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The Incidence Rate, Types, and External Causes of Traumatic Brain Injuries in Parkinson's Disease Patients in Nebraska 2008-2014

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Abstract

Background: Parkinson's disease (PD) patients are at higher risk of traumatic brain injury (TBI) due to disease characteristics like tremor, bradykinesia, and impaired balance. Most of the studies that have been done in the United States to investigate the incident rate and causes of TBI among PD patients have mainly focused on falls, while none of these studies have thoroughly addressed all causes of TBI among the PD population or have used a population-based database. Our study aims to investigate the incidence rate, types, and external causes of TBI stratified by age of PD diagnosis using a population-based database from Nebraska. The outcomes of this study will provide valuable insights regarding the cause of TBI episodes among the PD population.

Methods: We conducted a retrospective study comprising of patients diagnosed with PD between 2008-2014. A statewide linkage was done between Nebraska PD Registry data and the Nebraska hospital discharge database (HDD). 4037 PD patients were enrolled in the study. PD patients were grouped based on their age of diagnosis into four categories; 30-59 years, 60-69 years, 70-79 years, and ≥80 years. The overall incidence rate and age-specific incidence rate of TBI in the Nebraska PD population was calculated. A chi-square test and multivariable logistic regression model was used to determine the age-specific difference of TBI among those with PD. Frequencies were used to describe the subtypes and external causes of TBI among the four age groups of PD patients.

Results: Between 2008 and 2014, 216 (5.35%) PD patients and 43,530 (4.1%) non-PD residents sustained TBI in Nebraska. The age-adjusted incidence rate of TBI was eight times higher in the PD subject than the general population (4,109 per 100,000 vs. 513 per 100,000). Among PD subjects, logistic regression analysis revealed that age of diagnosis and disease duration were significantly associated with TBI, ($p=0.0008$ and $p=0.0079$, respectively). Among PD patients

with TBI, unspecified head injury was the most frequent type of TBI (68.5%) followed by concussion (27.5%). Falls accounted for 88.9% of TBI incidents among the PD population.

Conclusion: PD patients experienced more TBI events than the general population. After adjusting for age, gender, disease duration, and location of residence, age and disease duration were significantly associated with TBI among the PD population. The analysis also revealed that unspecified head injury and concussion were the most common types of TBI in both PD and the general population. Further analysis showed that falls accounted for the majority of TBI episodes among PD and the general population. Nonetheless, PD patients suffered from a higher rate of falls compared to general population.

Introduction

Problem Statement

The risk of traumatic brain injury (TBI) is higher among the Parkinson's Disease (PD) population than any other population (Rumalla, Gondi, Reddy, & Mittal, 2017). However, the incidence rate, subtypes, and external causes of TBI have not been compared among different age of diagnosis-groups of PD patients in Nebraska.

Hypothesis

We hypothesize that the incidence rate, subtypes, external causes of TBI differ by the age of PD diagnosis in Nebraska.

Literature Review

Parkinson's Disease (PD) is a chronic, progressive neurodegenerative disease which is the result of the loss of dopamine-producing brain cells, called neurons, which are found in the substantia nigra, affecting the body's motor system (National Institute of Neurological Disorders and Stroke [NINDS], 2017). Dopamine is a neurotransmitter chemical responsible for transmitting messages within the brain to produce smooth, purposeful muscle movement (NINDS, 2017). By the time of diagnosis, the patient would typically have lost 60-80% of their dopamine-producing cells (NINDS, 2017). Death or failure of the normal functions of these neurons induces the development of PD and the appearance of the hallmark symptoms including tremors (involuntary shaking), bradykinesia (slowness of movement and reflexes), stiffness in their limbs or the trunk of their body, and impaired balance (NINDS, 2017). As these symptoms progress, walking, talking, swallowing, and completing other simple tasks can become challenging (NINDS, 2017).

The disease affects approximately 50,000 Americans every year, most of them over the age of 60 (NINDS, 2017).

Factors like age, family history, pesticides, decline in estrogen level, genetic and head trauma have been found to increases the risk of PD (Wirdefeldt, Adami, Cole, Trichopoulos, & Mandel, 2011). In the past two decades, studies have focused on the relationship between traumatic brain injury (TBI) and PD. For example, studies have consistently found that people who had mild-to-moderate TBI, including concussion, are at higher risk of developing PD later in their lives (Bower et al., 2003; Goldman et al., 2006; Jafari, Etminan, Aminzadeh, & Samii, 2013; Perry et al., 2016; Rugbjerg, Ritz, Korbo, Martinussen, & Olsen, 2008). In a population-based study, researchers found that there is an association between PD and TBI-related hospitalization occurring within a period of months to a year before PD confirmation (Fang et al., 2012; Rugbjerg et al., 2008).

TBI is defined by the Center for Disease Control and Prevention (CDC) as a disruption in the normal function of the brain that can be caused by a bump, blow, or jolt to the head, or penetrating head injury (Center for Disease Control and Prevention [CDC], 2017). TBI is a serious public health problem in the United States, where about 1.7 million TBI-related cases are reported every year between 2002-2006, including TBI-related emergency visits, hospitalizations, and death (TBI-EDHD) (Faul, Xu, Wald, & Coronado, 2010). Another study showed that in 2013, about 2.8 million TBI-related events happened in the United States (C. Taylor, 2017). Approximately 80-90% of all TBIs required ED visit, 10-16% needed hospitalization, and 2-3% of the patients died (Faul et al., 2010; C. Taylor, 2017). TBI is accountable for 30% of all injuries resulting in death with approximately 50,000 deaths annually (Faul et al., 2010).

In Nebraska, TBI-related hospitalizations and ED visits markedly increased between 2004 and 2008. Hospitalization rate rose from 42.2 per 100,000 persons in 2004 to 62.0 per 100,000 persons in 2008, while ED visits rate increased from 255.0 per 100,000 in 2004 to 412 per 100,000 in 2008 (Welsh, Marcum, Xu, Nebraska, & Department of Health and Human, 2011). The increase in TBI-EDHD cases was mostly among children age 0-14 years and adults age 65 and older (Welsh et al., 2011). The rates of TBI-related hospitalization and death were higher among the age-group >65 than other age-groups; however, young people aged 0-14 are more prone to TBI-related ED visits than others (Welsh et al., 2011). When comparing Nebraska rates from the period of 2004-2008 to the national rates from the period of 2002-2006, it appears that TBI-related deaths in Nebraska decreased by 5% compared to 3.5% increase in the national rate (Faul et al., 2010). However, TBI-related hospitalization and ED visit rates increased in both; these increases were higher in Nebraska compared to national rates, 46% vs. 19.5% hospitalization and 61.9% vs. 14.4% ED visits (Faul et al., 2010; Welsh et al., 2011). More than half of this increase is attributed to falls and motor vehicle injuries (Faul et al., 2010; C. Taylor, 2017; Welsh et al., 2011).

TBI outcomes can range from recovery to death. These outcomes vary based on the severity of the TBI (Sariaslan, Sharp, D'Onofrio, Larsson, & Fazel, 2016). Moreover, recurrent TBIs cause poorer outcomes than single TBIs (Amir Sariaslan et al., 2016). Up to 50% of TBI patients develop adverse outcomes like forgetfulness, fatigue, feeling irritable, vision problem and making more mistakes within a year of the TBI event (Selassie et al., 2008; Whiteneck et al., 2004). Researchers have concluded that there is an association between TBI and developing neurological diseases later in life among those who sustained a TBI (Fang et al., 2012; Goldman et al., 2006; Perry et al., 2016). These neurological illnesses may take some time to reach a clinical stage (Bower et al., 2003; K. M. Taylor et al., 2016).

On the other hand, some neurological diseases have been found to play a role in increasing the risk of having TBI due to their characteristic features. One of these diseases is PD, which typically would increase the risk of TBIs, mainly due to falls. Many studies reported about the risk of falls among PD patients. In these studies, the risk of falls was found to be higher in PD than non-PD patients (Balash et al., 2005; Gazibara et al., 2014; Gray & Hildebrand, 2000; Martignoni et al., 2004; Rudzińska, Bukowczan, Stożek, Zajdel, Mirek, Chwata, et al., 2013; Wood, Bilclough, Bowron, & Walker, 2002). Age, disease duration, positive fall history, and increased motor impairment are significantly associated with falls (Bloem, Grimbergen, Cramer, Willemsen, & Zwinderman, 2001; Hiorth et al., 2017; Hiorth, Larsen, Lode, & Pedersen, 2014; Rudzińska, Bukowczan, Stożek, Zajdel, Mirek, Chwała, et al., 2013).

In studies that compared TBI among PD and non-PD populations; authors found that TBIs and hospitalization due to TBIs were more common among individuals with PD than individuals without PD (Rumalla, Gondi, Reddy, & Mittal, 2017; Wang et al., 2014). However, the risk factors, external causes, and subtypes of TBIs across different age groups of the PD population have not been studied. Therefore, this study aims to compare the incidence rate, subtypes, and external causes of TBI between different age-groups of PD patients in Nebraska.

Goals and Objectives

Aim #1: To estimate the incidence rate of TBI among different age of diagnosis groups of PD patients who were diagnosed with PD between 2008-2014.

Objective: Determine the incidence of TBI among different age of diagnosis groups of PD patients and identify the associated risk factors.

- Activity #1: Retrieve the data from the PD database and the merged PD-TBI database.

- Activity #2: Divide PD population into four age of diagnosis-groups based on 30-59, 60-69, 70-79, and ≥80.
- Activity #3: Analyze the data to determine the incidence rate of TBI among those with PD stratified by the age of PD diagnosis.
- Activity #4: Identify the factors influencing the incidence rate of TBI (e.g., gender and disease duration).

Aim #2: Describe the TBI subtypes among the different age groups of PD patients who were diagnosed with PD between the years 2008-2014 based on ICD-9-CM codes.

Objective: Identify the most common subtypes of TBI among different age of diagnosis groups of PD patients who were diagnosed with PD between 2008-2014.

- Activity: Analyze the data to identify the subtypes of TBI.

Aim #3: Describe the external causes of TBI among different age of diagnosis groups of PD patients who were diagnosed with PD between 2008-2014.

Objective: Identify the leading external causes of TBI among different age of diagnosis groups of PD patients who were diagnosed with PD between 2008-2014.

- Activity: Analyze the data to identify the external causes of TBI, for example, falls, motor vehicle accidents and firearms.

Methods

Data sources

Nebraska Parkinson's Disease

The Nebraska PD registry is a population-based registry maintained by the NE DHHS, established on January 1, 1997 (NE DHHS, 2017). The registry collects standard demographics and identifying information, diagnosis date, and information about prescribed medications and treating physician from pharmacists and physicians who are required by law to report every PD case (NE DHHS, 2015). Pharmacists are required to report any dispensation of drugs that are listed as PD medications based on the list issued by the NE DHHS in January of each year on a semi-annual basis (NE DHHS, 2015). Physicians have to report information on any individual diagnosed with PD or related movement disorder within 60 days of diagnosis date, or from receiving the request for confirmation that sent by the registry after receiving a pharmacy or patient report. The registry also collects information on PD cases from hospital discharge data, death certificates, and patient self-report which is done voluntarily by the patient through filling out a report form and sending it to the registry. Data regarding TBI were obtained from Nebraska hospital discharge data (HDD). The NE HDD collect data from 87 nonmilitary hospitals.

Research question

Does the incidence rate, external causes, and types of TBI differ by age of diagnosis for PD patients?

Study Design

A retrospective cohort study following PD patients from January 1, 2008 until December 31, 2014.

Study Population/Study sample/Data sources/ Data collection methods

We conducted a retrospective cohort study using patients with confirmed PD diagnosis to estimate the incidence rate, external causes, and subtypes of TBI among Nebraskan PD patients diagnosed between 2008 and 2014. PD data collected by the Nebraska PD Registry from January 1997 to 2014 were obtained. We also obtained data on TBI from HDD for the same period. Linkage of the datasets was done by the NE DHHS using Registry Plus™ Link Plus, a probabilistic record linking software developed by the CDC to link cancer registries and other registries that have fixed width or delimited format data (CDC, 2015). Data were linked by matching patient's first and last name, date of birth, gender. Combining the datasets was completed using SAS statistical software package. The study was reviewed and approved by Institutional Review Boards (IRB) at University of Nebraska Medical Center.

Inclusion Criteria

Subjects who lived in Nebraska and have a confirmed PD diagnosed between 2008 and 2014 will be included in this study.

Exclusion Criteria

Subjects missing information on gender, date of birth, diagnosis date, date of TBI injury for PD patient who sustained TBI, and type of injury will be excluded from the study. We also eliminated subject with TBI injury date before PD diagnosis date.

Case Ascertainment

PD case is identified as any person who is diagnosed and confirmed by a physician or reported by a pharmacist to use one of PD medications and confirmed by a physician.

Measurement of Outcomes

TBI case is defined as any person who is admitted to a hospital or rehabilitation center or treated in hospital, rehabilitation center, or in the office of physician or psychologist for one of the following brain or head injuries. Injuries are coded according to the International Classification of Disease, Ninth Revision, Clinical Modification Coding System of the World Health Organization (ICD-9-CM) as follow; 800.0-801.99: Fracture of the vault or base of the skull, 803.0-804.9: Other and unqualified and multiple fractures of the skull, 850.0-854.19: Intracranial injury, including concussion, contusion, laceration and hemorrhage; 907.0: Late effect of intracranial injury, 907.2: 950.1-950.3: Injury to optic chiasm, optic pathways, and visual cortex, and 959.01: Unspecified head injury. External causes will be identify based on the E-codes which is a subset of the ICD-9-CM as follow; E810-819: Motor vehicle traffic-related (unintentional), E880-E888: Falls, E960-E969 Assult (includes firearm), E916 and E817: struck by and against, and all other E-codes: other and unspecified.

Abstracted Variables

For the included cases, we retrieved the following variables; gender, date of birth, date of PD diagnosis, confirmation of PD diagnosis, date of injury, cause of injury, and final diagnosis or classification of the injury. The ICD-9-CM codes that used for final diagnosis or classification of the injury are 800.0-801.99: Fracture of the vault or base of the skull, 803.0-804.9: Other and unqualified and multiple fractures of the skull, 850.0-854.19: Intracranial injury, including concussion, contusion, laceration and hemorrhage; 907.0: Late effect of intracranial injury, 950.1-950.3: Injury to optic chiasm, optic pathways, and visual cortex, 953.0-953.9: Injury to nerve roots and spinal plexus; and 959.01: Unspecified head injury. While the ICD-9-CM E-codes that used for cause of injury are E810-819: Motor vehicle traffic-related (unintentional), E880-E886, E888,

and E897: Falls, E960-E969 Assult (includes firearm and other), E916 and E817: struck by and against, and all other E-codes: other and unspecified.

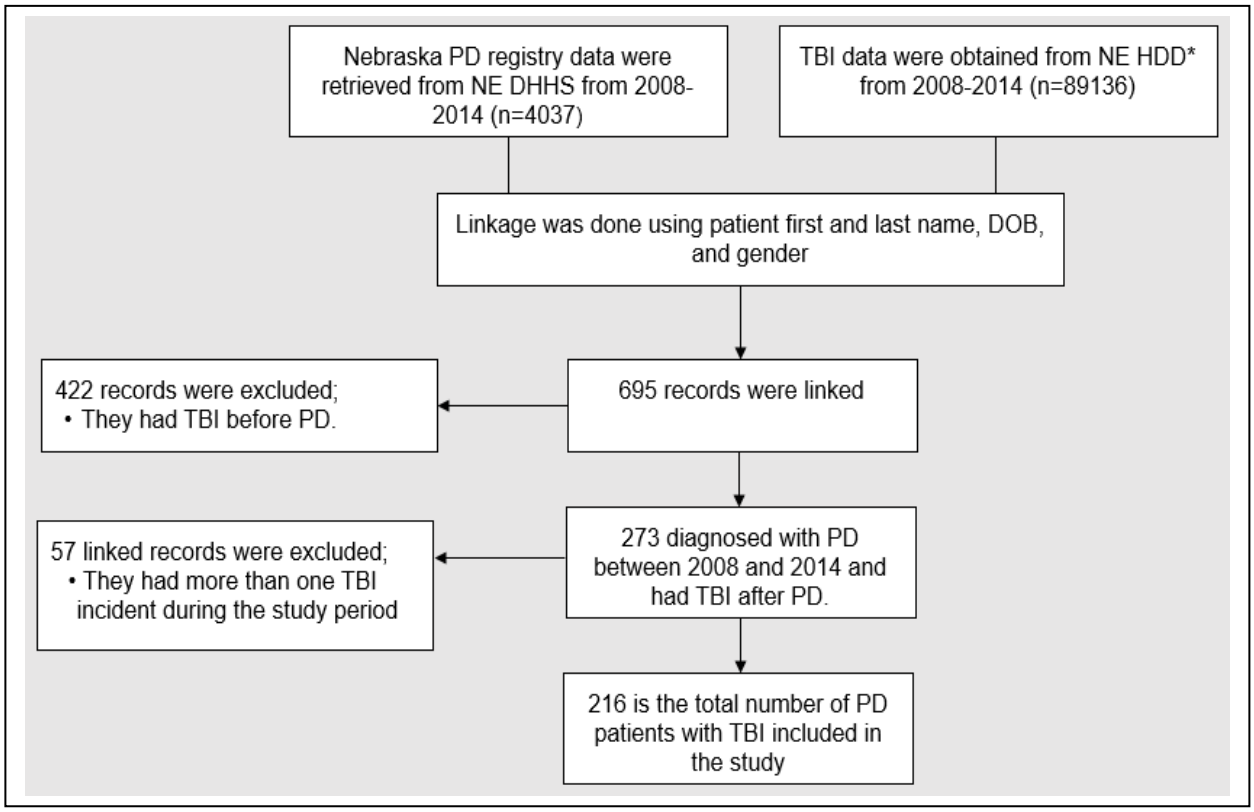
Follow-up

Included subjects were followed retrospectively from the date of PD diagnosis or date PD first reported to the registry to the date of first TBI, date of death, or to the end of the study date December 31, 2014.

Statistical Methods

The cohort stratified by age when first diagnosed with PD into four groups 1) 30-59 years-old, 2) 60-69 years-old, 3) 70- 79 years-old 4) ≥80 years-old. A descriptive analysis was performed to present the demographics of study population and to present the frequencies of the external causes and subtypes of TBI. The incidence rate of TBI was calculated for the four groups of the PD population as the number of TBI incidents divided by the total number of people at risk in the study and multiplied by 100,000. However, the incidence rate for the general population was calculated by taking the total number of TBI incidence occurred during the study period in the general population and divided it on the average number of the population for the same period then multiply it by 100,000. To compare the differences in the incident rate between the groups, multivariate logistic test was performed. To identify the risk factors associated with TBI, all significant variables form the binary tests were included in the multivariate logistic regression model. The results of the descriptive analysis will be reported using frequency, percent, mean, odds ratio, and 95% confidence interval (CI), while the incident rate will be reported using event/100,000 person-year. A p-value <0.05 was considered statistically significant. analysis was performed using SAS 9.4 TS Level 1M4 (SAS Institute Inc., Cary, NC).

Figure 1. Flowchart of inclusion and exclusion criteria of the study subjects.



*****HDD: Hospital Discharge Data.

Results

The retrospective cohort analysis of the data obtained from the PD registry and HDD from 2008 to 2014 contained information on 4,144 PD patients and 89,136 TBI patients. We excluded 107 subjects from the PD cohort because they had inaccurate PD diagnosis date, the date of diagnosis was after death date. Figure 1 illustrates the database linkage process and the inclusion and exclusion criteria of the study population. Basic demographic characteristics and disease duration of PD patients with and without TBI are presented in Table 1. Basic demographics of Nebraska residents with TBI, age 30 years or older, are demonstrated in Table 2.

The PD cohort composed of 4,037 patients (55.78% male, and 44.22% female). Age stratification revealed that about 9.05% were younger than 60 years when diagnosed with PD,

16.56% were diagnosed between the age of 60 and 69 years, 31.08% were diagnosed between the age of 70 and 79, and 43.31% were 80 years or older when diagnosed with PD. Approximately, 57.99% of those had a disease duration of less than three years, and 87.44% of them resided in urban counties.

Table 1. Demographic characteristics and disease duration of Parkinson's disease (PD) patients with and without traumatic brain injury (TBI) in Nebraska (2008-2014).

	Parkinson's Disease (PD)				
	TBI (n=216)	Non-TBI (n=3,821)	OR (95% CI)	*P* value[1]	*P* Adjusted[2]
Age of PD Diagnosis, n (%)					
30-60	14 (3.8)	352 (96.1)	1.0	0.0007	0.0008
60-69	18 (2.8)	624 (97.2)	0.72 (0.36-1.47)		
70-79	89 (7.0)	1179 (92.9)	1.83 (1.03-3.26)		
≥80	95 (5.3)	1666 (94.6)	1.30 (0.73-2.32)		
PD Duration, n (%)					
<3 Years	145 (6.1)	2196 (93.8)	1.0	0.005	0.0079
≥3 Years	71 (4.1)	1625 (95.8)	0.67 (0.50-0.01)		
Gender, n (%)					
Male	118 (5.2)	2134 (94.7)	1.0	0.72	0.7136
Female	98 (5.4)	1687 (94.5)	0.95 (0.72-1.25)		
Residence, n (%)					
Urban	194 (5.5)	3336 (94.5)	1.0	0.27	0.2112
Rural	22 (4.3)	485 (95.6)	1.28 (0.82-2.01)		

1. Chi-square test. 2. Logistic Regression. * Non-Significant.

Table 2. Demographic characteristics of the Nebraska population (≥30 years) with traumatic brain injury (TBI) (2008-2014).

Variables	TBIs in Nebraska Population (≥30 years)
	TBI n=43530
Age, n (%)	
30-59	21025 (2.9)
60-69	5949 (3.4)
70-79	6313 (6.1)
≥80	10243 (13.1)
Gender, n (%)*	
Male	48259 (9.1)
Female	40865 (7.6)

[a] Total Nebraska population is the average population (≥30 years) that resided in Nebraska between 2008 -2014. *Gender is divided based on the gender distribution of Nebraska population for 2010.

Of the PD subjects, 3,821 (94.65%) did not have TBI, and 216 (5.35%) had TBI after being diagnosed with PD. Males representation in TBI vs. non-TBI groups were 55.85% vs. 54.63%, respectively. Regarding the age of PD diagnosis in non-TBI and TBI groups, 9.21% and 6.48% were diagnosed under the age of 60 years, 16.33% and 8.33% diagnosed between 60-69 years, 30.86% and 41.2% diagnosed between 70-79 years, and 43.60% and 43.98% were 80 years or older when diagnosed. 57.47% of the non-TBI cohort and 67.13% of the TBI cohort had a disease duration of less than three years. About 87.31% of the non-TBI group and 89.81% of the TBI group resided in urban counties. From the logistic regression analysis (Table 1), we found significant differences between the TBI group and non-TBI group in terms of age of PD diagnosis ($P<0.001$) and disease duration (OR= 1.51; 95% CI, 1.12-2.02; $P=0.005$). However, we did not find any difference between the two group in terms of gender (OR= 0,95; 95% CI, 0.72-1.25; $P=0.725$), and county of residence (OR= 1.28; 95% CI, 0.82-2.01; $P=0.279$).

During the seven years, the average population density in Nebraska was 1,061,928 lives. The age distribution of the general population was opposite of that in the PD subjects. More than half (66.88%) of the population is found between 30 and 59 years of age, 16.19% were between 60 and 69 years old, 9.6% were between 70 and 79 years old, and 7.32% were at the age of 80 or older, and males were 49.8% of the population. Amongst those, 43530 (4.1%) had TBI, and 1018398 (95.9%) did not have TBI during the study period. People with TBI were representing 2.96% of the age-group 30-59 years of age, 3.46% of the age-group 60-69 years of age, 6.19% the age-group of 70-79 years, and 13.18% of the people who 80 years or older.

The overall age-adjusted incidence and the age-specific incidence rate of TBI for the general population, age 30 years and older, and PD population are presented in Table 3. The unadjusted crude incidence rate of TBI for the seven years period was 5,351 per 100,000 PD

patients compared to 374 per 100,000 persons in general population. After adjusting for age of diagnosis, the incidence rate dropped to 4,109 per 100,000 PD patients. However, the incidence rate in the general population rose after age adjustment to 513 per 100,000 persons. That means the incidence rate of TBI among PD patients is eight times higher than that among the general population. Despite the dramatic increase in the TBI incident rate in 2009, the trend of TBI incident rate over the seven years has dropped from 5,100 per 100,000 PD patients in 2008 to 396 per 100,000 PD patients in 2014 as presented in Figure 2. Age-specific incidence rate for <60, 60-69, 70-79, and ≥80 groups were 3,825 per 100,000 PD patients, 2,804 per 100,000 PD patients, 7,019 per 100,000 PD patients, and 5,395 per 100,000 PD patients, respectively.

Multivariate logistic regression model adjusted for gender and county of residence in Table 1 revealed that patient's age of PD diagnosis (*P adjusted*= 0.0008), and disease duration (OR= 0.67; 95% CI, 0.49-0.90 *P adjusted*= 0.0079) were independent risk factors for TBI. Comparison between the four age groups showed that there were significant differences between age group 70-79 and other groups; 70-79 vs. 30-59 (OR= 1.83; 95% CI, 1.03-3.26; *P*= 0.04), 70-79 vs. 60-69 (OR= 2.53; 95% CI, 1.51-4.25; *P*= 0.0004), and 70-79 vs. ≥80 (OR= 1.41; 95% CI, 1.04-1.90; *P*= 0.0267). In addition, there was significant difference between patient in age group ≥80 and patients in age group 60-69 (OR= 1.79; 95% CI, 1.07-3.01; *P*= 0.0259).

Table 4. reveals the most common types and of TBI among PD patients. The most prevalent types of TBI in PD and general population were as follows: unspecified head injury (68.52% vs. 56.43%) followed by concussions in PD subjects with (27.52% vs. 3.21%). Fracture of the skull was the second most common cause of TBI among general population with 5.31% compared to 3.21% in PD patients. Intracranial injury including concussion, contusion, laceration, and hemorrhage were the least common cause of TBI among both PD population and the general

population (0.46% vs. 0.15%). The external causes of TBI are presented in Table 5. Falls were accounted for 88.89% of TBI incidents among PD patients and 49.68% of the episodes in the general population, followed by other accidents, such as struck by and against, accident caused by machinery, and an accident caused by electric current (6.02% vs. 34.16%), motor vehicle accidents (2.78% vs. 15.6%), activity (1.39% vs. 0.26%); and drugs, medicinal and biological substances creating adverse effects in therapeutic use (0.93% vs. 0.3%).

Table 4. Type of traumatic brain injury in Parkinson's disease (PD) patients Nebraska (2008-2014).

Types of Traumatic Brain Injury, n (%)	All TBI in Nebraska n=43,530*	PD patients with TBI, n=216
Concussion	9,116 (3.21%)	60 (27.5%)
Fracture of the skull	2,313 (5.31%)	7 (3.2%)
Intracranial injury including concussion contusion laceration and hemorrhage	67 (0.15%)	1 (0.4%)
Unspecified head injury	24,565 (56.43%)	148 (68.5%)

*Including Nebraska patients ≥30 years old at the time of TBI occurrence, 2008-2014.

Table 5. Causes of traumatic brain injury (TBI) in general population in Parkinson's disease (PD) patients stratified by the age of PD diagnosis in Nebraska (2008-2014).

Causes of Traumatic Brain Injury, n (%)	Total TBI in Nebraska n=43,530*	PD patients with TBI n=216
Falls	41,903 (48.2%)	193 (88.8%)
Motor Vehicle Accidents	13,644 (15.7%)	6 (2.7%)
Other Accidents	19,461 (22.4%)	14 (6.0%)
Drug Adverse Effects	140 (0.1%)	1 (0.9%)
Activity[a]	628 (0.7%)	2 (1.3%)

*Including only patients who are ≥30 years old at the time of TBI occurrence. [a] Daily activities such as cooking, animal care, and work.

Discussion

The study utilized a statewide population-based PD registry data in the United States to investigate the incident rate, types, and external causes of TBI among PD patients. Our study states that only 5.35% of PD patients, diagnosed between 2008 and 2014, had TBI during the study period with an overall age-adjusted incident rate of 4,109 per 100,000 PD patients. The main findings of our study are; 1) Age is an associated risk factor with TBI in PD patients. About 85.18% of TBI episodes occurred in older patients. 2) The likelihood of TBI is 1.5 times higher for patients with disease duration of less than three compared to patients with longer disease duration. 3) Unspecified head injury and concussion are the most common forms of TBI among the study cohort with 68.52% and 27.52%, respectively. 4) Falls accounted for 88.89% of all TBIs in our study subjects.

Consistent with previous study, PD patients have higher TBI incidence rate than the non-PD subjects (Eric Nyam et al., 2018). However, our study shows a higher proportion of TBI incidence among PD population (5.4% vs. 2.6%) than that in a recent study conducted in Taiwan (Eric Nyam et al., 2018). This difference continues even among the general population (4.1% vs. 1.8%). The variance in TBI incidence among the general population between the United States and Taiwan could explain the difference between the two studies. For example, according to the CDC, the incidence rate TBI in the United States is 823.7 per 100,000 (CDC, 2018). While in Taiwan the TBI incidence rate is 344 per 100,000 (Chiu et al., 1997). The first study only estimated the incidence rate TBI-related hospitalization, which might lead to missing mild form of TBI cases that did not require hospitalization (Eric Nyam et al., 2018).

Our results suggest that patients diagnosed with PD at the age of 80 years or older have a lower rate of TBI incidence than those who diagnosed between the age of 70 to 79 years. The first

reason that could explain the decrease in TBI incidence rate among this group is living in nursing home or long-term care facility (LTCF), which is prepared to suit their condition to prevent further complications. A study found that the average age of LTCF residents with PD is 82.3 years compared to 78.7 years in the community-dwelling patients with PD (Safarpour et al., 2015). Another study reported that about 57% of PD patients were 80 years of age or older at the time of admission to the nursing homes and most of them were physically dependent (Buchanan, Wang, Huang, Simpson, & Manyam, 2002). Decline daily physical activity rate or activity avoidance might also explain the reduction in TBI incidence in that group compared to patients diagnosed with between the age 70 and 79 years. Patients with old-age PD onset were found to have greater motor impairment than those with middle-age PD onset (Diederich, Moore, Leurgans, Chmura, & Goetz, 2003).

We found patients with shorter PD duration, less than three years, to have higher TBI incidence rate than longer PD duration patients. This is consistent with previous studies that reported increase rate of TBI (Mactier, Lord, Godfrey, Burn, & Rochester, 2015), head injury (Wang et al., 2014), and falls (Eric Nyam et al., 2018; Lord et al., 2016; Mactier et al., 2015; Voss et al., 2012) among patients with PD duration of less than three years than patient with longer PD duration. The study findings suggest that early intervention for newly diagnosed PD patients in important to reduce the incidence of TBI.

The frequency of unspecified head injury and concussion were found to be the most common types of TBI among PD patients and the general population. However, the analysis shows that PD patients have higher frequencies of unspecified head injury and concussion than the general population (68.52% vs. 56.43%) and (27.52% vs. 3.21%), respectively. This is expected since most of the TBI episodes were caused by falls.

We found that falls are accounted for the majority of the TBI cases among PD population and the general population. Our analysis of the frequency of falls among PD patients seems to exceed the frequency of falls among the general population, which is similar to what we found in the literature. However, our results revealed higher frequency of falls among PD subject 88.89% than that reported in pervious retrospective studies (38%-81%) (Ashburn, Stack, Pickering, & Ward, 2001; Hely, Morris, Reid, & Trafficante, 2005; Koller, Glatt, Vetere-Overfield, & Hassanein, 1989; Paulson, Schafer, & Hallum, 1986) and up to 70% in prospective studies (Bloem et al., 2001; Rudzińska, Bukowczan, Stożek, Zajdel, Mirek, Chwała, et al., 2013; Wood et al., 2002). The difference in frequencies of falls between our study and previous published one is because the nature of the study. Our study aimed to measure the frequency of falls among PD patients who had TBI, while the other studies estimate the number of falls all included PD subjects. Even in a similar study conducted in Taiwan, they reported that fall was accounted for 50% of the TBI cases (Eric Nyam et al., 2018). The nature of TBI incidence between the two countries might explain the difference in the frequency of fall between the two studies. As mentioned earlier, the United States has higher TBI incidence than Taiwan.

Studies found postural instability and gait difficulties (Hiorth et al., 2017; Matinolli, Korpelainen, Sotaniemi, Myllylä, & Korpelainen, 2011; Rudzińska, Bukowczan, Stożek, Zajdel, Mirek, Chwata, et al., 2013; Wood et al., 2002), freezing (Rudzińska, Bukowczan, Stożek, Zajdel, Mirek, Chwata, et al., 2013), were the most common causes of fall among PD patients. Meanwhile about 89% of TBI cases in PD patients are due to falls, helping PD patients overcome these causes would reduce the risk of fall among those people which eventually decrease the TBI incidence among them. General exercises program, strength training, and Tai Chi training may improve motor function in PD patients (Carvalho et al., 2015; Dashtipour et al., 2015; Li et al., 2012). In

patients with advanced PD, using assistive mobility devices like four-wheeled walkers might help with gait difficulties (Kegelmeyer, Parthasarathy, Kostyk, White, & Kloos, 2013).

To our knowledge this is the first study to investigate the incidence, types, and external causes of TBI among PD patients using a population-based data in the United States. A strength of this study is that we were able to catch all PD patients in Nebraska. However, our study has several limitations that should be considered. First, HDD has lots of missing information that may result in losing a number of cases during the linkage process. Second, a limited number of variables in the database prevent us from accounting for covariates like race/ethnicity, and confounders like BMI, and diseases for example Alzheimer. Also, addressing the effect of marital status, having family support and living accommodation cannot be assessed due to the lack of information. Finally, the registry does not collect information on PD severity, because of that we could not evaluate the relationship between PD severity and TBI. Further prospective studies are needed to determine other risk factors for TBI in PD patients. The results of this study prompt analysis of these issues followed by intervention actions.

Conclusion

PD patients experienced more TBI events than the general population. After adjusting for age, gender, disease duration, and location of residence, age and disease duration were significantly associated risk factors with TBI among PD population. The analysis also revealed that unspecified head injury and concussion were the most common types of TBI in both PD and general population; however, PD patients had a higher incidence. Further analysis showed that fall was accounted for the majority of TBI episodes among PD and general population. Nonetheless, PD patients suffered from a higher rate of fall compared to general population.

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Service Learning/Capstone Experience Reflection

I did my service learning activities at the Division of Public Health in the NE DHHS, Lincoln, NE, from November 28th, 2017 to February 26th, 2018. The DHHS, Nebraska's largest agency, was established in 1997. The Division of Public Health was founded by governor Mike Johanns in 2000. The Division of Public Health is one of six divisions within the DHHS (NE DHHS, 2016). The Division of Public Health has two main sections Health Licensure and Health Data, and Community and Environmental Health (NE DHHS, 2017). The Health Licensure and Health Data is in charge of epidemiology and informatics, licensure, investigations, public health preparedness and emergency response, and vital records. Community and Environmental Health is responsible for community and rural health planning, environmental health, health promotion, and lifespan health services (NE DHHS, 2017).

Working at the NE DHHS has given me the opportunity to learn how to apply the theoretical knowledge I have acquired from the College of Public Health to the real world. During the time I spent at the NE DHHS I was able to work and help the division on four public health-related topics. First, I helped the division to complete a survey on laboratory's testing for HIV, STD, hepatitis C, antibiotic susceptibility and Clostridium difficile (C. diff). The survey was part of funding requirements from the CDC to monitor changes in laboratory practice in the state. I was one of a three member-team who was tasked to contact the laboratories located in Nebraska and fill out the survey. The questioner was divided into five sections. The first one was asking about the lab name, the name of the person completed the survey, and contact information, email and phone number, in case of the need for more information. The sections from second to five were looking for information about HIV, STD, Heb. C., antibiotic susceptibility and C. diff. tests. The questions in these sections were about whether the lab does any of these tests on-site or refer it to

another lab and if so, what is the name of that lab. What technique do they use to perform these tests? What method do they use to confirm their results?

The second activity was entering immunization data into the Nebraska State Immunization Information System (NESIIS) program. NESIIS aims to generate standardized immunization records for each patient to help providers track their patient immunization status as well as to reduce the risk of administering duplicate immunizations. Second, identify the needed vaccination for each patient and remind clients when it is the time for the next shoot or boost to reduce the risk of the missing vaccine. Third, helping providers to track their inventory and notify them when a vaccine is about to expire or run out. In this task, I worked on data entry. These data were taken from immunization records of NE residents that NE DHHS received from immunization providers located in Nebraska. From this activity, I learned how NESIIS works and the benefit of such system.

The third activity was finalizing the mailing list for NESIIS survey. The list included providers not sharing the immunization information of their clients with NE DHHS. This list was used later to mail the survey to the included providers. The goal of the survey was to measure the interest rate of sharing the immunization information among the providers with the NE DHHS through NESIIS. Additionally, the survey aims to identify the barriers that prevent the providers from sharing the immunization information with the NE DHHS in order find solutions to ease these barriers.

I finalized the mailing list after ruling out all providers who are already sharing their immunization records with NE DHHS. Creating the final mailing list was completed in three steps. Initially, I created a list that contains the providers who did not share their immunization information with the NE DHHS from the one I got from my supervisor on the survey project, Michelle Hood, and

compare it with the list on the NE DHHS website that contains providers who are already sharing their records with the NE DHHS. Then I sent my list to the other two persons who are responsible of maintaining the list of providers who are sharing the immunization records with the NE DHHS, so they can rule out any provider who shares immunization information with the NE DHHS but not listed in the website list. Finally, after I received the file back from them, I cleaned the list and removed the duplicates and send to my supervisor.

Fourth, mailing address labels and preparing a cover letter that we sent along with a brochure about the NESIIS. The letter and brochure give an overview of NESIIS functionality and benefits to both clients and providers. We included in the letter has a link that will give the providers access to complete the survey. The letter was drafted from an existing letter that I got from my supervisor, and I made some changes on it to fit the purpose of our survey. After I made the changes, a copy of the letter was sent to my supervisor for the approval and signature. Finally, once the I got approval on the cover letter I printed the address labels and 203 cover letters. Then I prepared 203 envelops, each one has a cover letter and brochure inside it, and on the outside, there were the address label and the billing code.

For the capstone part, the activities included on data cleaning, and analysis, meeting with my committee members, writing my final paper and preparing my oral presentation. The process involved performing a quality check of the data I will use, using SAS software, meeting with my committee members to revise the final paper. During the quality check, I had several meetings with Dr. Ming, from those meeting I learned how to do quality check for the data to detect if the dataset truly represents the target population. After receiving the datasets, I had serval meetings with Dr. LeVan and Dr. Smith to revise the results and discussion sections. The capstone experience gave an opportunity to expand my knowledge about data cleaning and scientific writing. This experience

taught me how to apply the knowledge I got from the public health school to the scientific research, starting from finding a public health problem then developing the research question to building a study design and specifying the aims, inclusion and exclusion criteria, the statistical methods that will be used to answer the research question. Also, through the capstone experience I got exposed to the IRB application process.

The most significant challenge in this project was obtaining the correct dataset. The first problem started when I realized discrepancies in the TBI, that I showed to my preceptor to find after that the person responsible of the trauma registry had sent a wrong file to be linked with the PD data. The second problem raised when got a very small sample size after cleaning the data to find out that the linkage was performed using so many factors to match between the cases that resulted in losing a huge number of the cases. The third problem appeared during the analysis to figure out that the data I received do have the external causes of the TBI because when the file was sent without the external causes to be linked with the PD data. I overcome those problem by involving my preceptor and having several meetings with him and the people responsible of preparing the data for me, and later my preceptor changed the person who oversees the linkage process. Finally, I got the correct data files, that cost me three months of my capstone time and I was able to start the analysis. This problem showed the importance of the quality check of the data which is essential to do before starting the data analysis to ensure the quality of the results section.

Acknowledgement

I would like to thank Dr. Ming Qu, Michelle Hood, Jill Krause, Andrew, Fei, and Peibei Sun of the NE DHHS for helping me through my project by providing the data, explain to me the linkage process, and answering all my questions regarding the data.

I am very grateful for Dr. Tricia LeVan for her work and guidance from which I learned so many things. I also would like to thank Dr. Lynette Smith for helping me with the statistical part of the project.

Finally, I would like to thank my family for their support, especially my wife for her endless support.

Appendix

Table 6. Types of traumatic brain injury (TBI) in Parkinson's disease (PD) stratified by age of PD diagnosis in Nebraska (2008-2014)

Types of Traumatic Brain Injury, n (%)	PD patients with TBI (Age of Diagnosis)				
	30-59 n=14	60-69 n=18	70-79 n=89	≥80 n=95	P value*
Concussion	4 (28.5)	6 (33.3)	22 (24.7)	28 (29.4)	0.908
Unspecified head injury	10 (71.43)	12 (66.67)	61 (68.5)	65 (68.4)	

*****Fisher's exact test.

Table 7. Causes of traumatic brain injury (TBI) in Parkinson's disease (PD) patients stratified by the age of PD diagnosis in Nebraska (2008-2014).

Causes of Traumatic Brain Injury, n (%)	PD patients with TBI (Age of Diagnosis)				
	30-59 n=14	60-69 n=18	70-79 n=89	≥80 n=95	P value*
Falls	11 (78.5)	15 (83.3)	79 (88.8)	88 (92.6)	0.219
Other Accidents	3 (21.3)	3 (16.6)	10 (11.2)	7 (7.4)	

*****Fisher exact test.

Figure 2. Age-specific incidence rate of traumatic brain injury (TBI) in Parkinson's disease (PD) population by age of PD diagnosis in Nebraska (2008-2014).

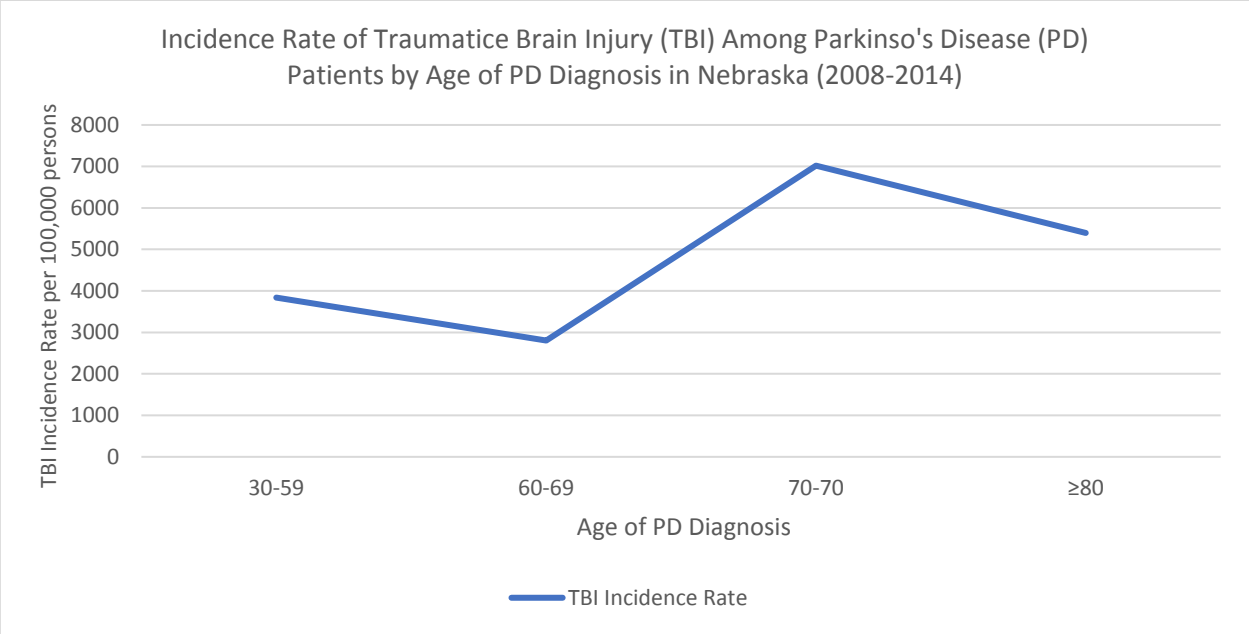

Figure 3. Age-specific incidence rate of traumatic brain injury (TBI) among Nebraska (NE) population (≥30 years) by age of TBI Occurrence (2008-2014).

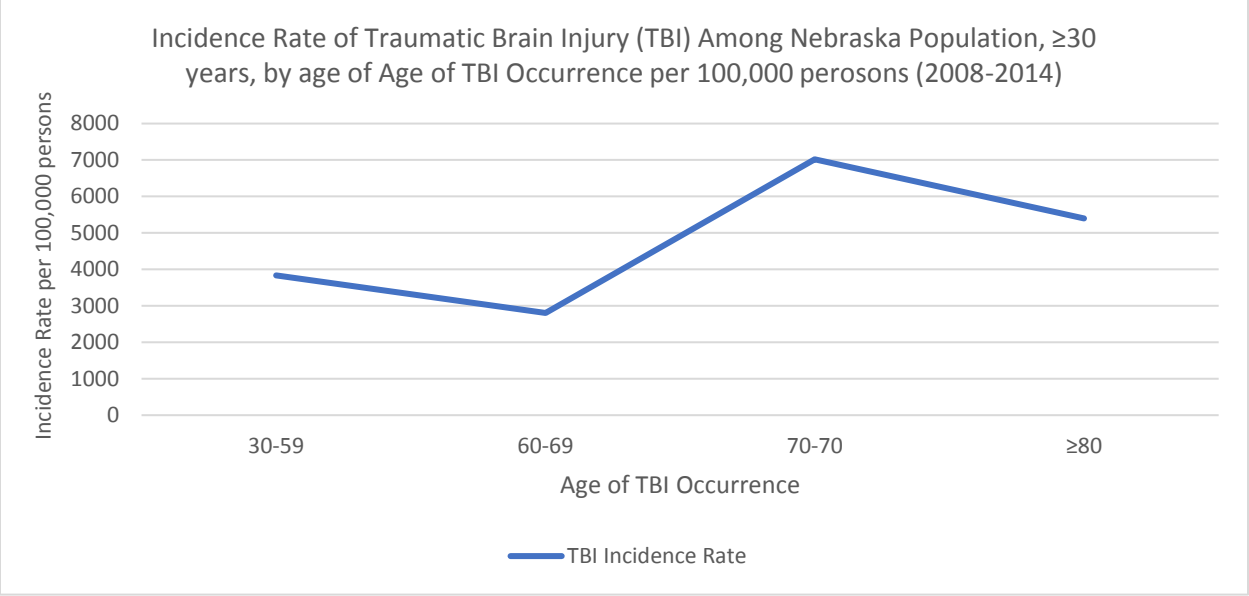

Figure 4. Incidence rate of traumatic brain injury among Parkinson's disease (PD) patients by year of PD diagnosis (2008-2014)

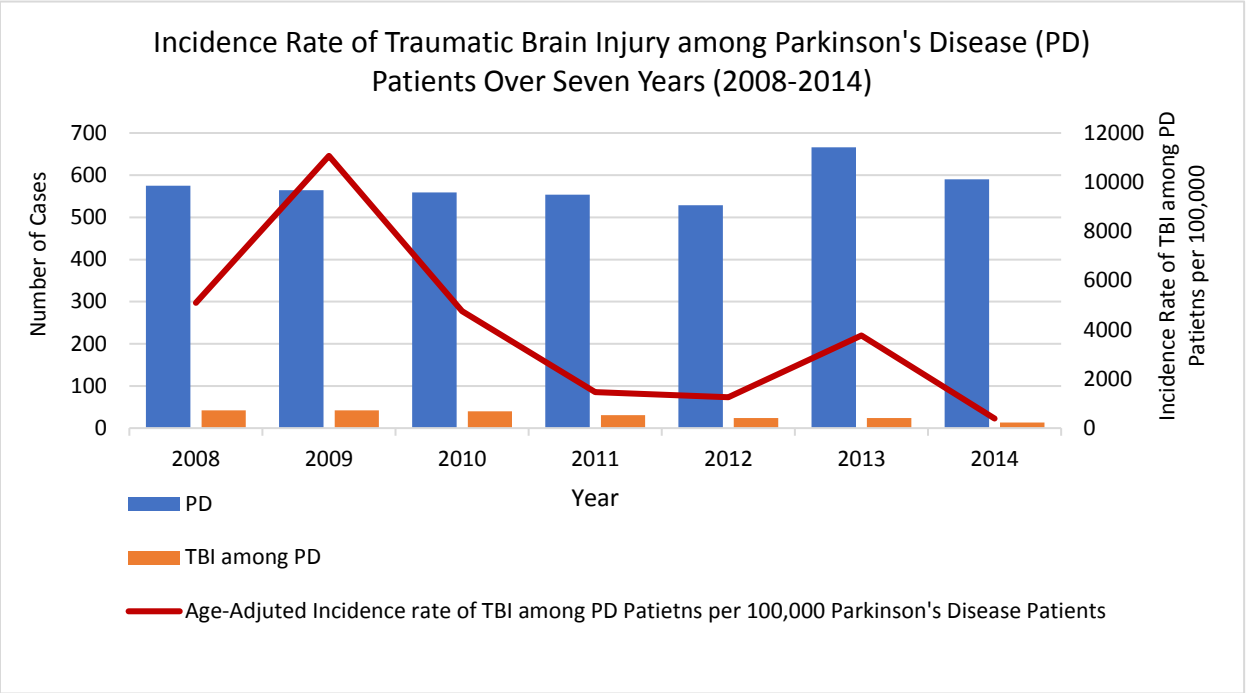

Figure 5. Prevalence and Number of Parkinson's disease in Nebraska by year of diagnosis (2008-2014)

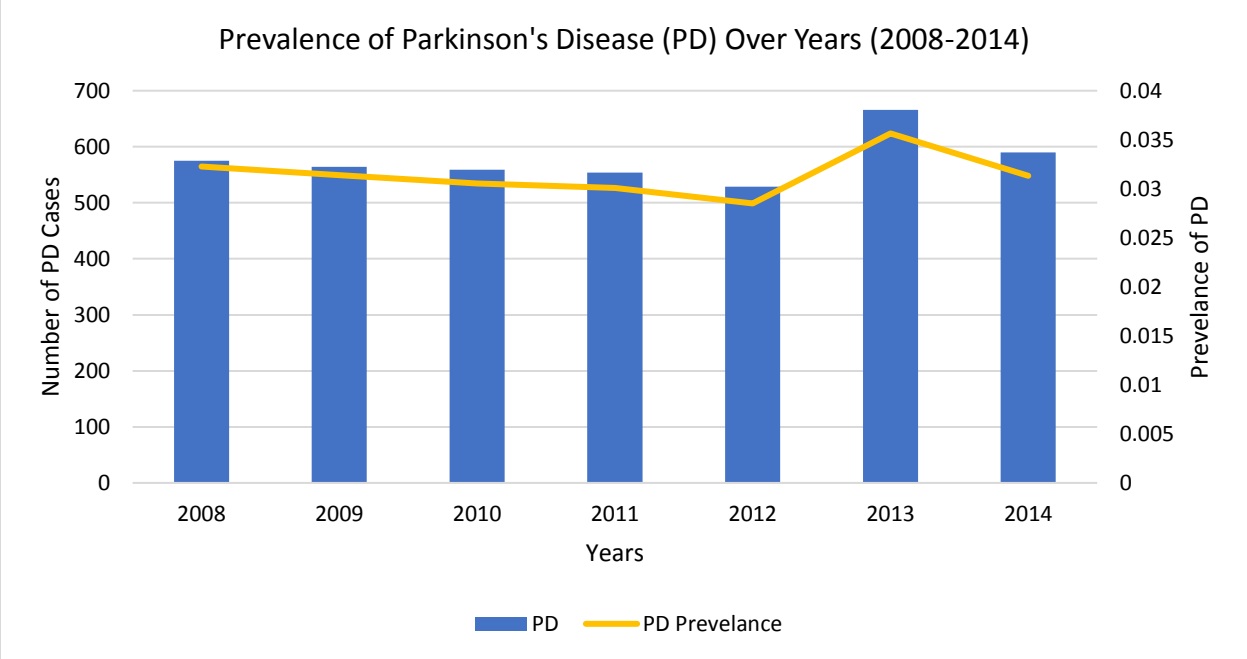

Figure 5. Parkinson's disease (PD) distribution by age group and year (2008-2014)

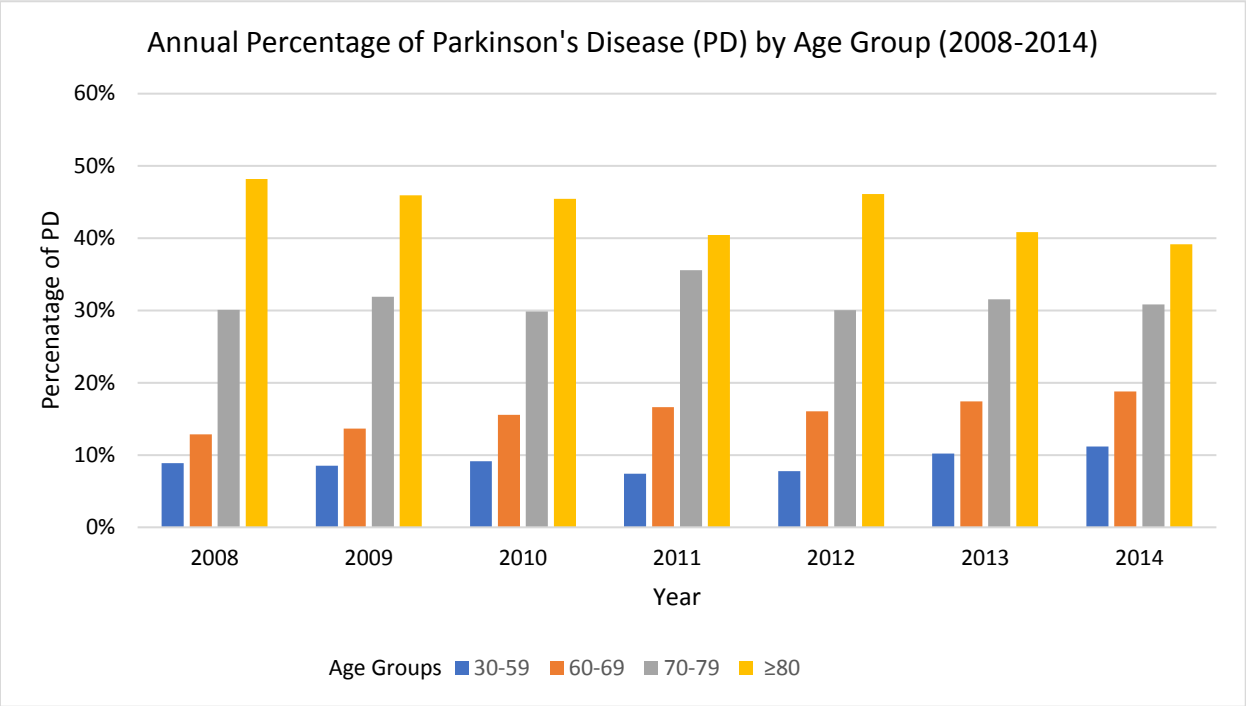

Figure 6. Distribution of traumatic brain injury (TBI) in Nebraska population (≥30 years) by year (2008-2014)

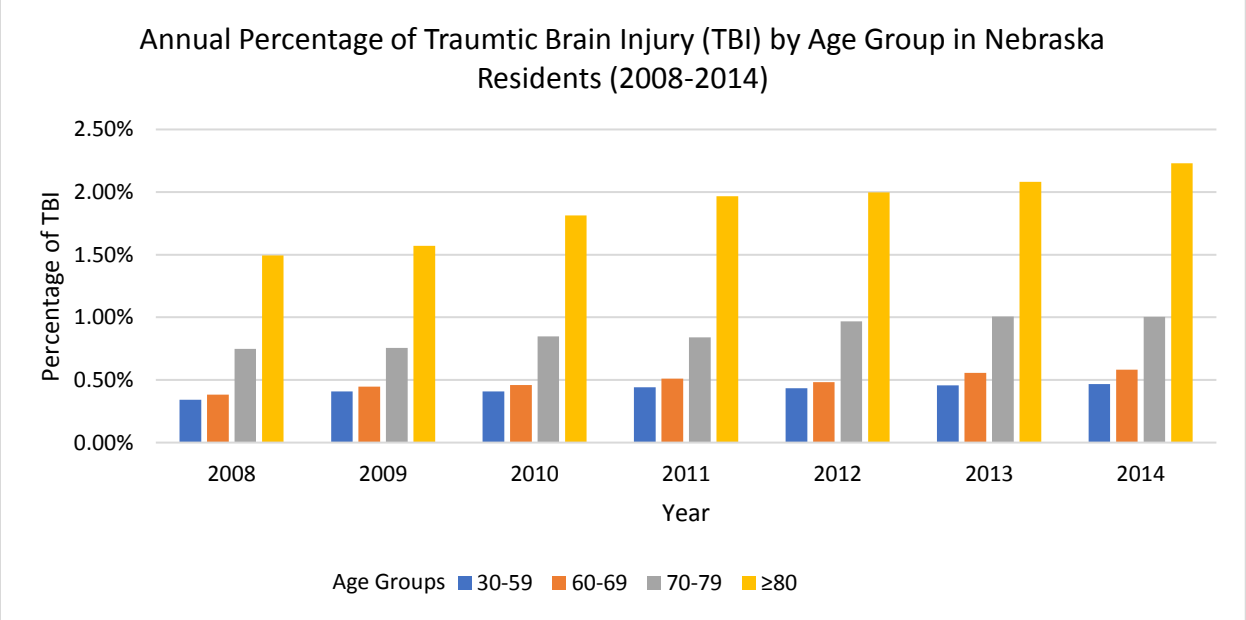

Figure 7. Distribution of traumatic brain injury (TBI) in Nebraska population (≥30 years) by year (2008-2014)