HHS Public Access

Author manuscript

Bone. Author manuscript; available in PMC 2021 April 24.

Published in final edited form as:

Bone. 2019 December ; 129: 115060. doi:10.1016/j.bone.2019.115060.

The effect of low-trauma fracture on one-year mortality rate among privately insured adults with and without neurodevelopmental disabilities

Daniel G. Whitney, PhD[a,b], **Daniel Whibley, PhD**[a,c], **Karl J. Jepsen, PhD**[d]

[a]Department of Physical Medicine and Rehabilitation, University of Michigan, 325 E. Eisenhower, Ann Arbor, MI 48108

[b]Institute for Healthcare Policy and Innovation, University of Michigan, 2800 Plymouth Rd., Ann Arbor, MI 48109

[c]Epidemiology Group, School of Medicine, Medical Sciences and Nutrition, University of Aberdeen, Foresterhill, Aberdeen AB25 2ZD, Scotland, UK

[d]Department of Orthopaedic Surgery, University of Michigan, 1540 E Hospital Dr., Ann Arbor, MI 48109

Abstract

Background: Individuals with neurodevelopmental disabilities (NDDs) have poor development and preservation of skeletal health throughout the lifespan, and are especially vulnerable to low-trauma fracture and post-fracture health complications. However, no studies have examined if adults with NDDs have greater post-fracture mortality risk compared to adults without NDDs. The purpose of this study was to determine whether adults with NDDs have greater 12-month mortality rates following a low-trauma fracture compared to adults without NDDs.

Methods: Data from 2011 to 2017 was leveraged from Optum Clinformatics® Data Mart; a nationwide claims database from a single private payer in the U.S. Data were extracted from adults (18+ years) with and without NDDs that sustained a low-trauma fracture between 01/01/2012-12/31/2016, as well as pre-fracture chronic diseases (i.e., cardiovascular diseases, cerebrovascular diseases, diabetes, chronic obstructive pulmonary diseases, cancer). Mortality rate was estimated for adults with and without NDDs, and the mortality rate ratio (RR) and 95% confidence interval (CI) was calculated. Cox regression was used to estimate hazard ratio (HR) and 95% CI for 1-, 3-, 6-, and 12-month post-fracture mortality rates between adults with and without NDDs after adjusting for age, sex, race, U.S. region, and pre-fracture chronic diseases.

Results: Mean age (SD) at baseline was 56.7 (20.6) for adults with NDDs (n=3749; 45.2% men) and 63.9 (19.2) for adults without NDDs (n=585910; 34.4% men). During the 12-month follow-up period, 182 adults with NDDs (mean age [SD]=69.8 [14.7]; 46.2% men) and 25456 adults without NDDs (mean age [SD]=78.9 [9.8]; 38.3% men) died. Crude mortality rate was not different

Address of Correspondence: Daniel G. Whitney, PhD, Department of Physical Medicine and Rehabilitation, University of Michigan, 325 E. Eisenhower, Ann Arbor, MI, Phone: 734-647-2967 Fax: 734-615-1770 dgwhit@umich.edu.

Declarations of interest: none.

between adults with and without NDDs for any time points (e.g., 12-months: 5.40 vs. 4.96 per 100 person years; RR=1.09; 95% CI=0.94–1.26); however, it was greater for adults with intellectual disabilities compared to adults without NDDs (RR=1.46; 95% CI=1.23–1.79). After adjustments, adults with NDDs had greater post-fracture mortality rates for 3-, 6-, and 12-month time points (e.g., 12-months: HR=1.46; 95% CI=1.27–1.69). When stratified by the type of NDD, adults with intellectual disabilities and adults with autism spectrum disorders, but not adults with cerebral palsy, had greater 12-month post-fracture mortality risk. When stratified by fracture location, lower extremities were associated with greater crude mortality rate (RR=1.69; 95% CI=1.22–2.35) and adjusted mortality risk (HR=2.41; 95% CI=1.73–3.35), while upper extremities were associated with greater adjusted mortality risk (HR=1.76; 95% CI=1.23–2.50) for adults with vs. without NDDs.

Conclusions: Among privately insured adults with NDDs, low-trauma fracture is associated with greater mortality risk within 1 year of the fracture event, even after adjusting for pre-fracture chronic diseases. Study findings suggest the need for earlier fracture prevention strategies and improved post-fracture healthcare management.

Keywords

neurodevelopmental disabilities; low-trauma fracture; mortality

Introduction

Fractures represent a major public health issue in terms of disease [1] and medical cost [2] burdens. Among older adults, fracture is a primary cause of functional disability [3], morbidity [4], poor quality of life [5], and premature mortality [3, 6, 7]. Pre-fracture health status is a strong predictor of post-fracture health, functional, and survival outcomes [3]. As such, fracture risk and its related sequela (e.g., chronic diseases, premature mortality) may disproportionately impact adults with neurodevelopmental disabilities (NDDs), due to barriers for these individuals in acquiring adequate skeletal and overall health throughout the lifespan. However, the burden of low-trauma fracture, an indicator of skeletal fragility, for adults with NDDs is largely unknown.

Three common NDDs include intellectual disabilities, cerebral palsy, and autism spectrum disorders, which can be comorbid with one another. While the etiology of these conditions vary, what links all individuals with NDDs is the potential for having complex and unmet healthcare needs due to factors that are inherent (e.g., genetic predisposition) and secondary (e.g., communication impairments) to the disability, as well as lack of clinical knowledge of their aging process [8–11]. Collectively, these factors increase risk for developing health complications throughout the lifespan. Throughout growth, children with NDDs exhibit low fitness levels [12, 13], excess body fat [14–17], poor psychosocial development [18–21], and an underdeveloped musculoskeletal system [14, 22–24]. As children with NDDs age into and throughout their adult years, there is potential for a further decline of function and mobility [25] with subsequent loss in regular weight-bearing activities. As such, the pediatric to adult transition is accompanied by a concerning prevalence of musculoskeletal diseases leading to a substantially increased risk for skeletal fragility and fracture [26–29].

Furthermore, adults with NDDs are at risk for early mortality compared to adults without NDDs. Population-based studies have shown that adults with intellectual disabilities [30], cerebral palsy [31], and autism spectrum disorders [32] die approximately 15–30 years premature (i.e., earlier compared to adults without NDDs). This premature mortality is likely governed, at least in part, by early development of chronic diseases across several biological systems for these NDD populations [30, 31], including an elevated prevalence of cardiometabolic diseases [26, 33], mental health disorders [33, 34], and kidney and liver diseases [35] compared to adults without NDDs.

Despite the increased risk for skeletal fragility throughout the lifespan and the overall poor health status in adulthood, no studies have examined how skeletal fragility contributes to health and survival outcomes for adults with NDDs. A better understanding of the potential link between skeletal fragility with poor health and premature mortality among these vulnerable populations is needed. If skeletal fragility increases risk for premature mortality for adults with NDDs as compared to adults without NDDs, clinicians should be alerted to the heightened need for strategies to prevent skeletal fragility and intensively manage low-trauma fractures when they do occur in their patients with NDDs as compared to their patients without NDDs, with the ultimate aim of improving healthful aging throughout the lifespan. Accordingly, the primary objective of this study was to compare the 1-, 3-, 6-, and 12-month mortality rates following a low-trauma fracture, and by location of low-trauma fracture, between adults with vs. without NDDs. We hypothesized that adults with NDDs would have greater post-fracture mortality rates compared to adults without NDDs, even after adjusting for pre-fracture chronic diseases.

Methods

Data source

Data from 2011 to 2017 were extracted from the Clinformatics® Data Mart Database (OptumInsightTM, Eden Prairie, MN, USA), which is a U.S. nationwide de-identified single private payer administrative claims database. The claims data includes all health service utilization (e.g., inpatient, outpatient) for each beneficiary throughout enrollment. Date of death is also recorded. To preserve patient identity, researchers leveraging this database are allowed either the Date of Death or Socioeconomic Status table. This study leveraged the Date of Death table and therefore some information regarding socioeconomic status (i.e., income, education) were not available. Since data are de-identified, the university Institutional Review Board approved this study as non-regulated.

Sample selection

All medical conditions (e.g., NDDs, fracture) were identified using the International Classification of Diseases, Ninth and Tenth Revision (ICD-9 and ICD-10), Clinical Modification codes to account for the shift in reporting codes on October 1st, 2015. We identified adults ≥18 years of age that had at least one claim for a low-trauma fracture between 2012 to 2016 of the vertebral column, hip (including proximal femur), non-proximal femur, tibia/fibula, humerus, ulna/radius, or unspecified location. We defined low-trauma fracture as the first fracture in at least 12 months from the participant's index date of

health plan enrollment without trauma codes (e.g., motor vehicle accident) 7 days before to 7 days after the index date of fracture, as guided by previous studies [36, 37]. We included individuals that had at least 12 full months of continuous enrollment in a health plan prior to their index date of low-trauma fracture to sequester baseline chronic disease data. The single claim-based definition has shown excellent accuracy (up to 98% positive predictive value) for fractures, which was similar or better than other algorithms (e.g., 2+ claims) [38].

Individuals with NDDs were identified by at least one claim for intellectual disabilities, cerebral palsy, or autism spectrum disorders. The comparison group included individuals with no claims for any of these NDDs. This single claim-based definition has shown good accuracy for identifying individuals with pediatric-onset conditions using administrative claims data with 99% sensitivity and a positive predictive value of 79% [39].

Outcome measure

Mortality rate for 1-, 3-, 6-, and 12-months post-fracture was determined as the number of days from the index date of low-trauma fracture to date of death. The Date of Death table from Optum is kept up-to-date and is sourced by the Death Master File which is maintained by the Social Security Office.

Covariates

Covariates were selected based on their relevance to adults with NDDs, fracture, mortality, and availability in the administrative claims database [26, 40, 41]. Sociodemographic variables included age, sex, race, and U.S. region of residence (West, Midwest, South, and Northeast). Data regarding severity of cerebral palsy or autism spectrum disorders using common clinical measures (e.g., gross motor function classification system for cerebral palsy) are not available in administrative claims, and >70% of the cerebral palsy cohort had “other” or “unspecified” cerebral palsy [35]. Since analyses were unable to stratify or statistically account for clinical subtypes of cerebral palsy (e.g., spasticity/athetoid, hemiplegic) or autism spectrum disorders, intellectual disabilities were not stratified by severity (e.g., mild, severe) for consistency.

Baseline chronic disease comorbidities were identified by at least two claims on separate days, and the date of the first claim had to be within 12 months prior to the index date of low-trauma fracture. Using the algorithm of at least 2 claims on separate days was selected to omit “rule out” scenarios for these chronic diseases, which has been shown to improve accuracy in identifying non-event chronic diseases, such as diabetes and cardiovascular diseases [42, 43]. Chronic disease comorbidities were grouped as cardiovascular diseases, diabetes, chronic obstructive pulmonary diseases, and cancer. Cardiovascular disease comorbidities included: (1) ischemic heart diseases (i.e., angina pectoris, acute or old myocardial infarction, other acute ischemic heart diseases [e.g., coronary thrombosis], and chronic ischemic heart diseases [e.g., atherosclerosis of coronary arteries, aneurysm]); (2) heart failure; (3) cerebrovascular diseases (i.e., intracranial hemorrhage, cerebral infarction, occlusion and stenosis of precerebral and cerebral arteries, and other cerebrovascular diseases); and (4) hypertension. Diabetes included type 1 or type 2. Chronic obstructive pulmonary diseases included: (1) chronic bronchitis; (2) emphysema; and (3) other chronic

obstructive pulmonary diseases. Cancer anywhere in the body included malignant, secondary, in situ, and benign neoplasms, as well as neoplasms of unspecific behavior.

Statistical analysis

Baseline descriptive characteristics for the entire sample and for the sample that died during the 12-month follow up were summarized. Group differences between adults with vs. without NDDs were examined using independent t-tests for continuous variables or Chi-square tests for categorical variables.

Crude mortality rates (and 95% confidence intervals [CI]) for 1-, 3-, 6-, and 12-month time points were estimated for adults with and without NDDs, and by NDD subgroups, as the number of mortality cases divided by the amount of person-years, and expressed per 100 person-years. Mortality rate ratios (RR and 95% CI) were calculated as the mortality rate for the groups with NDDs divided by the mortality rate for the group without NDDs. The NDD subgroups included adults with intellectual disabilities (ID only), cerebral palsy (CP only), autism spectrum disorders (ASD only), and comorbid NDDs, including ID+CP, ID+ASD, CP+ASD, and all three NDDs.

Cox proportional hazards regression models were developed to estimate hazard ratios (HR and 95% CI) for 1-, 3-, 6-, and 12-month post-fracture mortality rates, comparing each exposure groups (e.g., entire sample with NDDs; NDD subgroups) with the reference group without NDDs, adjusting for covariates. Model 1 adjusted for age, sex, race, and US region; and Model 2 adjusted for the variables in Model 1 and chronic disease comorbidities. Analyses were performed when the number of mortality cases in the NDD group and subgroups were 5–9 per number of covariates, as this range provides coverage and bias within acceptable levels, which is similar to the more established rule of thumb of 10 or more events per number of covariates for Cox models [44]. Individuals were right censored if they discontinued enrollment within the follow-up periods following the index date of low-trauma fracture or if they were alive at the end of the follow-up periods. Possible interactions between exposure status (NDD vs. no NDD) and sex were assessed by conducting separate analyses for sex strata (to estimate NDD effects) and by including product terms in the Cox models (to test for interactions).

Subsequent Cox proportional hazards regression models compared the 12-month post-fracture mortality rate between adults with and without NDDs stratified by location of low-trauma fracture (vertebral column, hip, lower extremities, upper extremities), adjusting for the variables in model 1 and 2 where appropriate.

$P \leq 0.05$ (two-tailed) was used to determine statistical significance. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Baseline descriptive characteristics of adults with (n=3,749) and without (n=585,910) NDDs that sustained a low-trauma fracture are presented in Table 1. Compared to adults without NDDs, adults with NDDs were on average 7.2 years younger at baseline and had a higher

proportion of men, Black race, and residency in the Northeast region of the U.S. Adults with NDDs had higher unadjusted prevalence of heart failure, cerebrovascular diseases, diabetes, and chronic obstructive pulmonary disease, but lower prevalence of cancer, compared to adults without NDDs. Over the 12-month study period, 182 adults with NDDs died (4.9% of sample) and 25,456 adults without NDDs died (4.3%). Among those that died (Table 2), adults with NDDs were on average 9.1 years younger than adults without NDDs.

Post-fracture mortality rate

Post-fracture crude mortality rate and RR between adults with and without NDDs, and by NDD subgroups, is presented in Table 3. For adults without NDDs, the crude mortality rate for 1-, 3-, 6-, and 12-months was 13.60, 9.02, 6.61, and 4.96, respectively. For adults with NDDs, it was 12.46 (RR=0.92; 95% CI=0.67), 8.48 (RR=0.94; 95% CI=0.75–1.18), 7.16 (RR=1.08; 95% CI=0.91–1.29), and 5.40 (RR=1.09; 95% CI=0.94–1.26), respectively. When examined by the NDD subgroups, adults with ID only had greater crude mortality rate for 6-months (RR=1.46; 95% CI=1.17–1.83) and 12-months (RR=1.49; 95% CI=1.23–1.79). The crude mortality rate was similar for adults with CP and ASD only compared to adults without NDDs where analyses were able to be performed.

Adjusted post-fracture mortality risk for any fracture

Adjusted post-fracture mortality risk between adults with and without NDDs, and by NDD subgroups, is presented in Table 4. For the entire sample of adults with NDDs, post-fracture mortality risk was significantly greater for 3-, 6-, and 12-months after adjusting for the variables in model 1 and model 2. For adults with ID only, post-fracture mortality risk was significantly greater for 1-month after adjusting for the variables in model 1 (insufficient mortality cases for model 2 adjustment), and 3-, 6-, and 12-months after adjusting for the variables in model 1 and model 2. For adults with ASD only, there were insufficient mortality cases to compare model 1 adjusted mortality rates at 1-, 3-, and 6-months, and model 2 adjusted 12-month mortality rate. Post-fracture mortality risk was significantly greater for 12-months after adjusting for the variables in model 1. Post-fracture mortality risk was similar for adults with CP only compared to adults without NDDs where analyses were able to be performed.

Post-fracture mortality rate and risk by fracture location

Twelve-month post-fracture mortality rate, RR, and risk between adults with and without NDDs, stratified by fracture location, is presented in Table 5. Low-trauma fracture of the lower extremities, but not vertebral column or hip, was associated with greater mortality RR and risk among adults with NDDs compared to adults without NDDs. Low-trauma fracture of the upper extremities was associated with greater mortality risk among adults with NDDs compared to adults without NDDs. Further, there was a significant group by sex interaction for upper extremities (P=0.027). When stratified by sex and adjusted for age (due to small sample size), men with NDDs (HR=2.71; 95% CI=1.72–4.27), but not women with NDDs (HR= 1.22; 95% CI=0.69–2.14), with an upper extremity fracture had greater 12-month mortality risk compared to adults without NDDs.

Discussion

Despite the younger age of death by nearly a decade, adults with NDDs had greater mortality risk within 12-months following a low-trauma fracture compared to adults without NDDs. Of the fracture locations, the lower extremities were associated with greater unadjusted and adjusted mortality risk, while the upper extremities were associated with greater adjusted mortality risk among adults with vs. without NDDs. In line with previous work [27–29], study findings corroborate the need for earlier strategies to detect and delay skeletal fragility for adults with NDDs. Previous studies in non-NDD populations have shown that screening for fracture risk [45], modest improvements in detecting skeletal fragility [46], and exercise and pharmaceutical intervention [1, 45, 47] have the potential to prevent fractures and reduce post-fracture burdens. Whether such strategies could be immediately implemented to reduce the burden of fracture for adults with NDDs, or if population- or patient-specific modifications are needed, requires further investigation.

Findings from the current study found no difference in crude post-fracture mortality rate between adults with and without NDDs. However, as individuals with NDDs have compromised health at younger ages and are more likely to be male, age and sex adjustment is needed to better understand post-fracture mortality risk beyond group differences in these characteristics. After statistically accounting for age, sex, and other demographic variables using Cox regression, the HR for post-fracture mortality was greater for adults with vs. without NDDs for the 3-, 6-, and 12-month time points. The greater mortality risk for these time points remained elevated after further adjustment for pre-fracture chronic diseases.

When analyses were stratified by fracture location, results suggest site-specific effects on mortality risk for adults with NDDs. Specifically, lower extremity fractures were associated with 69% greater unadjusted mortality rate and 141% greater adjusted mortality risk for adults with vs. without NDDs. Upper extremity fractures were associated with 39% greater unadjusted mortality rate, but this was not statistically significant (95% CI=0.97–1.98). However, after adjusting for age, sex, and other demographic variables, adults with NDDs had 76% greater mortality risk following an upper extremity fracture. Moreover, there was a group by sex interaction for the upper extremities, with the difference in mortality risk present among men, but not women, with vs. without NDDs. This study did not find evidence of difference in mortality rate or risk between adults with and without NDDs based on low-trauma fracture of the vertebral column or hip. The differential association of site-specific fracture location with post-fracture complications and may be due to many factors. Individuals with NDDs exhibit inadequate development of bone and altered biomechanical loading patterns (e.g., due to physical disabilities) throughout growth, and adults with NDDs have poor skeletal preservation. The chronic burden of skeletal fragility throughout the lifespan may lead to site-specific vulnerability to fractures unique to these populations (e.g., distal femur fractures most common for cerebral palsy [48]), which may in turn impact health and survival outcomes. Better understanding site-specific effects of fracture on health outcomes requires further research, as this may lead to more targeted interventions to mitigate fracture and its disease sequela for adults with NDDs.

When analyses were stratified by the NDD subgroups, adults with ID only had greater crude post-fracture mortality rate compared to adults without NDDs at the 6- and 12-month time points. However, after statistically accounting for age, sex, and other demographic variables using Cox regression where analyses were able to be performed, the HR for post-fracture mortality was greater for adults with ID only and ASD only, but not CP only, compared to adults without NDDs. Although, stratifying by NDD subgroups resulted in a small number of mortality cases for some groups, possibly leading to unreliable point estimates and CI. Therefore, interpretations for the NDD subgroups should be done so with caution.

The finding of similar mortality risk between adults with CP only and adults without NDDs raises an important issue, in that the post-fracture mortality rates in this study may be underestimating the extent of the problem for these adult NDD populations. Study findings were derived from a nationwide private insurance database, which represents a healthier segment of the NDD populations [29, 49]. To support this notion, we found that the prevalence of comorbidity among the NDD groups, which increases the medical complexity and needs of the individual [50], was only 9.8%. This estimate is lower than expected based on other population-based studies [50, 51]. Further, the average age of death for our sample of adults with NDDs that sustained a low-trauma fracture was 69.8 years, which is higher than previously reported from large-scale studies [30–32]. In regards to CP, the study sample may have been disproportionately biased to reflect a less skeletally fragile patient population, relative to ID and ASD. Part of the severity spectrum for CP includes motor function deficits and ranges from independent ambulation (i.e., no need for assistive walking devices) to using an electric-powered wheelchair for mobility. This considerable range in mechanical loading ability leads to large variation in the extent of skeletal fragility for this population. In previous studies, we have found the prevalence of osteoporosis, a predictor of low-trauma fracture, among privately-insured adults aged 18–64 years with CP (n=5,555; osteoporosis prevalence, 5.5%) [29] was higher than adults without CP (1.3%), but considerably lower than what we previously published from a clinical-based sample of adults with CP (n=1,395; osteoporosis prevalence, ~10% for 18–40 year olds, ~15% for 41–50 year olds, ~26% for >50 year olds) [52]. In that clinical-based study [52], over half of the sample had moderate to severe forms of CP, and the prevalence of musculoskeletal morbidities among adults with moderate to severe forms of CP are about double compared to adults with milder forms [26]. Therefore, study findings with regards to CP should be interpreted with caution. Further research is required that leverages data that better represents the diversity of the CP population.

While factors that explain fracture-induced premature mortality still need to be elucidated, there may be a different set of risk factors contributing to short- and long-term post-fracture mortality [53], which may be further confounded by the NDD condition and fracture site. Among older adults, pre-fracture presence of chronic diseases [54], functional ability [55], and physical capacity (e.g., muscle strength) [56] are predictors of early post-fracture mortality, and a subsequent fracture exacerbates premature mortality [56]. In general, the overall physiological stress induced by a low-traumatic fracture may create an unfavorable biological environment that increases risk for post-fracture complications and premature death, either through direct or indirect mechanisms [53]. This places individuals with NDDs at particular risk for post-fracture complications because of the greater lifetime burden of

unhealthful aging caused by low fitness levels [12, 13], excess health problems experienced in childhood (e.g., excess body fat) [14–17, 20, 22–24], and elevated prevalence of chronic diseases in adulthood [26, 29, 34, 57]. Therefore, adults with NDDs may already have a vulnerable physiological environment and skeletal fragility (e.g., history of fractures), and sustaining a low-trauma fracture may increase susceptibility to post-fracture complications. Unfortunately, we were not able to ascertain lifetime fracture history.

Further, each NDD group has a considerable spectrum of severity, concomitant with a range of health complications and medical needs. For example, the multimorbidity prevalence (≥2 chronic diseases) among 18–30 year olds with severe forms of cerebral palsy is more than double that of 18–30 year olds with mild to moderate forms (33.9% vs. 15.2%, respectively) [26], and the mortality rate is increased among lower vs. higher functioning individuals with autism spectrum disorders [32]. In summary, the risk factors for immediate and long-term post-fracture premature mortality among adults with NDDs may encompass general risk factors, such as pre-fracture chronic diseases, but there may also be risk factors unique to these NDD populations, such as the type and severity of the NDD condition, use of assistive walking device or wheelchair, and medications/polypharmacy. Future studies are needed to disentangle the general and patient-specific risk factors that may differentially associate with post-fracture premature mortality, and to what extent the fracture-mortality association is mediated by post-fracture complications, such as chronic diseases, pneumonia, for example.

The limitations of this study must be discussed. First, as noted above, the sample may reflect a higher functioning and healthier segment of the NDD population, which may explain the relatively small number of deaths and older than expected age of death. It is therefore possible that there is a bigger population health issue than the current database can capture. Study conclusions, especially for CP, should be considered within the scope of this particular population of privately-insured adults. Second, we were unable to reliably determine severity of these NDD conditions, which could have provided further clinical interpretation with stratification by severity levels. Third, the observational design of the study introduces inherent bias due to unmeasured confounding. We therefore computed e-values to estimate the extent of unmeasured confounding, which determines the minimum strength of association with the exposure and outcome needed to fully explain away a specific exposure-outcome association, conditional on the set of covariates [58, 59]. The highest level covariate-adjusted Cox models for the 12-month time point were used for the NDDs groups where appropriate (e.g., model 2 for NDDs; model 1 for ASD only). The estimated e-value (lower 95% CI) needed to fully explain away the effect for the NDD group variable was 2.28 (1.86) for the entire sample of adults with NDDs, 3.00 (2.34) for adults with ID only, and 2.64 (1.49) for adults with ASD only. For fracture locations, it was 4.25 (2.85) for the lower extremities and 2.92 (1.76) for the upper extremities. Given the large e-values, it appears unlikely that unmeasured confounding largely biased effect estimates for the exposure variable. Fourth, this study was underpowered to examine differences in post-fracture mortality rate for adults with NDDs by race and for many of the NDD subgroups, such as comorbid NDDs. Studies of the general population have shown racial differences for post-fracture mortality rates [60]; whether adults with NDDs follow a similar racial pattern requires further investigation. Fifth, there may be other factors or comorbidities associated with premature mortality among adults with NDDs that were not assessed in the current

study. Sixth, while the medical conditions examined have shown good accuracy, it is unknown if there are substantive differences in the diagnostic accuracy of these conditions between groups.

Conclusion

We report for the first time that adults with NDDs have greater mortality risk within 12 months following a low-trauma fracture compared to adults without NDDs, despite an age difference of about a decade for those that died. Of the fracture sites, lower and upper extremities may be more strongly associated with 12-month mortality risk for adults with vs. without NDDs. Conducting similar analyses using a more general (i.e., not privately insured) population may reveal larger disparities and we suggest such an investigation is warranted given our findings. Further research is needed to identify risk factors for excess premature mortality post-fracture and post-fracture complications that may exacerbate premature mortality among adults with NDDs.

Acknowledgements

Funding: This work was supported by the University of Michigan Office of Health Equity and Inclusion Diversity Fund (Dr. Whitney).

Role of funder: The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Abbreviations:

NDD	neurodevelopmental disabilities

References

[1]. Papadimitriou N, Tsilidis KK, Orfanos P, Benetou V, Ntzani EE, Soerjomataram I, Kunn-Nelen A, Pettersson-Kymmer U, Eriksson S, Brenner H, Schottker B, Saum KU, Holleczek B, Grodstein FD, Feskanich D, Orsini N, Wolk A, Bellavia A, Wilsgaard T, Jorgensen L, Boffetta P, Trichopoulos D, Trichopoulou A, Burden of hip fracture using disability-adjusted life-years: a pooled analysis of prospective cohorts in the CHANCES consortium, Lancet Public Health 2(5) (2017) e239–e246. [PubMed: 29253489]

[2]. Burge R, Dawson-Hughes B, Solomon DH, Wong JB, King A, Tosteson A, Incidence and economic burden of osteoporosis-related fractures in the United States, 2005–2025, J Bone Miner Res 22(3) (2007) 465–75. [PubMed: 17144789]

[3]. Neuman MD, Silber JH, Magaziner JS, Passarella MA, Mehta S, Werner RM, Survival and functional outcomes after hip fracture among nursing home residents, JAMA Intern Med 174(8) (2014) 1273–80. [PubMed: 25055155]

[4]. Veronese N, Stubbs B, Crepaldi G, Solmi M, Cooper C, Harvey NC, Reginster JY, Rizzoli R, Civitelli R, Schofield P, Maggi S, Lamb SE, Relationship Between Low Bone Mineral Density and Fractures With Incident Cardiovascular Disease: A Systematic Review and Meta-Analysis, J Bone Miner Res 32(5) (2017) 1126–1135. [PubMed: 28138982]

[5]. Harvey-Kelly KF, Kanakaris NK, Obakponovwe O, West RM, Giannoudis PV, Quality of life and sexual function after traumatic pelvic fracture, J Orthop Trauma 28(1) (2014) 28–35. [PubMed: 23481925]

[6]. Kumar A, Rahman M, Trivedi AN, Resnik L, Gozalo P, Mor V, Comparing post-acute rehabilitation use, length of stay, and outcomes experienced by Medicare fee-for-service and

Medicare Advantage beneficiaries with hip fracture in the United States: A secondary analysis of administrative data, PLoS Med 15(6) (2018) e1002592.

[7]. Uriz-Otano F, Pla-Vidal J, Tiberio-Lopez G, Malafarina V, Factors associated to institutionalization and mortality over three years, in elderly people with a hip fracture-An observational study, Maturitas 89 (2016) 9–15. [PubMed: 27180154]

[8]. Berry JG, Berry SD, Caring for Patients With Neurological Impairment: Conversations Between a Pediatrician and Geriatrician, JAMA Pediatr (2018).

[9]. Ahmedani BK, Hock RM, Health care access and treatment for children with co-morbid autism and psychiatric conditions, Soc Psychiatry Psychiatr Epidemiol 47(11) (2012) 1807–14. [PubMed: 22322982]

[10]. Vohra R, Madhavan S, Sambamoorthi U, St Peter C, Access to services, quality of care, and family impact for children with autism, other developmental disabilities, and other mental health conditions, Autism 18(7) (2014) 815–26. [PubMed: 24353274]

[11]. Aisen ML, Kerkovich D, Mast J, Mulroy S, Wren TA, Kay RM, Rethlefsen SA, Cerebral palsy: clinical care and neurological rehabilitation, Lancet Neurol 10(9) (2011) 844–52. [PubMed: 21849165]

[12]. Tyler K, MacDonald M, Menear K, Physical activity and physical fitness of school-aged children and youth with autism spectrum disorders, Autism Res Treat 2014 (2014) 312163.

[13]. Garcia CC, Alcocer-Gamboa A, Ruiz MP, Caballero IM, Faigenbaum AD, Esteve-Lanao J, Saiz BM, Lorenzo TM, Lara SL, Metabolic, cardiorespiratory, and neuromuscular fitness performance in children with cerebral palsy: A comparison with healthy youth, Journal of exercise rehabilitation 12(2) (2016) 124–31. [PubMed: 27162775]

[14]. Whitney DG, Singh H, Miller F, Barbe MF, Slade JM, Pohlig RT, Modlesky CM, Cortical bone deficit and fat infiltration of bone marrow and skeletal muscle in ambulatory children with mild spastic cerebral palsy, Bone 94 (2017) 90–97. [PubMed: 27732905]

[15]. Whitney DG, Singh H, Zhang C, Miller F, Modlesky CM, Greater Visceral Fat but No Difference in Measures of Total Body Fat in Ambulatory Children With Spastic Cerebral Palsy Compared to Typically Developing Children, J Clin Densitom (2018).

[16]. Whitney DG, Miller F, Pohlig RT, Modlesky CM, BMI does not capture the high fat mass index and low fat-free mass index in children with cerebral palsy and proposed statistical models that improve this accuracy, Int J Obes (Lond) (2018).

[17]. Corvey K, Menear KS, Preskitt J, Goldfarb S, Menachemi N, Obesity, Physical Activity and Sedentary Behaviors in Children with an Autism Spectrum Disorder, Matern Child Health J 20(2) (2016) 466–76. [PubMed: 26515467]

[18]. Whitney DG, Peterson MD, Warschausky SA, Mental health disorders, participation, and bullying in children with cerebral palsy, Dev Med Child Neurol (2019).

[19]. Whitney DG, Warschausky SA, Peterson MD, Mental health disorders and physical risk factors in children with cerebral palsy: a cross-sectional study, Dev Med Child Neurol 61(5) (2019) 579–585. [PubMed: 30362114]

[20]. Whitney DG, Shapiro DN, Warschausky SA, Hurvitz EA, Peterson MD, The contribution of neurologic disorders to the national prevalence of depression and anxiety problems among children and adolescents, Ann Epidemiol 29 (2019) 81–84 e2.

[21]. Whitney DG, Shapiro DN, Peterson MD, Warschausky SA, Factors associated with depression and anxiety in children with intellectual disabilities, J Intellect Disabil Res 63(5) (2019) 408–417. [PubMed: 30588708]

[22]. Neumeyer AM, Cano Sokoloff N, McDonnell E, Macklin EA, McDougle CJ, Misra M, Bone Accrual in Males with Autism Spectrum Disorder, J Pediatr 181 (2017) 195–201 e6.

[23]. da Silva VZ, de Franca Barros J, de Azevedo M, de Godoy JR, Arena R, Cipriano G Jr., Bone mineral density and respiratory muscle strength in male individuals with mental retardation (with and without Down Syndrome), Res Dev Disabil 31(6) (2010) 1585–9. [PubMed: 20541908]

[24]. Modlesky CM, Whitney DG, Singh H, Barbe MF, Kirby JT, Miller F, Underdevelopment of trabecular bone microarchitecture in the distal femur of nonambulatory children with cerebral palsy becomes more pronounced with distance from the growth plate, Osteoporos Int 26(2) (2015) 505–12. [PubMed: 25199575]

[25]. Day SM, Wu YW, Strauss DJ, Shavelle RM, Reynolds RJ, Change in ambulatory ability of adolescents and young adults with cerebral palsy, Developmental medicine and child neurology 49(9) (2007) 647–53. [PubMed: 17718819]

[26]. Whitney DG, Hurvitz EA, Ryan JM, Devlin MJ, Caird MS, French ZP, Ellenberg EC, Peterson MD, Noncommunicable disease and multimorbidity in young adults with cerebral palsy, Clin Epidemiol 10 (2018) 511–519. [PubMed: 29750055]

[27]. Schrager S, Kloss C, Ju AW, Prevalence of fractures in women with intellectual disabilities: a chart review, J Intellect Disabil Res 51(Pt 4) (2007) 253–9. [PubMed: 17326806]

[28]. Neumeyer AM, O'Rourke JA, Massa A, Lee H, Lawson EA, McDougle CJ, Misra M, Brief report: bone fractures in children and adults with autism spectrum disorders, J Autism Dev Disord 45(3) (2015) 881–7. [PubMed: 25193141]

[29]. Whitney DG, Alford AI, Devlin MJ, Caird MS, Hurvitz EA, Peterson MD, Adults with Cerebral Palsy have Higher Prevalence of Fracture Compared with Adults Without Cerebral Palsy Independent of Osteoporosis and Cardiometabolic Diseases, J Bone Miner Res 34(7) (2019) 1240–1247. [PubMed: 30730595]

[30]. Glover G, Williams R, Heslop P, Oyinlola J, Grey J, Mortality in people with intellectual disabilities in England, J Intellect Disabil Res 61(1) (2017) 62–74. [PubMed: 27489075]

[31]. Ryan JM, Peterson MD, Ryan N, Smith KJ, O'Connell N E, Liverani S, Anokye N, Victor C, Allen E, Mortality due to cardiovascular disease, respiratory disease, and cancer in adults with cerebral palsy, Dev Med Child Neurol (2019).

[32]. Hirvikoski T, Mittendorfer-Rutz E, Boman M, Larsson H, Lichtenstein P, Bolte S, Premature mortality in autism spectrum disorder, Br J Psychiatry 208(3) (2016) 232–8. [PubMed: 26541693]

[33]. Croen LA, Zerbo O, Qian Y, Massolo ML, Rich S, Sidney S, Kripke C, The health status of adults on the autism spectrum, Autism 19(7) (2015) 814–23. [PubMed: 25911091]

[34]. Whitney DG, Warschausky SA, Ng S, Hurvitz EA, Kamdar NS, Peterson MD, Prevalence of mental health disorders among adults with cerebral palsy: A cross-sectional analysis, Annals of Internal Medicine In Press (2019).

[35]. Whitney DG, Kamdar NS, Ng S, Hurvitz EA, Peterson MD, Prevalence of high-burden medical conditions and healthcare resource utilization and costs among adults with cerebral palsy Clinical Epidemiolgy In Press (2019).

[36]. Buchele G, Becker C, Cameron ID, Auer R, Rothenbacher D, Konig HH, Rapp K, Fracture risk in people with developmental disabilities: results of a large claims data analysis, Osteoporos Int 28(1) (2017) 369–375. [PubMed: 27553444]

[37]. Keshishian A, Boytsov N, Burge R, Krohn K, Lombard L, Zhang X, Xie L, Baser O, Examining the Effect of Medication Adherence on Risk of Subsequent Fracture Among Women with a Fragility Fracture in the U.S. Medicare Population, J Manag Care Spec Pharm 23(11) (2017) 1178–1190. [PubMed: 29083977]

[38]. Narongroeknawin P, Patkar NM, Shakoory B, Jain A, Curtis JR, Delzell E, Lander PH, Lopez-Ben RR, Pitt MJ, Safford MM, Volgas DA, Saag KG, Validation of diagnostic codes for subtrochanteric, diaphyseal, and atypical femoral fractures using administrative claims data, J Clin Densitom 15(1) (2012) 92–102. [PubMed: 22071028]

[39]. Reeves S, Garcia E, Kleyn M, Housey M, Stottlemyer R, Lyon-Callo S, Dombkowski KJ, Identifying sickle cell disease cases using administrative claims, Acad Pediatr 14(5 Suppl) (2014) S61–7. [PubMed: 24882379]

[40]. Ryan JM, Peterson MD, Ryan N, Smith KJ, O'Connell NE, Liverani S, Anokye N, Victor C, Allen E, Incidence of mortality due to cardiovascular disease, cancer, and respiratory disease in adults with cerebral palsy, Developmental Medicine and Child Neurology In Press (2019).

[41]. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016, Lancet 390(10100) (2017) 1151–1210. [PubMed: 28919116]

[42]. Chang HY, Weiner JP, Richards TM, Bleich SN, Segal JB, Validating the adapted Diabetes Complications Severity Index in claims data, Am J Manag Care 18(11) (2012) 721–6. [PubMed: 23198714]

[43]. Solberg LI, Engebretson KI, Sperl-Hillen JM, Hroscikoski MC, O'Connor PJ, Are claims data accurate enough to identify patients for performance measures or quality improvement? The case of diabetes, heart disease, and depression, Am J Med Qual 21(4) (2006) 238–45. [PubMed: 16849780]

[44]. Vittinghoff E, McCulloch CE, Relaxing the rule of ten events per variable in logistic and Cox regression, Am J Epidemiol 165(6) (2007) 710–8. [PubMed: 17182981]

[45]. Viswanathan M, Reddy S, Berkman N, Cullen K, Middleton JC, Nicholson WK, Kahwati LC, Screening to Prevent Osteoporotic Fractures: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force, JAMA 319(24) (2018) 2532–2551. [PubMed: 29946734]

[46]. Lewiecki ME, Ortendahl JD, Vanderpuye-Orgle J, Grauer A, Arellano J, Harmon LJ,AL, Singer BMS,AJ, Healthcare policy changes in osteoporosis can improve outcomes and reduce costs in the US, Journal of Bone and Mineral Research (2019) In Press.

[47]. Singh NA, Quine S, Clemson LM, Williams EJ, Williamson DA, Stavrinos TM, Grady JN, Perry TJ, Lloyd BD, Smith EU, Singh MA, Effects of high-intensity progressive resistance training and targeted multidisciplinary treatment of frailty on mortality and nursing home admissions after hip fracture: a randomized controlled trial, J Am Med Dir Assoc 13(1) (2012) 24–30. [PubMed: 21944168]

[48]. Presedo A, Dabney KW, Miller F, Fractures in patients with cerebral palsy, Journal of pediatric orthopedics 27(2) (2007) 147–53. [PubMed: 17314638]

[49]. Whitney DG, Prevalence of high-burden medical conditions among young and middle-aged adults with pediatric-onset medical conditions: findings from U.S. private and public administrative claims data, International Journal of Health Policy and Management In Press (2019).

[50]. Reid SM, Meehan EM, Arnup SJ, Reddihough DS, Intellectual disability in cerebral palsy: a population-based retrospective study, Dev Med Child Neurol 60(7) (2018) 687–694. [PubMed: 29667705]

[51]. Tonnsen BL, Boan AD, Bradley CC, Charles J, Cohen A, Carpenter LA, Prevalence of Autism Spectrum Disorders Among Children With Intellectual Disability, Am J Intellect Dev Disabil 121(6) (2016) 487–500. [PubMed: 27802102]

[52]. Whitney DG, Hurvitz EA, Devlin MJ, Caird MS, French ZP, Ellenberg EC, Peterson MD, Age trajectories of musculoskeletal morbidities in adults with cerebral palsy, Bone 114 (2018) 285–291. [PubMed: 29981509]

[53]. Schousboe JT, Mortality After Osteoporotic Fractures: What Proportion Is Caused by Fracture and Is Preventable?, J Bone Miner Res 32(9) (2017) 1783–1788. [PubMed: 28691759]

[54]. Katsoulis M, Benetou V, Karapetyan T, Feskanich D, Grodstein F, Pettersson-Kymmer U, Eriksson S, Wilsgaard T, Jorgensen L, Ahmed LA, Schottker B, Brenner H, Bellavia A, Wolk A, Kubinova R, Stegeman B, Bobak M, Boffetta P, Trichopoulou A, Excess mortality after hip fracture in elderly persons from Europe and the USA: the CHANCES project, J Intern Med 281(3) (2017) 300–310. [PubMed: 28093824]

[55]. Tosteson AN, Gottlieb DJ, Radley DC, Fisher ES, Melton LJ 3rd, Excess mortality following hip fracture: the role of underlying health status, Osteoporos Int 18(11) (2007) 1463–72. [PubMed: 17726622]

[56]. Bliuc D, Nguyen ND, Milch VE, Nguyen TV, Eisman JA, Center JR, Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women, JAMA 301(5) (2009) 513–21. [PubMed: 19190316]

[57]. Cashin A, Buckley T, Trollor JN, Lennox N, A scoping review of what is known of the physical health of adults with autism spectrum disorder, J Intellect Disabil 22(1) (2018) 96–108. [PubMed: 27623754]

[58]. Mathur MB, Ding P, Riddell CA, VanderWeele TJ, Website and R package for computing E-values., Epidemiology 29(5) (2018) e454–e47.

[59]. VanderWeele TJ, Ding P, Sensitivity Analysis in Observational Research: Introducing the E-Value, Ann Intern Med 167(4) (2017) 268–274. [PubMed: 28693043]

[60]. Jacobsen SJ, Goldberg J, Miles TP, Brody JA, Stiers W, Rimm AA, Race and sex differences in mortality following fracture of the hip, Am J Public Health 82(8) (1992) 1147–50. [PubMed: 1636840]

Table 1.

Baseline descriptive characteristics of participants with and without neurodevelopmental disabilities (NDDs) that sustained a low-trauma fracture.

	With NDDs (n=3749)	Without NDDs (n=585910)	
	No. (%)	No. (%)	*P* value
NDD characteristics			
Intellectual disabilities only	1670 (44.5)	0	
Cerebral palsy only	1094 (29.2)	0	
Autism spectrum disorders only	619 (16.5)	0	
NDD comorbidity	366 (9.8)	0	
1st Fracture characteristics			
Fracture distribution			<0.001
Unspecified location	105 (2.8)	22546 (3.9)	
Vertebral column	857 (22.9)	147453 (25.2)	
Hip	698 (18.6)	96180 (16.4)	
Femur, non-proximal	147 (3.9)	15219 (2.6)	
Tibia/fibula	966 (25.8)	135942 (23.2)	
Humerus	412 (11.0)	57908 (9.9)	
Ulna/radius	564 (15.0)	110662 (18.9)	
Demographic characteristics			
Age, mean (SD)	56.7 (20.6)	63.9 (19.2)	<0.001
18–39 years	827 (22.1)	79332 (13.5)	
40–59 years	1025 (27.3)	127745 (21.8)	
60–79 years	1372 (36.6)	225529 (38.5)	
80+ years	525 (14.0)	153304 (26.2)	
Sex			<0.001
Women	2056 (54.8)	384237 (65.6)	
Men	1693 (45.2)	201673 (34.4)	
Race			<0.001
White	2406 (64.2)	394034 (67.3)	
Black	383 (10.2)	42185 (7.2)	
Hispanic	278 (7.4)	47968 (8.2)	
Asian	93 (2.5)	14439 (2.5)	
Unknown/missing	589 (15.7)	87284 (14.9)	
US region			<0.001
West	1018 (27.2)	164639 (28.1)	
Midwest	873 (23.3)	141098 (24.1)	
South	1366 (36.4)	220110 (37.6)	
Northeast	492 (13.1)	60063 (10.3)	

	With NDDs (n=3749)	Without NDDs (n=585910)	
	No. (%)	**No. (%)**	***P* value**
Chronic disease comorbidities			
Ischemic heart diseases	525 (14.0)	82674 (14.1)	0.852
Heart failure	369 (9.8)	48084 (8.2)	<0.001
Cerebrovascular diseases	357 (9.5)	44548 (7.6)	<0.001
Hypertension	1885 (50.3)	301701 (51.5)	0.139
Diabetes	844 (22.5)	115892 (19.8)	<0.001
Chronic obstructive pulmonary disease	500 (13.3)	71646 (12.2)	0.039
Cancer	598 (16.0)	124577 (21.3)	<0.001

*Some individuals may have more than one NDD and are represented across multiple NDD groups.

Table 2.

Baseline descriptive characteristics of participants with and without neurodevelopmental disabilities (NDDs) that died during the 12-month follow up.

	With NDDs (n=182)	Without NDDs (n=25456)	
	No. (%)	**No. (%)**	***P* value**
Mortality characteristics			
Mortality			
1-month	38 (20.9)	6461 (25.4)	
3-months	76 (41.8)	12521 (49.2)	
6-months	127 (69.8)	18023 (70.8)	
12-months	182 (100)	25456 (100)	
NDD characteristics *			
Intellectual disabilities	110 (60.4)	0	
Cerebral palsy	37 (20.4)	0	
Autism spectrum disorders	27 (14.8)	0	
NDD comorbidity	8 (4.4)	0	
1st Fracture characteristics			
Fracture distribution			0.006
Unspecified location	7 (3.9)	730 (2.9)	
Vertebral column	52 (28.6)	9397 (36.9)	
Hip	56 (30.8)	8779 (34.5)	
Femur, non-proximal	10 (5.5)	744 (2.9)	
Tibia/fibula	26 (14.3)	2046 (8.0)	
Humerus	18 (9.9)	2151 (8.5)	
Ulna/radius	13 (7.1)	1609 (6.3)	
Demographic characteristics			
Age, mean (SD)	69.8 (14.7)	78.9 (9.8)	<0.001
18–39 years	9 (5.0)	117 (0.5)	
40–59 years	31 (17.0)	1269 (5.0)	
60–79 years	85 (46.7)	8397 (33.0)	
80+ years	57 (31.3)	15673 (61.6)	
Sex			0.029
Women	98 (53.9)	15717 (61.7)	
Men	84 (46.2)	9739 (38.3)	
Race			0.476
White	129 (70.9)	17834 (70.1)	
Black	19 (10.4)	2395 (9.4)	
Hispanic	12 (6.6)	1654 (6.5)	

	With NDDs (n=182)	Without NDDs (n=25456)	
	No. (%)	**No. (%)**	***P* value**
Asian	6 (3.3)	497 (2.0)	
Unknown/missing	16 (8.8)	3076 (12.1)	
US region			<0.001
West	31 (17.0)	7007 (27.5)	
Midwest	28 (15.4)	4882 (19.2)	
South	80 (44.0)	9423 (37.0)	
Northeast	43 (23.6)	4144 (16.3)	
Chronic disease comorbidities			
Ischemic heart diseases	59 (32.4)	8248 (32.4)	0.996
Heart failure	47 (25.8)	7438 (29.2)	0.316
Cerebrovascular diseases	44 (24.2)	4486 (17.6)	0.021
Hypertension	137 (75.3)	19788 (77.7)	0.427
Diabetes	69 (37.9)	8223 (32.3)	0.107
Chronic obstructive pulmonary disease	50 (27.5)	7714 (30.3)	0.408
Cancer	49 (26.9)	8338 (32.8)	0.095

*Some individuals may have more than one NDD and are represented across multiple NDD groups.

Table 3.

Crude post-fracture mortality rate and rate ratio (RR) between adults with and without neurodevelopmental disabilities (NDDs).

	1-month mortality	3-month mortality	6-month mortality	12-month mortality
Mortality cases	**N**	**N**	**N**	**N**
Without NDDs	6461	12521	18023	25456
With NDDs	38	76	127	182
ID only	24	45	76	110
CP only	7	16	27	37
ASD only	6	10	18	27
Comorbid NDDs *	1	5	6	8
Crude mortality rate	**N per 100 person years**	**N per 100 person years**	**N per 100 person years**	**N per 100 person years**
Without NDDs	13.60	9.02	6.61	4.96
With NDDs	12.46	8.48	7.16	5.40
ID only	17.70	11.31	9.66	7.38
CP only	**	6.10	5.19	3.74
ASD only	**	**	6.12	4.84
Comorbid NDDs *	**	**	**	**
Mortality RR	**RR (95% CI)**	**RR (95% CI)**	**RR (95% CI)**	**RR (95% CI)**
Without NDDs	Reference	Reference	Reference	Reference
With NDDs	0.92 (0.67, 1.26)	0.94 (0.75, 1.18)	1.08 (0.91, 1.29)	1.09 (0.94, 1.26)
ID only	1.30 (0.87, 1.94)	1.25 (0.94, 1.68)	1.46 (1.17, 1.83)	1.49 (1.23, 1.79)
CP only	**	0.68 (0.41, 1.10)	0.79 (0.54, 1.15)	0.75 (0.55, 1.04)
ASD only	**	**	0.93 (0.58, 1.47)	0.98 (0.67, 1.42)
Comorbid NDDs *	**	**	**	**

ID, intellectual disabilities; CP, cerebral palsy; ASD, autism spectrum disorders; CI, confidence interval.

* Comorbid NDDs were grouped together due to insufficient sample size and include: ID+CP; ID+ASD; CP+ASD; or ID+CP+ASD.

** Number of mortality cases insufficient for analysis (N≤10).

Table 4.

Risk of post-fracture mortality rate between adults with neurodevelopmental disabilities (NDDs) and adults without NDDs (reference).*

	With NDDs	ID only	CP only	ASD only
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
1-month mortality				
Model 1	1.27 (0.92, 1.75)	1.62 (1.09, 2.42)	**	**
Model 2	**	**	**	**
3-month mortality				
Model 1	1.31 (1.04, 1.64)	1.57 (1.17, 2.10)	**	**
Model 2	1.27 (1.02, 1.59)	1.53 (1.14, 2.05)	**	**
6-month mortality				
Model 1	1.50 (1.26, 1.79)	1.82 (1.45, 2.28)	0.98 (0.67, 1.43)	**
Model 2	1.45 (1.22, 1.73)	1.76 (1.41, 2.21)	**	**
12-month mortality				
Model 1	1.51 (1.31, 1.75)	1.86 (1.55, 2.25)	0.94 (0.68, 1.29)	1.63 (1.12, 2.38)
Model 2	1.46 (1.27, 1.69)	1.80 (1.49, 2.17)	**	**

ID, intellectual disabilities; CP, cerebral palsy; ASD, autism spectrum disorders; HR, hazard ratio; CI, confidence interval. N=589,659 for all models. Model 1 adjusted for age, sex, race, and US region. Model 2 adjusted for age, sex, race, US region, cardiovascular diseases (i.e., ischemic heart diseases, heart failure, cerebrovascular diseases, and/or hypertension), diabetes (i.e., type 1 or 2, primary or secondary), chronic obstructive pulmonary diseases, and cancer.

* Number of mortality cases insufficient for analysis for comorbid NDD group.

** Number of mortality cases insufficient for analysis (model 1, N<20; model 2, N<40).

Table 5.

Crude 12-month post-fracture mortality rate and rate ratio (RR) and adjusted hazard ratio (HR) between adults with neurodevelopmental disabilities (NDDs) and without NDDs (reference) by fracture location.

	Mortality cases	Crude mortality rate	Mortality RR	Model 1	Model 2
	N	N per 100 person years	RR (95% CI)	HR (95% CI)	HR (95% CI)
Vertebral column					
Without NDDs	9397	7.38	Reference	Reference	Reference
With NDDs	52	6.87	0.93 (0.71, 1.22)	1.17 (0.89, 1.54)	1.16 (0.88, 1.52)
Hip					
Without NDDs	8779	11.00	Reference	Reference	Reference
With NDDs	56	9.39	0.85 (0.66, 1.11)	1.25 (0.96, 1.63)	1.26 (0.97, 1.65)
Lower extremities					
Without NDDs	2790	2.07	Reference	Reference	Reference
With NDDs	36	3.51	1.69 (1.22, 2.35)	2.41 (1.73, 3.35)	*
Upper extremities					
Without NDDs	3760	2.48	Reference	Reference	Reference
With NDDs	31	3.45	1.39 (0.97, 1.98)	1.76 (1.23, 2.50)	*

ID, intellectual disabilities; CP, cerebral palsy; ASD, autism spectrum disorders; CI, confidence interval. Model 1 adjusted for age, sex, race, and US region. Model 2 adjusted for age, sex, race, US region, cardiovascular diseases (i.e., ischemic heart diseases, heart failure, cerebrovascular diseases, and/or hypertension), diabetes (i.e., type 1 or 2, primary or secondary), chronic obstructive pulmonary diseases, and cancer. Vertebral column, N=148,310; hip, N=96,878; lower extremities, N=152,274; upper extremities, N=169,546.

*Number of mortality cases insufficient for analysis (N<40).