Adverse Medication Events Related to Hospitalization in the U.S.: A comparison between Adults with Intellectual/Developmental Disabilities and those Without

Corresponding Author:
Steven R. Erickson, Pharm.D., Associate Professor
serick@med.umich.edu
University of Michigan
College of Pharmacy
428 Church Street
Ann Arbor, Michigan 48109-1065

Co-Authors:
Neil Kamdar, MA, Lead Statistician
neilseal@umich.edu
University of Michigan
Institute for Healthcare Policy & Innovation
2800 Plymouth Rd, NCRC Building 16
Ann Arbor MI 48109-2800

Chung-Hsuen Wu, Ph.D., Associate Professor
chunghwu@tmu.edu.tw
Taipei Medical University
College of Pharmacy
No.250, Wu-hsing St.
Xinyi Dist., Taipei 11031
Taiwan

Acknowledgement: Dawn Russell, for secretarial support for the manuscript. She is an Administrative Assistant, University of Michigan Institute for Healthcare Policy & Innovation

This study was conducted without funding. This study has not been presented as a poster or podium presentation.

Adverse Medication Events Related to Hospitalization in the U.S.: A comparison between Adults with Intellectual/Developmental Disabilities and those Without

Abstract

This study examined the proportion of hospitalizations associated with adverse medication events (AMEs) for adults with IDD and adults from the general population in the United States using the 2013 National Inpatient Sample (NIS) dataset of the Healthcare Cost and Utilization Project (HCUP). Adults with IDD had greater odds of having a hospitalization associated with an AME than the general adult population. Unadjusted odds ratios (95% CI) for hospitalization due to any medication for IDD was 2.47 (2.31-2.65). In the multivariate logistic regression model, IDD was significantly associated, with an odds ratio of 1.28 (1.19-1.38). Adults who have IDD are at greater risk of having a hospital admission due to an AME.

Running Title:

Adverse Medication Events in Adults who have Intellectual/Developmental Disabilities

Key Words

Intellectual developmental disability, adverse medication events, hospital admission

Introduction

Adverse medication events are an important cause of hospitalizations in the general population, with almost half being potentially preventable (Leendertse, Egberts, Stoker, & van den Bemt, 2008). A recent analysis of hospitalizations over a one-year period in the U.S. found that adverse medication events were present on admission for 105.6 per 10,000 encounters (Weiss, Freeman, Heslin, & Barrett, 2018). Other research efforts, as well as systematic reviews, have identified adverse medication events as being an important cause for hospitalization (Budnitz, et al., 2006; Budnitz, Lovegrove, Shehab, & Richards, 2011; Kongkaew, Noyce, & Ashcroft, 2008; McDonnell & Jacobs, 2002). Determinants include impaired cognition, multiple comorbidities, dependent living situation, nonadherence to medication regimens, and polypharmacy. In several other studies of the general population, being of older age, receiving more than 5 medications, having greater comorbidity, and starting new high-risk drugs are factors associated with preventable hospital admissions associated with adverse medication events (Kongkaew et al., 2013; Nair, et al., 2016). Another study found that older age, greater comorbidity, and a greater number of prescribed medications, along with female gender and alcohol use, were associated with adverse medication events leading to hospitalization (Onder et al, 2002).

There is a paucity of research focused on identifying and remediating the factors associated with adverse medication events for people with intellectual or developmental disability (IDD). Information in the literature is derived from small observational studies which focus on psychotropic drug prescribing and related adverse effects (Hess, Matson, Neal, Mahan, Fodstad, Bamburg & Holloway, 2010; Valdovinos, Caruso, Roberts, Kim, & Kennedy, 2005; Scheifes, et al., 2016).

People who have IDD may be at greater risk for experiencing adverse medication events due to having a number of the predisposing risk factors identified in the general population. A recent study conducted at a single academic health system found that the complexity of medication regimens of

adults who have IDD and are patients of adult general internal medicine clinics was twice that of age and gender matched patients without IDD in the same clinical setting. The level of medication regimen complexity for patients who had IDD was at the same level as that reported in other studies to be associated with a higher risk for medication-associated medication nonadherence, hospitalizations, and emergency room visits. (Erickson, Nicaj, & Barron, 2018; Ferreira, Galato, & Melo, 2015; Willson, Greer, & Weeks, 2014; Wimmer, et al., 2014). Also noteworthy was that 80% of patients with IDD were prescribed five or more medications, and over 60% had 10 or more prescribed medications. Other studies have confirmed that polypharmacy and high comorbidity, especially with comorbid mental illness and neurological disorders, are problems for people who have IDD. (Robertson, et al., 2008; O'Dwyer, Peklar, Mccallion, Mccarron, & Henman, 2016; Doan, Lennox, Taylor-Gomez, & Ware, 2013). Elderly patients who have IDD may be at risk for adverse medication events due to prescribing errors. One study found that the prevalence of individuals with prescription errors in this population is 47.5%, with relevant errors were identified in 26.8% of the individuals (Zaal, Kaaij, Evenhuis, & Bemt, 2013). People who have IDD may have cognitive and adaptive limitations leading to reliance on other people for assistance in managing medications. Findings from a recent qualitative study of caregivers of patients with developmental disabilities identified a number of potential barriers to successful use of medications including communication gaps between health care providers, specialists, primary care providers, pharmacies, and patients/caregivers and lack of understanding of drug regimens by the caregiver (Erickson, Salgado, & Tan, 2016).

The present study was conducted to determine an estimate of the proportion of hospital admissions associated with a primary diagnosis of an adverse medication event for adults who have IDD and compared to the general adult population of the United States. It was hypothesized that individuals with IDD were more likely to experience hospitalizations due to adverse medication events than people who do not have IDD.

Methods

Conceptual Framework.

The Behavioral Model of Health Services Utilization by Aday and Andersen was the conceptual framework of this study (Aday, & Andersen, 1974; Andersen, 1995). The model proposes that use of health services is a function of individual and family/household predisposition to use services, factors that enable or impede use, and specific needs for care. We used the Model to identify the individual as well as system/ environmental factors that may be associated with the occurrence of hospitalization due to an adverse medication events. The model consists of environmental/system, predisposing, enabling, and illness level or need factors which are hypothesized to be the primary determinants of health services utilization. The predisposing component contains demographics, education level, health beliefs, cognitive ability, and autonomy. The enabling component includes the resources available to the individual in terms of personal income, education, and insurance status, access to care, health literacy, and social support. The illness level or need component is composed of subject perception of illness or illness burden determined by a health care provider. The environmental factors include availability of community resources, nature and extent of support, access to health personnel and facilities, price of services, and geographic location of residence. We identified hospital admission due to adverse medication events as the outcome of interest.

Database

This study used the 2013 National Inpatient Sample (NIS) dataset available through the Healthcare Cost and Utilization Project (HCUP). A description of the dataset can be found by accessing the web site https://www.hcup-us.ahrq.gov/. HCUP is a family of health care databases sponsored by the Agency for Healthcare Research and Quality (AHRQ). The HCUP datasets bring together a compilation of data from around the country with all-payer, encounter-level information. The National (Nationwide) Inpatient Sample (NIS) of the Healthcare Cost and Utilization Project (HCUP) dataset is a

publicly available all-payer inpatient health care database, yielding national estimates of hospital inpatient stays. Weighted, it estimates more than 35 million hospitalizations nationally.

Data Sample.

The sample consists of non-institutionalized adults age 18 years or older whose hospitalization event was captured in the 2013 NIS. The dataset contains two sets of variables related to diagnoses. The aggregated diagnoses categories called Clinical Classification Codes (CCCs), which are comprised of like-ICD9 codes, were used for this study. There are 25 CCC data elements searchable for diagnoses related to each admission. The CCC 654 (Developmental disorders), CCC 655 (Disorders usually diagnosed in infancy, childhood, or adolescence), and CCC 217 (Other congenital anomalies) were used to identify individuals who were considered to have an IDD-related condition. Additional details regarding the ICD9 codes that comprise each CCC is available from the corresponding author. Patients were categorized as being in the IDD group or the Non-IDD group.

Identification of cases with the principal diagnosis representing a medication-related cause for admission used the CCC 241 (Poisoning by Psychotropic Agent) and CCC 242 (Poisoning by other Medications and Drugs). These terms refer to diagnoses that may be due to excessive use of an agent (given too high of a dose, intentional ingestion, unintentional ingestion, inadvertently taking the wrong medicine), but also includes admissions where the cause is related to unintended medication effects. Based on HCUP documentation, the principle diagnosis associated with the reason for the hospitalization is the first diagnosis code position for the encounter. We used this code to search for medication-related causes for hospitalization.

Measures

The *primary dependent variable* was the proportion of hospitalizations in which the primary diagnosis was due to an adverse medication event. For this study, each category was used as a separate dependent variable, and a combined variable, “All Medications AME”, was created by merging

the psychotropic and other medication categories. The "poisoning by psychotropic agents" category was renamed "Psychotropic Medications AME" and included medications used for the treatment of anxiety, depression, bipolar, and schizophrenia. The "poisoning by other medications and drugs" category was renamed "Physical Medications AME" for this analysis.

Independent variables

Variables were grouped based on the categories of Predisposing, Enabling, Need, and Environmental based on the Andersen & Aday (1995) model. The Predisposing variables included the primary independent variable of interest which was group assignment to IDD or Non-IDD. The type of admission, elective or non-elective, is a predisposing variable included in an effort to control for the fact that elective admissions are most likely not related to a severe adverse medication event but rather for elective surgeries and other non-emergent, preplanned admissions. Other Predisposing variables include demographics (age, gender, and race). Enabling variable included the expected primary payer and the median household income category for patient's ZIP code of residence. The Need category used the count of unique chronic diagnoses reported on the discharge. The Environmental variable was the HCUP definition for urbanicity of residence (urban-rural designation of residence).

Statistical Analysis

Variables are presented as means with standard deviation (continuous) or frequency with percent (categorical). Determination of the proportion of patients having hospitalizations for adverse medication events was calculated by determining the total number of all-cause events within each group as the denominator, with the numerator being the number of events that are medication-related. Bivariate analyses were conducted between IDD and non-IDD groups to assess significance in baseline characteristics. Chi-Square tests were conducted on categorical variables to test for difference in proportions. For continuous variables, if the variable was normally distribution, parametric Student's T-test was conducted. All analyses utilized the sample weights made available in the dataset to account

for the sampling methodology used to obtain the data. The discharge weights (DISCWT) provided in the NIS were used in analyses in order to produce national estimates.

Analysis using multivariable logistic regression modelling was conducted for the primary dependent variables hospitalization due to Physical Medications AME, Psychotropic Medications AME, and All Medications AMEs. All independent variables entered into the model simultaneously.

Results

In the 2013 NIS dataset, there were 5,993,894 total admissions for patients age 18 years and older. Of these, 5,943,223 admissions (99.2%) were for patients in the Non-IDD while 50,671 (0.8%) were for patients with an IDD. These data represented 29,969,450 admissions when discharge weights were applied, with the weighted estimate $\pm$ standard error, and 95% confidence interval (95% CI) of 29,716,096.4$\pm$ 2,766.9 (95% CI of 29,710,673 to 29,721,519) admissions for Non-IDD patients and 253,354.8 $\pm$ 1,120.6 (95% CI of 251,158 to 255,551) for those with an IDD.

Patients in the IDD group were younger and more were male compared with the patients in the Non-IDD group. All comparisons were significantly different between the two groups. Refer to Table 1 for the description of the sample. The two groups were similar in distribution based on race. Patients in the IDD group had a greater number of chronic diagnoses. Both groups were similar in terms of the distribution of where they live (rural/urban measure) and household income of the ZIP code in which they live, although there was a somewhat higher proportion of patients with IDD living in ZIP codes with lower income. A greater proportion of patients in the IDD group had Medicaid insurance while a greater proportion of the patients in the Non-IDD group were covered by Medicare or private insurance. The proportion of admissions due to emergent reasons was higher for patients with IDD, while the proportion of admissions due to elective reasons was higher for patients in the Non-IDD group.

Patients with IDD had a higher percentage of hospital admissions for adverse medication events due to All Medication AME as a principle diagnosis (1.61%) than the patients Non-IDD group (0.7%) with

an odds ratio of 2.47 (95% confidence interval 2.31 to 2.65). This relationship held true when medication related reasons were further categorized and analyzed separately as Physical Medications AME (IDD group 0.9% versus 0.4% for non-IDD group, odds ratio 2.30 with 95% confidence interval of 2.1-2.53) and Psychotropic Medication AME (IDD group 0.7% versus 0.3% for non-IDD group, odds ratio of 2.70 with 95% confidence interval of 2.43 to 3.00).

In multivariate analysis, the independent variables significantly associated with being hospitalized for an adverse medication event were the same for all 3 models. Refer to Table 2. Having a diagnosis associated with IDD was still significantly associated with hospitalization for a medication-related event in all three models. Also significant were age, gender, race, type of admission, primary payer, income of the residential ZIP code, and overall number of diagnoses. Patients who had an IDD diagnosis, as well as those who were younger, female, Caucasian, non-elective admission, public or self-insured, home residence in a lower income ZIP code, and having a greater number of diagnoses were all associated with greater odds of the hospitalization being due to an adverse medication event. The environmental variable, urbanicity, was not a significant predictor variable in any of the multivariate models.

Discussion

This study demonstrated that a significantly greater proportion of hospitalizations for adults who have an intellectual or developmental disability were associated with adverse medication events compared to the general adult population. The present study found that 1.61% of hospital stays for patients with IDD were due to an adverse medication event (All Medications AME) compared to 0.7% of those from the general population. Both of these estimates are generally lower than the prevalence of AMEs that lead to hospitalization previously reported in the literature for the general population. Variation in rates of hospital admission or emergency room visits for adverse medication events

reported in the literature is due to varying definitions of hospital admission, the definition of an adverse drug event, the method of data collection, and the validation of the likelihood of an AME occurring such as a clinician review of event (Leendertse, Visser, Egberts, & van den Bemt, 2010). A review of the literature from 1966 to 1989 of studies characterizing drug-related hospital admissions found that between 0.2 to 21.7% of hospital admissions are due to outpatient medication adverse drug events, with a median value of 4.9% (Einarson, 1993). Other studies found values ranging from 3.4 to 6.5% from the Netherlands, United Kingdom, and Italy (Leendertse, et al.,2008; Onder, et al, 2002; Pirmohamed, et al., 2004). Two systematic reviews of the literature found rates of admission for adverse medication events ranging between 3.7 and 5.3% (Kongkaew, et al., 2008; Winterstein, Sauer, Hepler, & Poole, 2002). In one of the only studies in the literature examining all-cause hospitalizations of people with IDD, 8.5% of hospital admissions were primarily associated with injury or poisoning, which included adverse medication events (Balogh, Hunter, & Ouellette-Kuntz, 2005). In the end, the primary finding of the present study is that the prevalence of hospitalization for an adverse medication event for adults who have IDD was over twice that of adult patients from the general population.

Predisposing, Enabling, Need and Environmental Factors Associated with Hospital Admission Due to an Adverse Medication Event

The type of admission, categorized as either emergent or non-emergent, was significantly different between adult patients who have IDD and those without. In the multivariable models, this variable had the greatest association with the cause for hospitalization being medication related. The non-emergent reasons for admission were higher for the general population compared with the patients with IDD. Non-emergent reasons for admission are primarily associated with elective surgeries or planned admissions. It is not surprising that in the present study there was a significant difference in the association between the types of admission between the two groups. Generally, adult patients who have IDD have fewer elective surgical procedures such as hip replacements compared with the general

population, which may be the primary explanation for the difference (Balogh, et al., 2005; Kapell, et al., 1998).

Patients in middle age category experienced a greater likelihood of a hospitalization related to medication compared to younger patients, and relative to older patients. There are mixed results of the association between age and its association with the occurrence of adverse medication events in studies of the general population. For example, one study found that individuals age 65 and older were more likely than younger individuals to experience adverse medication events (annual estimate, 4.9 vs 2.0 per 1000; rate ratio [RR], 2.4; 95%CI, 1.8-3.0) and more likely to require hospitalization (annual estimate, 1.6 vs 0.23 per 1000; RR, 6.8; 95%CI, 4.3-9.2) (Budnitz, et al., 2006). However, another study of over 5000 patients found no age effect (Raschetti, et al., 1999). Further research is necessary to determine the reasons for the age difference for people who have IDD, such as the type of medications used, comorbid conditions, and potential social indicators, which may be different between age groups. For patients who have IDD, these variables may include the type of living environment as well as the experience and training of the support network. Older people with IDD may more likely live in a supervised setting as opposed to younger people who live with family. There may be a difference in training of caregivers as well as the systems that are used to distribute and administer medications between these two groups.

In the present study, female gender was associated with greater odds of experiencing a hospitalization associated with an adverse medication event. This is consistent with other research that included gender as a predictor variable (Forster, Murff, Peterson, Gandhi, & Bates, 2003; Sarkar, Lopez, Maselli, & Gonzales, 2011). Findings associated with race were relatively consistent with other studies, whereby minority patients had a lower risk of experiencing adverse medication events compared to the White category (Sarkar, et al., 2011). The IDD group had a higher proportion of patients who were

either White or who were Black compared with the general population group, which had higher proportion of other minority races documented.

Enabling and environmental variables may also be considered social indicators or determinants of health. In this study, these include insurance type, race, income (ZIP code of residence used as income for the present study), and a rating of urbanicity, a measure of population density. Being uninsured (self-pay) or having publically funded health insurance (Medicare, Medicaid) was associated with a greater chance that a hospitalization was due to an adverse medication event compared with patients who had private insurance. A much higher proportion of adults who have IDD had public insurance (Medicare, Medicaid) compared to the general population group. Having publically funded insurance may be associated with having lower household income. In this study, living in a ZIP code with lower household income was associated with greater odds of experiencing a hospitalization that was associated with an adverse medication event. The IDD group of patients had higher proportions of individuals who lived in the lower income ZIP codes, while the non-IDD group had greater proportions of patients who lived in middle to higher income ZIP codes.

The urban/rural variable, or population density categories, had a mixed results. The reason for including this variable in the analysis was that access to healthcare practitioners and pharmacies may be associated with adverse medication events. For example, rural areas have been found to have lower access to health care providers. Although studies provide a mixed assessment of the effect of rurality on health care outcomes, one study, using the access indicator of hospitalization for ambulatory-care sensitive conditions (ACSH), found that for adults, rates of ACSH increased with level of rurality (Laditka, Laditka, & Probst, 2009). Further, a review of studies by Lishner et al found that access to primary health-care for persons with disabilities living in rural areas was often limited (Lishner, Richardson, Levine, & Patrick, 1996). In the present study, there was no discernable pattern other than the “not metro or micro” category was consistently at lower odds of having hospitalization associated with

adverse medication event. For persons who have IDD, place of residence defined by population density is not significantly associated with the chance of experiencing an adverse medication event that led to hospitalization.

In the present study, the Need category of variables was operationalized using comorbidity, a measure of overall disease burden. Greater comorbidity was associated with higher odds that a hospitalization was associated with an adverse medication event. For the present study, people in the IDD group had a significantly higher number of comorbid conditions, or greater burden of illness compared with patients in the general population group. This finding is consistent with the literature. In a study of risk factors associated with adverse medication events among elderly people in the ambulatory setting, researchers found that greater comorbidity and number of medications to be associated with adverse medication events (Field, et al., 2004). The present study used a comorbidity variable that was a sum of the diagnoses present on discharge. A recent study of elderly people who have IDD noted that greater comorbidity is significantly associated with adverse outcomes (O'Dwyer, Mccallion, Mccarron, & Henman, 2018).

Limitations

This study was able to determine, to some extent, characteristics of the patients that were associated with adverse medication events leading to hospitalization. The variables available in this dataset, however, did not include more clinically detailed information that may help identify causes, nor did it include an in-depth set of social variables. The HCUP datasets contain only a limited set of independent or predictor variables. This limits the ability to identify the social determinants associated with hospitalization for an AME. Another example of a limitation of the dataset is that it does not include variables to identify specific medications prescribed, which precludes the documentation of the quantity of medication or the complexity of the medication regimens for patients. The clinical classification codes, or CCCs, were used to identify the hospitalizations due to an adverse medication

event. The CCCs are composed, for the most part, of multiple related ICD9 codes for specific drug categories. They usually are not specific enough to identify specific medications. Another potential limitation related to the CCCs is their use to identify people who have IDD. CCCs are aggregates of ICD9 diagnosis codes that are related. The problem is that upon aggregation, some CCCs may include an ICD9 code for chromosomal abnormalities, but they may include conditions that are not considered an intellectual or developmental disability. Alternatively, there may be under-coding of a CCC that includes IDD based on whether the hospital admission/discharge process included the code in the diagnosis fields. The inclusion of an IDD related diagnosis could be overlooked in favor of other more "billable" codes for an encounter. Lastly, this study is a cross sectional analysis, a limitation imposed by the data. Association between independent and dependent variables is all that can be inferred from the analysis.

Future work

Future analyses of either the HCUP database, or more likely datasets with more detailed information about the specific medication related to the adverse event leading to hospitalization are warranted. Information such as that found on medication reconciliation efforts on admission would be useful in identifying not only the drug, but other patient-specific factors that may be associated with the adverse event. Use of data warehouses from large integrated health systems may provide the type of data necessary to be able to more definitively identify the medications associated with both outpatient as well as emergency room visits and hospitalizations for adverse medication events. These datasets should also be able to provide more information about the clinical context associated with these events. In future projects, researchers should pursue testing related hypotheses using longitudinal data with a richer set of predictor variables.

Conclusion

Hospitalizations associated with adverse medication events are significantly more common in adults who have intellectual or developmental disability compared with the general population.

Clinicians need to be aware of the fact that their patients who have intellectual or developmental disabilities are at risk for experiencing poor outcomes associated with medication therapy. Clinicians do not receive adequate training in professional school or residency related to the care of people with IDD. More work needs to be undertaken to advance disability awareness and topics in curriculum of health professional schools and residency training programs. Becoming familiar with guidelines such as the Canadian Consensus Guidelines for primary care of adults who have IDD would help clinicians understand some of the unique needs and related treatments for people who have IDD (Sullivan, et al., 2018).

References

Aday, L., & Andersen R. (1974). A framework for the study of access to medical care. *Health Services Research, 9 (3),*208–220.

Andersen, R.M. (1995). Revisiting the behavioral model and access to medical care: does it matter? *Journal of Health and Social Behavior, 36(1),*1-10.

Balogh, R.S., Hunter, D., & Ouellette-Kuntz, H. (2005). Hospital utilization among persons with intellectual disability, Ontario, Canada, 1995-2001. *Journal of Applied Research in Intellectual Disabilities, 18(2),* 181-190.

Budnitz, D.S., Pollock, D.A., Weidenbach, K.N., Mendelsohn, A.B., Schroeder, T.J., & Annest, J.L. (2006). National surveillance of emergency department visits for outpatient adverse drug events. *Journal of the American Medical Association, 296(15),*1858-1866.

Budnitz, D.S., Lovegrove, M.C., Shehab, N., & Richards, C.L. (2011). Emergency hospitalizations for adverse drug events in older Americans. *New England Journal of Medicine, 365(21),* 2002-2012. DOI: 10.1056/NEJMsa110305.

Doan, T. N., Lennox, N. G., Taylor-Gomez, M., & Ware, R. S. (2013). Medication use among Australian adults with intellectual disability in primary healthcare settings: A cross-sectional study. *Journal of Intellectual & Developmental Disability*,*38*(2), 177-181. doi:10.3109/13668250.2013.778968

Einarson, T.R. (1993). Drug-related hospital admissions. *Annals of Pharmacotherapy, 27(7-8)*, 832-840.

Erickson, S.R., Salgado, T.M., & Tan, X. (2016). Issues in the medication management process in people who have intellectual/developmental disability: a qualitative study of the caregivers' perspective. *Intellectual and Developmental Disabilities,54(6),* 4412-426. DOI:10.1352/1934-9556-54.6.412.

Erickson, S.R., Nicaj, D., & Barron, S. (2018). Complexity of medication regimens of people with intellectual/developmental disabilities. *Journal of Intellectual & Developmental Disability, 43(3)*, 351-361. DOI: 10.3109/13668250.2017.1350836

Ferreira, J.M., Galato, D., & Melo, A.C. (2015). Medication regimen complexity in adults and the elderly in a primary healthcare setting: determination of high and low complexities. *Pharmacy Practice, 13(4),*:659. DOI: 10.18549/PharmPract.2015.04.659.

Field, T.S., Gurwitz, J.H., Harrold, L.R., Rothschild, J., DeBellis, K.R., Seger, A.C., Auger, J.C., Garber, L.A., Cadoret, C., Fish, L.S., Garder, L.D., Kelleher, M., & Bates, D.W. (2004). Risk factors for adverse drug events among older adults in the ambulatory setting. *Journal of the American Geriatric Society, 52(8),* 1349–1354.

Forster, A.J., Murff, H.J., Peterson, J.F., Gandhi, T.K., & Bates, D.W. (2003). The Incidence and severity of adverse events affecting patients after discharge from the hospital. *Annals of Internal Medicine, 138(3),* 161-167.

Hess, J.A., Matson, J.L., Neal, D., Mahan, S., Fodstad, J.C., Bamburg, J.A., & Holloway, J. (2010). A comparison of psychotropic drug side effect profiles in adults diagnosed with intellectual disabilities and autism spectrum disorders. *Journal of Mental Health Research in Intellectual Disabilities, 3(2)*, 85-96.

Kapell, D., Nightingale, B., Rodriguez, A., Lee, J.H., Zigman, W.B., & Schupf, N. (1998). Prevalence of chronic medical conditions in adults with mental retardation: comparison with the general population. *Mental Retardation, 36(4),* 269-279.

Kongkaew, C., Hann, M., Mandal, J., Williams, S. D., Metcalfe, D., Noyce, P. R., & Ashcroft, D. M. (2013). Risk Factors for Hospital Admissions Associated with Adverse Drug Events. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy,33*(8), 827-837. doi:10.1002/phar.1287

Kongkaew, C., Noyce, P.R., & Ashcroft, D.M. (2008). Hospital admissions associated with adverse drug reactions: a systematic review of prospective observational studies. *Annals of Pharmacotherapy, 42(7)*, 1017-1025. DOI:1 0.1345/aph.1 L037

Laditka, J.N., Laditka, S.B., & Probst, J.C. (2009). Health care access in rural areas: Evidence that hospitalization for ambulatory care-sensitive conditions in the United States may increase with the level of rurality. *Health & Place, 15(3),* 761-770.

Leendertse, A.J., Egberts, C.G., Stoker, L,J., & van den Bemt, P.M.L.A., for the HARM Study Group. (2008). Frequency of and risk factors for preventable medication-related hospital admissions in the Netherlands. *Archives of Internal Medicine, 168(17),* 1890-1896.

Leendertse, A.J., Visser, D., Egberts, A.C.G., & van den Bemt, P.M.L.A. (2010). The relationship between study characteristics and the prevalence of medication-related hospitalizations. A literature review and novel analysis. *Drug Safety, 33 (3),*233-244.

Lishner, D.M., Richardson, M., Levine, P., & Patrick, D. (1996). Access to primary health care among person with disabilities in rural areas: a summary of the literature. *The Journal of Rural Health, 12(1),*45-53.

McDonnell, P.J., & Jacobs, M.R. (2002). Hospital admissions resulting from preventable adverse drug reactions. *Annals of Pharmacotherapy, 36 (9),* 1331-1336.

Nair, N. P., Chalmers, L., Peterson, G. M., Bereznicki, B., Castelino, R. L., & Bereznicki, L. (2016). Hospitalization in older patients due to adverse drug reactions – the need for a prediction tool. *Clinical Interventions in Aging,*497. doi:10.2147/cia.s99097

O'Dwyer, M., Mccallion, P., Mccarron, M., & Henman, M. (2018). Medication use and potentially inappropriate prescribing in older adults with intellectual disabilities: A neglected area of research. *Therapeutic Advances in Drug Safety,9*(9), 535-557. doi:10.1177/2042098618782785

O'Dwyer, M., Peklar, J., Mccallion, P., Mccarron, M., & Henman, M. C. (2016). Factors associated with polypharmacy and excessive polypharmacy in older people with intellectual disability differ from the general population: A cross-sectional observational nationwide study. *BMJ Open,6*(4). doi:10.1136/bmjopen-2015-010505

Onder, G., Pedone, C., Landi, F., Cesari, M., Dell Vedova, C., Bernabei, R., & Gambassi, G. (2002). Adverse drug reactions as cause of hospital admissions: results from the Italian Group of Pharmacoepidemiology in the Elderly (GIFA). *Journal of the American Geriatric Society, 50(12),* 1962-1968.

Pirmohamed, M., James, S., Meakin, S., Green, C., Scott, A.K., Walley, T.J., Farrar, K., Park, B.K., & Breckenridge, A.M. (2004). Adverse drug reactions as cause of admission to hospital: prospective analysis of 18820 patients. *BMJ, 329(7456),*15-19.

Raschetti, R., Morgutti, M., Menniti-Ippolito, F., Belisari, A., Rossignoli, A., Longhini, P. & LaGuidara, C. (1999). Suspected adverse drug events requiring emergency department visits or hospital admissions *European Journal of Clinical Pharmacology, 54(12),* 959-963.

Robertson, J., Emerson, E., Gregory, N., Hatton, C., Kessissoglou, S., & Hallam, A. (2008). Receipt of psychotropic medication by people with intellectual disability in residential settings. *Journal of Intellectual Disability Research,44*(6), 666-676. doi:10.1111/j.1365-2788.2000.00307.x

Sarkar, U., Lopez, A., Maselli, J.H., & Gonzales, R. (2011). Adverse Drug Events in U.S. Adult Ambulatory Medical Care. *Health Services Research, 46(5),* 1517 – 1533. DOI: 10.1111/j.1475-6773.2011.01269.x

Scheifes, A., Walraven, S., Stolker, J. J., Nijman, H. L., Egberts, T. C., & Heerdink, E. R. (2016). Adverse events and the relation with quality of life in adults with intellectual disability and challenging behaviour using psychotropic drugs. *Research in Developmental Disabilities,49-50*, 13-21. doi:10.1016/j.ridd.2015.11.017

Sullivan, W.F., Diepstra, M.A., Heng, J., Ally, S., Bradley, E., Casson, I.,…Witherbee, S. (2018). Primary care of adults with intellectual and developmental disabilities. 2018 Canadian consensus guidelines. *Canadian Family Physician, 64*, 254-279.

Valdovinos, M. G., Caruso, M., Roberts, C., Kim, G., & Kennedy, C. H. (2005). Medical and Behavioral Symptoms as Potential Medication Side Effects in Adults With Developmental Disabilities. *American Journal on Mental Retardation,110*(3), 164. doi:10.1352/0895-8017(2005)1102.0.co;2

Willson, M.N., Greer, C.L., & Weeks, D.L. (2014). Medication regimen complexity and hospital readmission for an adverse drug event. *Annals of Pharmacotherapy, 48 (1)*,26-32. DOI: 10.1177/106002013510898

Wimmer, B.C., Dent, E., Bell, J.S., Wiese, M.D., Chapman, I., Johnell, K., & Visvanathan R. (2014). Medication regimen complexity and unplanned hospital readmissions in older people. *Annals of Pharmacotherapy, 48 (9)*, 1120-1128. DOI: 10.1177/1060028014537469

Winterstein, A.G., Sauer, B.C., Hepler, C.D., & Poole, C. (2002). Preventable drug-related hospital admissions. *Annals of Pharmacotherapy, 36(7-8),* 1238-1248.

Zaal, R. J., Kaaij, A. D., Evenhuis, H. M., & Bemt, P. M. (2013). Prescription errors in older individuals with an intellectual disability: Prevalence and risk factors in the Healthy Ageing and Intellectual Disability Study. *Research in Developmental Disabilities,34*(5), 1656-1662. doi:10.1016/j.ridd.2013.02.005

Table 1. Comparison of Independent Variables between Groups			
Variables	Intellectual Developmental Disability Group (Weighted estimate with percent)	General Population Group, without diagnosis of Intellectual/Developmental Disability (Weighted estimate with percent)	P-valve
Predisposing			
Age (years)			<0.001
18 to 29.9	42,565.9 (16.8%)	3,872,422.4 (13.0%)	
30 to 39.9	29,785.0 (11.8%)	3,409,413.0 (11.5%)	
40 to 49.9	35,290.0 (13.9%)	2,978,273.3 (10.0%)	
50 to 59.9	51,430.0 (20.3%)	4,574,622.2 (15.4%)	
60 to 69.9	42,285.0 (16.7%)	5,094,257.2 (17.1%)	
70 to 79.9	26,265.0 (10.4%)	4,756,302.1 (16.0%)	
80 and older	25,735.0 (10.2%)	5,030,806.2 (16.9%)	
Gender			<0.001
Female	109,899.9 (43.4%)	17,579,424.3 (59.2%)	
Male	143,424.9 (56.6%)	12,132,627.1 (40.8%)	
Race			<0.001
White	167,969.9 (70.5%)	19,256,472.8 (68.6%)	
Black	39,965.0 (16.8%)	4,129,377.6 (14.7%)	
Hispanic	19,405.0 (8.1%)	2,984,038.1 (10.6%)	
Asian	3,715.0 (1.6%))	701,659.6 (2.5%)	
Other	7,355.0 (3.1%)	979,184.6 (3.5%)	
Admission Type			<0.001
Elective	30,929.9 (12.2%)	7,451,871.3 (25.2%)	
Non-elective	221,674.9 (87.8%)	22,154,454.7 (74.8%)	
Enabling			
Payer			<0.001
Medicare	154,049.9 (60.9%)	13,816,025.4 (46.6%)	
Medicaid	58,314.9 (23.1%)	4,645,861.5 (15.7%)	
Private	26,534.9 (10.5%)	8,337,141.6 (28.1%)	
Self-pay	7,639.9 (3.0%)	1,640,503.5 (5.5%)	
Other	6,405.0 (4.1%)	1,229,459.6 (4.1%)	
ZIP Code of Residence Median Household Income Quartile ($)			<0.001
1-38,999	77,434.9 (31.5%)	8,536,694.2 (29.4%)	
39,000-47,999	68,179.9 (27.8%)	7,692,828.8 (26.5%)	

48,000-62,999	55,780.0 (22.7%)	6,976,282.4 (24.0%)	
63,000 or more	44,075.0 (18.0%)	5,822,646.9 (20.1%)	
Need			
Number of chronic conditions			<0.001
None			
1 to 3	0 (0.0%)	3,376,173.4 (11.4%)	
4 to 7	34,300.0 (13.5%)	7,660,813.6 (25.8%)	
8 or more	127,209.9 (50.2%)	11,648,046.6 (39.2%)	
	91,845.0 (36.3%)	7,031,062.9 (23.7%)	
Environmental			
Urban/Rural Designation			<0.001
Central counties of metro areas of >=1 million	69,645.0 (27.6%)	8,529,731.3 (28.9%)	
Fringe counties of metro areas >=1 million	56,950.0 (22.6%)	7,095,489.4 (24.0%)	
Counties in metro areas 250K-999K	49,079.9 (19.5%)	5,700,374.3 (19.3%)	
Counties metro areas 50K-249K	25,615.0 (10.2%)	2,795,973.9 (9.5%)	
Micropolitan counties	30,959.9 (12.3%)	3,262,973.6 (11.0%)	
Not metro or micropolitan counties	19,805.0 (7.9%)	2,179,353.9 (7.4%)	

Table 2. Multivariable Logistic Regression Models Determining the Association between Predisposing, Enabling and Need Variables with the Outcome of being Hospitalized for an Adverse Medication Event

Variable	Physical Medications AME Only Odds Ratio (95% CI)	Psychotropic Medications AME Only Odds Ratio (95% CI)	All Medications AME Odds Ratio (95% CI)
Predisposing			
Age category			
18 to 29 versus:	1	1	1
30 to 39	0.82 (0.78-0.86)	0.86 (0.82-0.90)	0.84 (0.81-0.86)
40 to 49	0.70 (0.67-0.74)	0.68 (0.64-0.71)	0.69 (0.66-0.71)
50 to 59	0.48 (0.45-0.50)	0.39 (0.37-0.42)	0.43 (0.42-0.45)
60 to 69	0.23 (0.22-0.25)	0.15 (0.13-0.16)	0.19 (0.18-0.20)
70 to 79	0.13 (0.12-0.14)	0.05 (0.048-0.059)	0.095 (0.09-0.10)
80 and over	0.09 (0.08-0.091)	0.02 (0.018-0.024)	0.054 (0.05-0.057)
Gender:			
Male versus Female	1.11 (1.08-1.15)	1.32 (1.28-1.37)	1.19 (1.17-1.22)
Race			
White versus:	1	1	1
Black	0.71 (0.68-0.74)	0.29 (0.28-0.31)	0.52 (0.50-0.54)
Hispanic	0.62 (0.59-0.65)	0.45 (0.43-0.48)	0.54 (0.52-0.57)
Asian	0.68 (0.61-0.76)	0.44 (0.38-0.51)	0.58 (0.53-0.63)
Other	0.89 (0.83-0.95)	0.62 (0.56-0.69)	0.77 (0.72-0.81)
Elective versus Non-Elective	11.04 (10.14-12.02)	14.47 (12.92-16.21)	12.35 (11.54-13.22)
Non-IDD versus IDD	1.27 (1.15-1.40)	1.29 (1.15-1.45)	1.28 (1.19-1.38)
Enabling			
Primary Payer			
Private versus:	1	1	1
Medicare	1.50 (1.43-1.56)	1.53 (1.45-1.62)	1.51 (1.46-1.56)
Medicaid	1.44 (1.38-1.50)	1.37 (1.31-1.44)	1.41 (1.37-1.46)
Self	2.52 (2.31-2.53)	2.22 (2.11-2.34)	2.35 (2.27-2.43)
Other	1.55 (1.46-1.65)	1.52 (1.41-1.63)	1.54 (1.47-1.62)
Annual ZIP Code Income ($)			
63,000 or more versus:	1	1	1
1 to 38,999	1.16 (1.11-1.22)	1.07 (1.01-1.13)	1.13 (1.09-1.17)
40,000 to 47,999	1.09 (1.05-1.14)	1.04 (0.99-1.10)	1.07 (1.04-1.11)
48,000 to 62,999	1.05 (1.00-1.10)	1.03 (0.97-1.09)	1.04 (1.006-1.08)
Need			
Number of diagnoses			
None versus	1	1	1
1 to 3	8.93 (8.04-9.92)	15.06 (12.96-17.49)	10.99 (10.09-11.99)

4 to 7	12.99 (11.66-14.46)	23.48 (20.16-27.35)	16.53 (15.14-18.05)
8 or more	10.94 (9.78-12.24)	15.37 (12.11-18.02)	12.69 (11.58-13.91)
Environmental			
Place/Urbanicity			
Central Metro > 1 Million versus:	1	1	1
Fringe Metro > 1 Million	0.92 (0.89-0.96)	1.02 (0.97-1.07)	0.96 (0.93-0.99)
Metro 250K to 99K	0.10 (0.96-1.04)	1.12 (1.07-1.18)	1.04 (1.01-1.08)
Metro 50K to 249K	1.02 (0.97-1.08)	1.13 (1.06-1.20)	1.06 (1.02-1.11)
Micropolitan	0.97 (0.93-1.02)	1.06 (1.00-1.13)	1.01 (0.97-1.05)
Not Metro or Micro	0.86 (0.81-0.92)	0.93 (0.86-1.01)	0.88 (0.84-0.93)
Model diagnostics			
R^2 Nagelkerke	0.09	0.13	0.12

AME = Adverse Medication Event

Unweighted total = 7,119,563. Valid = 5,743,359. Invalid (missing data) = 1,376,204

Weighted sample total = 27,485,908 people

The p values for each variable in the model were statistically significant ($p < 0.001$)