using Medicare Claims Data for Utilization Analysis The American Journal of Medicine 2006 **4**(21):269-75.

11. Ogundimu EA, Douglas Collins, Gary Adequate Sample Size for Developing Prediction Models is Not Simply Related to Events per Variable Journal of Clinical Epidemiology 2016 175-82.

12. Charlson MP, Kathy Ales, Kathy, et al. . A New Method of Classigying Prognostic Comorbidity in Longitudinal Studies: Development & Validation Journal Of Chronic Diseases 1987;**40**(5):373-83.

13. Smith BS, Tyler Kaplan Meier & Cox Proprtional Hazards Modeling: Hands-On Survival Analysis Department of Defense Center for Deployment Health Research 2014.

14. De JW, Anne. Delirium Screening: A Systematic Review of Delirium Screening Tools The Gerontologist 2015 **55**(6):1079-99.

15. Wei LF, Michael, Sternberg Eea. The Confusion Assessment Method (CAM): A Systematic Review of Current Usage Journal of American Geriatics Society 2008 **56**(5):823-30.

16. Mariz J, Castanho TT, Jorge et al. . Delirium Diagnostic and Screening Instruments in the Emergency Department: An Up-to-Date Systematic Review Journal of American Geriatics Society 2016

17. Grover SK, Natasha Assessement Scales of Delirium World Journal of Psychiatry 2012 **2**(4):58-70.

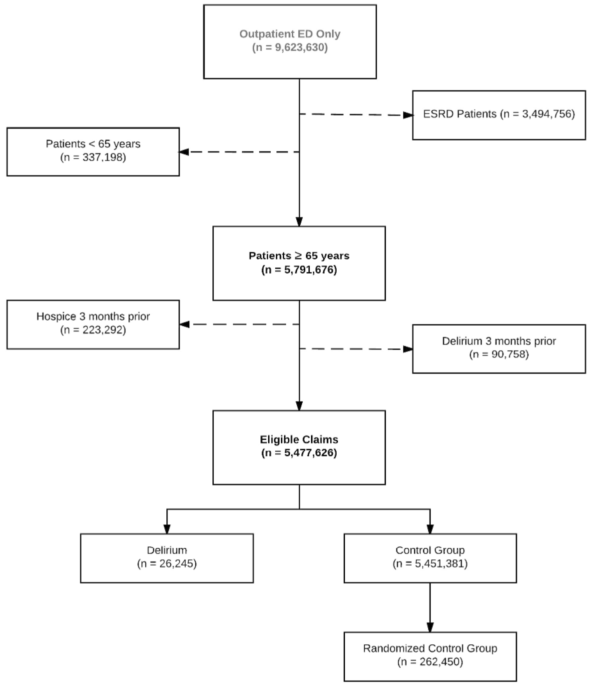

Figure 1. Flowchart for inclusion/exclusion criteria

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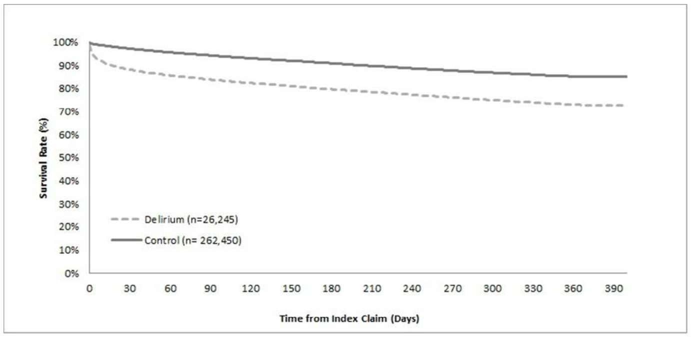

Figure 2. Kaplan-Meier Survival Curves
Assessing changes over time in the unadjusted effect of delirium on mortality in comparison to the control group (no delirium). The dotted line represents patients with delirium and when compared to the control group the survival rate decreased rapidly during the first 30 days after the index visit and continued to decline slowly.

304x190mm (96 x 96 DPI)

Supplemental File

Appendix 1. Diagnosis Related Group (DRG) codes for Delirium with ICD-9

ICD-9 Code	Description
293.0	Acute Delirium (also documented as acute confusional state)
290.41 & 437.0	Arteriosclerotic Dementia with Delirium
293.89	Chronic Delirium
780.09	Delirium, not otherwise specified
293.81	Drug Induced Delirium
300.11	Hysterical Delirium
290.11	Presenile Dementia with Delirium
290.3	Senile Dementia with Delirium
293.1	Subacute Delirium
308	Exhaustion Delirium
584-586	Uremic Delirium

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DELIRIUM AS A PREDICTOR OF MORTALITY IN US MEDICARE BENEFICIARIES DISCHARGED FROM THE EMERGENCY DEPARTMENT: A NATIONAL CLAIMS LEVEL ANALYSES UP TO 12 MONTHS

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021258.R1
Article Type:	Research
Date Submitted by the Author:	08-Mar-2018
Complete List of Authors:	Israni, Juhi; West Health Institute, Clinical Lesser , Adriane ; West Health Institute, Clinical Kent , Tyler ; West Health Institute Ko , Kelly ; West Health Institute, Clinical
Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	Emergency medicine
Keywords:	GERIATRIC MEDICINE, Delirium, Mortality, Claims Data

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Abstract: 300

Word Count: 3,618

References: 17

Figures: 2

Tables: 2

ABSTRACT

Background: Delirium is common among seniors discharged from the Emergency Department (ED) and associated with increased risk of mortality. Prior research has addressed mortality associated with seniors discharged from the ED with delirium, however has generally relied on data from one or a small number of institutions and at single time points.

Objectives: Analyze mortality rates among seniors discharged from the ED with delirium up to 12 months at the national level.

Design: Retrospective Cohort Study

Setting: Analyzed data from the Center for Medicare & Medicaid Services (CMS) limited datasets for 2012 to 2013.

Participants: Medicare fee-for-service beneficiaries aged 65 years or older discharged from the ED. We focused on new incidence cases of delirium, patients with any prior claims for delirium, hospice claims, or End-Stage Renal Disease (ESRD) were excluded. Sample size included 26,245 delirium claims, and a randomly selected sample of 262,450 controls.

Outcome Measures: Mortality within 12 months after discharge from the ED, excluding patients transferred or admitted as inpatients.

Results: Among all beneficiaries, 46,508 (16.1%) died within 12 months. Of which 39,404 (15.0%) were in the non-delirium (i.e., control group) and 7,104 (27.1%) were in the delirium cohort respectively. Mortality was strongest at 30 days with an adjusted hazard ratio of 4.82 (95%, 4.60-5.04). Over time, delirium was consistently associated with increased mortality risk compared to controls up to 12-months (HR 2.07; 95%, 2.01-2.13). Covariates that affected mortality included older age, comorbidity, and presence of dementia.

Conclusions: Our results demonstrate delirium is a significant marker of mortality among seniors in the ED, and mortality risk is most salient in the first 3 months following an ED visit. Given the significant clinical and financial implications, there is a need to increase delirium screening and management within the ED to help identify and treat this potentially fatal condition.

KEY WORDS: ***Geriatrics, Delirium, Mortality, Claims Data***

Strengths & Limitations of this Study

- This study included the entire Medicare population aged 65 and older with outpatient claims in the United States, over 5.8 million patients.
- A limitation of this study is that we could not control for delirium severity or duration of illness prior to the diagnosed event as this information was not available in the claims-level data used in our analysis.

INTRODUCTION

The Emergency Department (ED) is often the point of entry for seniors into the healthcare system, and as such plays a unique role in setting the trajectory of care for this rapidly growing and often vulnerable segment of the population. Thus, timely screening of life-threatening conditions such as delirium is critical in the ED.

Delirium is broadly defined as an acute decline in attention and global cognitive functioning,[1] which is not only common, but often fatal in older adults.[2] In the United States alone, of the nearly 20 million older adults seen in the ED each year,[3] approximately 8-17% present to the ED suffering from delirium.[4] Prior research indicates that patients with delirium have a 12-month mortality rate between 10-26%,[5] which is comparable to patients with sepsis or acute myocardial infraction.[6] Additionally, the increased mortality risk for delirium patients in the ED has been identified at multiple time points, specifically at 3, 6, and 12 months. [3 5 7]

Furthermore, delirium is also costly and management can be resource intensive. For example, delirium is often associated with increased length of stay among hospitalized patients, may require use of restraints, sedative medications, or additional staffing (e.g. sitters) and generally linked to greater functional and cognitive decline. [8]

Despite the growing body of research demonstrating delirium is an independent predictor of mortality, as well as increased costs, management of delirium in the ED has not been well studied. In fact, some studies suggest delirium goes undiagnosed by up to 80% of ED physicians [8 9], highlighting the magnitude of the missed opportunity to improve recognition and management of this potentially fatal condition.

While prior research has addressed the mortality risk associated with seniors discharged from the ED with delirium, much of this research has relied on data from a few, if not a single institution. Furthermore, previous research has typically examined mortality at only single points in time. Our work builds off this growing body of literature by leveraging national claims data to analyze mortality rates among seniors discharged from the ED with delirium at multiple time points up to 12 months, with implications for screening and treatment recommendations.

METHODS

Patient & Public Involvement

Patients or the public were not directly involved as the analysis was conducted utilizing US claims-level data.

Study Design & Data Source

Our study was a retrospective analysis of all available national claims-level data from 2012 to 2013. We analyzed data from the Center for Medicare & Medicaid Services (CMS) Research Data Assistance Center (ResDAC) dataset which includes data for approximately 98 percent of the U.S. population aged 65 years and older. [10] CMS data is one of the richest sources of utilization information nationally with sizable samples, documented procedures and diagnoses, verified deaths, beneficiary demographic information, and revenue center details. For our study, we utilized data for each institutional and non-institutional claim type with each record representing a beneficiary claim.

Inclusion/exclusion criteria

An ED-associated claim qualified as an index encounter if it was the beneficiary's initial ED outpatient-only claim during the study period and if the claim had subsequent claims-level data available for three months before and 12 months after index encounter (15 months of available data in total). The three-month control period prior to index ED encounter was used to exclude beneficiaries with any prior claims for delirium, hospice claims, or End-Stage

Renal Disease (ESRD) to reduce the potential confounding nature of these factors and to focus largely on new incident cases of delirium. We excluded ESRD patients from our sample population as prior literature suggests claims data for ESRD is often incompletely documented or not tracked in the Medicare data system with as much rigor as the general Medicare population.[11] Index encounters that resulted in observation or an inpatient stay were also excluded due to likelihood of that these cases may represent higher acuity conditions. Once exclusion criteria were applied, we removed a total of 3,808,806 claims (90,758 delirium, 223,292 Hospice, and 3,494,756 ESRD claims) leaving us with a total of 5,477,626 claims for our analyses. See Figure 1 for a flowchart showing application of the inclusion/exclusion criteria.

Cohort Selection

Of the 5,477,626 claims, we focused our analyses on two cohorts: A delirium cohort, and a control group of beneficiaries without delirium. The groups were constructed as follows:

Delirium cohort: Of the 5,477,626 eligible claims, delirium was identified based on presence of a qualifying outpatient diagnosis claim that included ICD-9 codes (293.0, 290.41, 293.89, 780.09, 292.81, 300.11, 290.11, 290.3, 293.1, and categories 308, and 584 to 586) (see Appendix 1 for a more detailed description of codes). We limited delirium diagnoses to claims where at least one of these ICD-9 codes was documented at least once within any diagnosis, at which point the claim was flagged as a delirium encounter. We identified a total of 25,980 beneficiaries with qualifying index encounters and a total of 26,245 delirium claims.

Control cohort: The control group consisted of beneficiaries with no delirium diagnosis present. Of the eligible 5,477, 626 claims for our analyses, 5,451,381 qualifying index ED claims were eligible for the control group after selection of the delirium cohort from the eligible claims. Considering the size of our control group, we randomly selected from the 5,451,381 potential control beneficiaries using a 10:1 ratio following prior research on recommended statistical practice based on simulation studies of a minimum of 10 events per variable. [12] Following random selection, our control group included a total of 251,971 beneficiaries and a total of 262,450 claims.

Mortality

Mortality was flagged for all individuals who died within 12-months from index encounter and flagged only if the death date was verified at 30 days, 90 days, 6 months, and 12 months. Total number of deaths recorded for the delirium and control groups at 12 months were 7,104 (27.1) and 39,404 (15.0%) respectively. See Table 1 for mortality rate by death date.

Statistical Analysis

Our analyses focused on two primary areas: (1) the role of delirium as an independent predictor for mortality; and (2) identifying the effect of covariates (age, gender, dementia, & Charlson Comorbidity Index (CCI)) on mortality.

We first compared the two cohorts using independent group t-test and X^2 test for quantitative and categorical variables and found significant differences between the cohorts with respect to demographic and clinical measures. Members of the delirium cohort were more likely than controls to be older (mean age: 79 vs. 77), more likely to have a lower level of illness and severity burden (mean CCI: 4 vs. 6),[13] and more likely to have a primary diagnosis of mental/neurological clinical classification. The cohorts did not differ with respect to gender or ethnicity as both cohort's members were more likely to be Caucasian females (See Table 1).

Time 0 was defined as date of index encounter and days between death date and index encounter was calculated for the model. In addition, beneficiaries were censored at the end of the 12-month follow-up period if death did not occur or loss of follow-up, whichever occurred earlier. We then used the exponential model for the survival time distribution to estimate yearly mortality rates for the delirium and control cohort using an unadjusted Kaplan-Meier survival curve. In addition, a score test (univariate Cox proportional hazards model) was utilized as a comparison to the unadjusted Kaplan-Meier survival curves. [14]

Table 1: Cohort Characteristics

Characteristics	Delirium	Control (No Delirium)
Total	26,245 (100)	262,450 (100)
Age	…	…
65-74	8,723 (33.2)	106,163 (40.4)
75-84	9,500 (36.2)	96,998 (37.0)
≥85	8,022 (30.6)	59,272 (22.6)
Mean Age	79	77
Gender	…	…
Female	16,279 (62.1)	160,421 (61.1)
Male	9,966 (37.9)	102,012 (38.8)
Race	…	…
Caucasian	22,699 (86.5)	222,177 (84.7)
African American	2,243 (8.5)	27,328 (10.4)
Asian	345 (1.3)	3,115 (1.2)
Hispanic	473 (1.8)	4,683 (1.8)
Native American	134 (0.51)	1,389 (0.53)
Other/Unknown	281 (1.1)	2,852 (1.1)
Charlson Comorbidity Scores	…	…
None (0)	12,423 (47.3)	113,743 (43.3)
Low (1-4)	13,182 (50.2)	141,832 (54.0)
Moderate (5-9)	595 (2.3)	6,553 (2.5)
High (10+)	45 (0.17)	305 (0.12)
Mean CCI Score	4	6
Primary Diagnosis (ICD-9 Codes)	…	…
Infectious Diseases (0-139)	252 (1.0)	2,235 (0.9)
Neoplasms (140-239)	93 (0.4)	926 (0.4)
Mental/Neurological (240-289)	4,651 (17.7)	8,547 (3.3)
Cardiovascular (390-429)	1,396 (5.3)	17,038 (6.5)
Cerebrovascular (430-459)	1,117 (4.3)	7,814 (3.0)
Respiratory (460-519)	794 (3.0)	15,802 (6.0)
Digestive (460-519)	312 (1.2)	13,927 (5.3)
Urogenital (580-629)	1,552 (5.9)	14,509 (5.5)
Musculoskeletal (710-739)	412 (1.6)	19,779 (7.5)
Symptoms (782-789)	1,803 (6.9)	60,126 (22.9)
Injuries (790-799)	151 (0.6)	1,593 (0.6)
Ill-defined, Skin, or Missing (680-709)	58 (0.2)	5,299 (2.0)
Endocrine (240-289)	1,463 (5.6)	10,788 (4.1)
Mortality		
30 Days	3,129 (11.9)	7,649 (2.9)
90 Days	4,251 (16.2)	15,267 (5.8)
6 Months	5,364 (20.4)	24,453 (9.3)
12 Months	7,104 (27.1)	39,404 (15.0)

Additionally, to adjust for possible prognostic factors of delirium on mortality, we used a multivariable Cox proportional hazards model with the following covariates: age, gender, dementia, and comorbidity (as defined by CCI). To address the potential interaction of delirium on mortality based on these characteristics, we evaluated all covariates in the multivariable Cox model, and then selected statistically significant interactions for further testing. In addition, to confirm results we re-ran these analyses using multiple randomly selected samples from within the control group and found no statistically significant differences.

RESULTS

During the 12-month study period 288,695 claims were included in our analysis sample, of which 26,245 comprised the delirium cohort and 262,450 control claims. Beneficiaries were largely similar with respect to gender, and primary diagnosis distributions, however when evaluating comorbidity scores, beneficiaries had higher scores in the control group suggesting higher risk of mortality (see Table 1). Among all beneficiaries, 46,508 (16.1%) died within 12 months. Of which 39,404 (15.0%) were in the non-delirium (i.e., control group) and 7,104 (27.1%) were in the delirium cohort respectively. In the delirium cohort, Kaplan-Meier survival decreased rapidly during the first 30 days after the index visit and thereafter continued to decline at a slower pace in comparison to the control group. At 30 days after index visit, the survival rate for beneficiaries with delirium was 88.2%, while the control group had a survival rate of 97.6%.

Results from the univariate and multivariate Cox proportional hazard models for 30 days, 90 days, 6 months, and 12 months are reported in Table 2. Our unadjusted results for delirium and mortality was strongest at 30 days as illustrated in the Kaplan-Meier survival curve (HR, 4.35; 95% CI, 4.17-4.54) (see Figure 2). Even after adjusting for covariates, delirium was still independently associated with approximately a five-fold increase in mortality during the 30-day follow-up period (HR 4.82; 95% CI, 4.60-5.04). Over time from index ED encounter, delirium was still c associated with an increased risk of mortality compared to the control group. However, mortality risk (while still significant) did decrease over time up until 12 months (HR 2.07; 95%, 2.01-2.13).

Table 2: Cox Proportional Hazard Ratios in Intervals to 12-Month Mortality

Mortality Rate	Variable	Univariate	Multivariate
30 Days	Delirium/Control	4.35† (4.17-4.54)	4.82 † (4.60-5.04)
…	Age	1.06† (1.05-1.06)	1.06 † (1.05-1.06)
…	Male/Female	0.72 † (0.69-0.74)	0.70 † (0.67-0.73)
…	CCI	1.29† (0.77-1.28)	1.30 † (1.29-1.31)
…	Dementia	1.84† (1.75-1.94)	1.44 † (1.35-1.53)
…	Delirium*Dementia	…	0.41 † (0.36-0.45)
90 Days	Delirium/Control	3.02 † (2.14-2.30)	3.27 † (3.15-3.40)
…	Age	1.06 † (1.05-1.06)	1.06 † (1.05-1.06)
…	Male/Female	0.74 † (0.72-0.76)	0.72 † (0.70-0.75)
…	CCI	1.32 † (1.31-1.32)	1.32 † (1.31-1.33)
…	Dementia	2.12 † (2.04-2.20)	1.58 † (1.51-1.65)
…	Delirium*Dementia	…	0.48 † (0.44-0.52)
6 months	Delirium/Control	2.42 † (2.35-2.49)	2.55 † (2.47-2.64)
…	Age	1.06 † (1.05-1.06)	1.06 † (1.05-1.06)
…	Male/Female	0.76 † (0.74-0.78)	0.73 † (0.71-0.75)
…	CCI	1.31 † (1.30-1.31)	1.31 † (1.31-1.32)
…	Dementia	2.25 † (2.18-2.31)	1.64 † (1.58-1.70)
…	Delirium*Dementia	…	0.53 † (0.49-0.57)
12 months	Delirium/Control	2.02 † (1.96-2.07)	2.07 † (2.01-2.13)
…	Age	1.06 (1.05-1.06)	1.06 † (1.05-1.06)
…	Male/Female	0.76 † (0.75-0.78)	0.73 † (0.71-0.74)
…	CCI	1.30 † (1.29-1.31)	1.30 † (1.29-1.31)
…	Dementia	2.28 ‡ (2.23-2.34)	1.62 † (1.57-1.66)
…	Delirium*Dementia	…	0.60 † (0.56-0.64)

Data are hazard ratios for univariate & multivariate for time periods to 1-year mortality rate (95% confidence interval). Of 277,951 patients, 46,508 died (16.7%) in both groups. Of which 39,404 (15.0%) were in the control group (no delirium) & 7,104 (27.1%) were in the delirium cohort, respectively.
Note(s): †P-value < 0.001; * indicates interaction

Other covariates that affected mortality rate included older age and higher comorbidity scores. However, women with delirium had a decreased risk of mortality, compared to males with delirium (HR 0.73; 95% CI, 0.71-0.74) at 12 months (see Table 2).

The presence of dementia, on the other hand, had a stronger association in the univariate model, however our adjusted multivariate model indicated dementia was not a significant predictor of mortality and instead associated with a significant protective effect on mortality. This protective effect is demonstrated by the significant statistical interaction between delirium and dementia ($P \geq 0.001$) while adjusting for covariates (HR 0.60; 95% CI, 0.56-0.64).

DISCUSSION

Our study found that delirium is an independent predictor of mortality among ED patients diagnosed with delirium in the ED compared to ED patients without delirium, even after adjusting for confounding factors such as age, gender, comorbidity, and dementia. While delirium had a strong effect on mortality during the entire 12-month follow-up period, the strongest association was at 30 days following index ED visit.

Generally, our findings are consistent with prior research examining delirium and mortality risk. For example, Lewis et al. observed that patients with delirium discharged from the ED had a significantly higher mortality risk at 3 months compared to a comparable control group (14% verses 8%), and we found similar unadjusted results at 3 months (16% verses 6%). Similarly, our findings report a two-fold mortality risk for delirium patients at 12 months following an ED visit (HR 2.07; 95%, 2.01-2.13) in line with McCusker et al (HR 2.11; 95%, 1.18-3.77), after adjusting for covariates. However, our results indicate a higher risk of mortality compared to prior research at 6 months, as Han et al. found seniors to be 1.7 times more likely to be at risk for mortality (HR 1.72; 95% CI, 1.04-2.86), compared to our study which found the risk to be over 2.5 times more likely at 6 months (HR 2.55, 95% CI, 2.47-2.64). In addition, our findings are also consistent with prior research on delirium as an independent indicator for mortality in the inpatient setting.[3] For instance, past studies report a two-fold increase in mortality risk among delirium patients, and our results point to a similar two-fold increase in mortality during 12-month follow-up.

Our findings are also in line with prior research highlighting the role of dementia superimposed on delirium and its protective effect on mortality.[3] Others have theorized as to why this is the case, however further research is needed in distinguishing acute behavioral changes of delirium with the longer-term changes associated with dementia to properly evaluate its impact. One reason may be that delirium may be harder to distinguish in patients with dementia, leading to misclassification in claims data. Further research is needed in distinguishing acute behavioral changes of delirium with the longer-term changes associated with dementia and the proper screening and measurements.

Given the clinical as well as cost implications, our results call for an increase in screening and management of delirium in the ED. A practical first step is through implementation of a validated delirium screening tool into the ED clinical workflow. Since the majority of patients with delirium have a clinically subtle presentation, it is often missed by providers, which is likely to be the case in a busy ED. While multiple resources exist for delirium screening, the most widely used in the inpatient setting is the Confusion Assessment Method (CAM). The brief CAM (b-CAM) is a modified and validated screening tool for delirium and is one of, if not the only instrument validated for use in the ED setting.[15 16] The b-CAM takes less than 2 minutes to perform, is highly reliable, easy to use, and requires minimal training, all of which make it an ideal instrument for an ED.[17] While other validated screening instruments are available such as the Delirium Rating Scale, the Nurses Delirium Screening Checklist, or the 4As test, many of these tools were not designed for use in the ED and either require specialized training or more time to complete than is often available in an ED encounter.[18]

A growing number of EDs specializing in geriatric care (i.e., Geriatric Emergency Departments) are already incorporating delirium protocols and screening instruments into their ED workflow. In fact, the Geriatric Emergency Department Guidelines, endorsed by leading professional societies in Emergency Medicine, Nursing and Geriatrics, identify delirium screening, and specifically the b-CAM as a recommended screening instrument for use in the ED's. The Society for Academic Emergency Medicine has even recommended delirium screening as a key quality indicator for geriatric emergency care underscoring the importance of detection and management of delirium in the ED. [2 15]

While screening for delirium is an important first step, screening alone is insufficient and must be followed by clinical intervention to be effective. Based on screening results, decreased use of psychoactive medication or other non-pharmacologic approaches such as increased mobilization (i.e., reduced of physical restraints, bladder catheters), and re-orienting the patient through cognitive stimulation are examples of interventions used in the inpatient setting that may also be appropriate for the ED.[7] While it remains unclear whether instruments such as the b-CAM or follow-up interventions used in the inpatient setting are associated with reduced mortality risk in the ED, incorporating a delirium instrument into ED workflows represents an important first step to more reliably detect delirium in the ED. Future research will then need to address the most effective screening and treatment protocols.

Limitations

Our study utilized national claims-level data, which poses several limitations. The date of claims submission does not necessarily reflect date of service however these differences are often considered marginal. Additionally, claims data lack information on severity and duration of illness prior to the diagnosed event. While we attempted to address this issue by including a three-month control period prior to qualifying index encounters and focusing on outpatient claims only, this still did not address the severity of delirium, which is likely to impact mortality risk.

Furthermore, we identified 26,245 (0.35%) patients ≥ 65 with delirium which is lower compared to rates of delirium in the ED widely reported in literature, which ranges anywhere from 3.6-35% with a mean of 17.5%.[4 5 9] Our lower incidence of delirium based on available claims may reflect a failure to diagnose, failure to code, or a lower rate of delirium patients in ED's. This potential absence of delirium diagnoses from a national claims database may limit the generalizability of our findings in helping capture the true impact of delirium on mortality.

CONCLUSIONS

Our study of national claims-level data demonstrates that delirium is a significant marker of mortality among seniors visiting the ED, and that mortality risk is most prominent in the first three months following an ED visit. Given the significant clinical as well as financial implications associated with seniors discharged from the ED with delirium, there is a need to increase delirium screening and management within the ED to help identify and treat underlying conditions. Specifically, future research is needed to focus on implementation and dissemination of existing delirium protocols (i.e., screening and follow-up interventions) for the ED and whether doing so helps reduce mortality risk in seniors discharged from the ED with this fatal and potentially avoidable condition.

FOOTNOTES

Figure Legends

Figure 1. Flowchart for inclusion/exclusion criteria

Figure 2. Kaplan-Meier Survival Curves
Assessing changes over time in the unadjusted effect of delirium on mortality in comparison to the control group (no delirium). The dotted line represents patients with delirium and when compared to the control group the survival rate decreased rapidly during the first 30 days after the index visit and continued to decline slowly.

Contributors Statement: JI, TK, AL, and KK contributed to study design. JI and TK performed the data analysis. JI led drafting of the manuscript, with additional manuscript writing performed by AL and KK All authors had full access to all the data including statistical reports and tables in the study and can take full responsibility for the integrity of the data and the accuracy of the data analysis.

Funding: This project received no specific funding.

Competing Interests: All authors declare no financial relationships with any organizations that might have an interest in the submitted work or other relationships or activities that could appear to have influenced the submitted work.

Data Sharing Statement: No additional data available

Transparency: The lead author affirms that the manuscript is an honest, accurate and transparent account of the study analyzed and reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

REFERENCES

1. Albert M, McCaig L, Ashman J. Emergency Department Visits by Persons Aged 65 and Over: United States. NCHS Data Brief 2013 (130).
2. Fong T, Tulebaev S, Inouye S. Delirium in Elderly Adults: Diagnosis, Prevention, and Treatment Nature Reviews Neurology 2009;**5**:210-20.
3. Ritsuko Kakuma GGDF, Louise Arsenault, Anne Perrault, Robert W. Platt, Johanne Monette, Yola Moride, & Christina Wolfson Delirium in Older Emergency Department Patients Discharged Home: Effect on Survival Journal of the American Geriatrics Society 2003;**51**(4):443-50.
4. Inouye S, Westendorp R, Sacynski J. Delirium in Elderly People Lancet 2015 **383**(9920):911-22.
5. Jane McCusker MC, Michal Abrahamowicz, Francois Primeau, & Eric Belzile Delirium Predicts 12- Month Mortality JAMA Internal Medicine 2002 **162**(4):457-63.
6. Gower L, Gatewood M, Kang C. Emergency Department Management of Delirium in the Elderly Western Journal of Emergency Medicine 2012 **2**(13):194-201.
7. Han J, Wilson A, Ely W. Delirium in the Older Emergency Department Patient - A Quiet Epidemic Emergency Medicine Clinics of North America 2010 **3**(28):611-31.
8. Han J, Zimmerman E, Cutler N, et al. Delirium in Older Emergency Department Patients: Recognition, Risk Factors, and Psychomotor Subtypes Journal of the Society for Academic Emergency Medicine 2009 **16**:193-200.
9. Han J, Shintani A, Eden S, et al. Delirium in the Emergency Department: an Independent Predictor of Death Within Six Months. Annals of Emergency Medicine 2010 **3**(56):244-52.
10. Tyree P, Lind B, Lafferty W. Challenges and Advantages of Using Medicare Claims Data for Utilization Analysis The American Journal of Medicine 2006 **4**(21):269-75.
11. Wolfe, R. (1991). "Survival Analysis Methods for the End Stage Renal Disease Program in Medicare " Kidney Failure & the Federal Government: 353-375.
12. Ogundimu E, Altman D, Collins G. Adequate Sample Size for Developing Prediction Models is Not Simply Related to Events per Variable Journal of Clinical Epidemiology 2016 175-82.
13. Charlson M, Pompei K, Ales K, et al. A New Method of Classigying Prognostic Comorbidity in Longitudinal Studies: Development & Validation Journal Of Chronic Diseases 1987;**40**(5):373-83.
14. Smith B, Smith T. Kaplan Meier & Cox Proprtional Hazards Modeling: Hands-On Survival Analysis Department of Defense Center for Deployment Health Research 2014.
15. De J, Wand A. Delirium Screening: A Systematic Review of Delirium Screening Tools The Gerontologist 2015 **55**(6):1079-99.
16. Wei L, Fearing M, Sternberg E, et al. The Confusion Assessment Method (CAM): A Systematic Review of Current Usage Journal of American Geriatics Society 2008 **56**(5):823-30.
17. Mariz J, Castanho T, Teixeira J, et al. Delirium Diagnostic and Screening Instruments in the ED: An Up-to-Date Systematic Review Journal of American Geriatics Society 2016
18. Grover S, Kate N. Assessement Scales of Delirium World Journal of Psychiatry 2012 **2**(4):58-70.

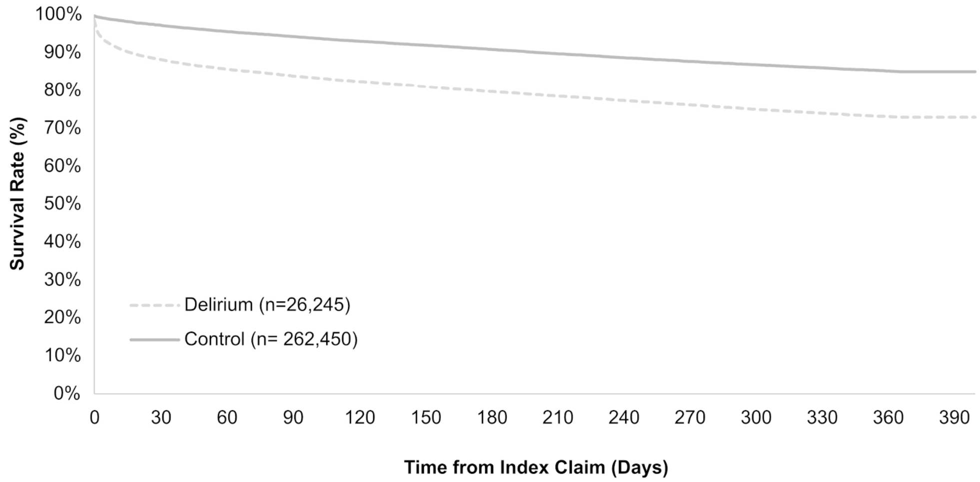

Figure 2: Kaplan- Meier Survival Curves
Assessing changes over time in the unadjusted effect of delirium on mortality in comparison to the control group (no delirium). The dotted line represents patients with delirium and when compared to the control group the survival rate decreased rapidly during the first 30 days after the index visit and continued to decline slowly.

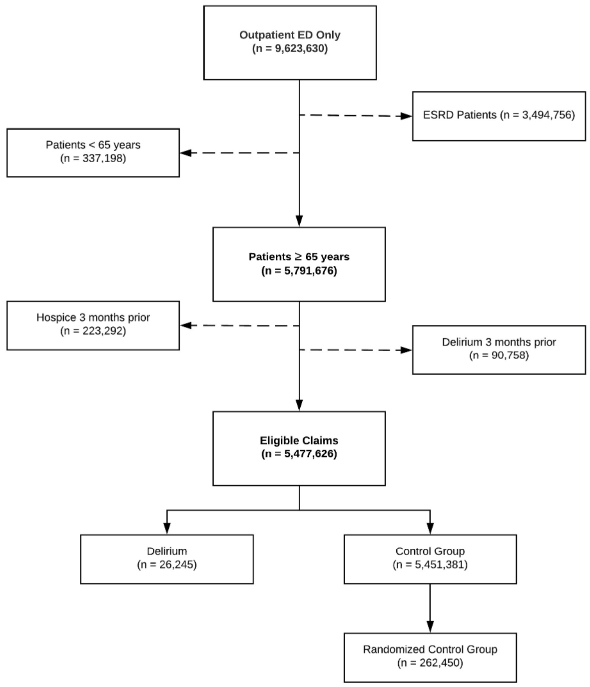

Figure 1: Inclusion/Exclusion Flowchart

280x217mm (300 x 300 DPI)

Supplemental File

Appendix 1. Diagnosis Related Group (DRG) codes for Delirium with ICD-9

ICD-9 Code	Description	Number of Claims
293.0	Acute Delirium (also documented as acute confusional state)	3,056
290.41 & 437.0	Arteriosclerotic Dementia with Delirium	538
293.89	Chronic Delirium	18
780.09	Delirium, not otherwise specified	17,226
293.81	Drug Induced Delirium	46
300.11	Hysterical Delirium	239
290.11	Presenile Dementia with Delirium	1,714
290.3	Senile Dementia with Delirium	576
293.1	Subacute Delirium	108
308	Exhaustion Delirium	978
584-586	Uremic Delirium	1,746