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The Impact of Drug Burden Index on Unplanned Hospital Readmission and Length of Hospital Stay

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ABSTRACT

Background: The Drug Burden Index (DBI) is a pharmacotherapy risk assessment tool explored to evaluate its association with unplanned hospital-related outcomes.
Objective: To evaluate the DBI association with unplanned hospital readmissions, develop a prediction model for unplanned readmissions. To investigate DBI association with length of hospital stay (LOS).
Setting: Unplanned readmission data were collected for 1000 adult hospitalized patients at Antrim Area Hospital in Northern Ireland.
Method: The study was designed as a retrospective analysis. Logistic regression models were developed to determine the prediction power. Discriminative ability testing was carried out using the Receiver Operating Characteristic (ROC) curve. Youden's index formula was used to detect the cut-off points. Analysis of covariance (ANCOVA) was performed to determine whether LOS differed based on the DBI score. Finally, negative binomial regression was used to predict LOS based on DBI.
Results: Of the 1000 patient records, 43% were females, and a total of 885 (88.5%) were exposed to sedative and anticholinergic medications (DBI>0). Readmission rates at 7, 14, 30 and 90 days were 5.4%, 9.0%, 15.0% and 28.8% respectively. The odds ratio (OR) of readmission within seven days for patients with DBI>1 was 3.42 times higher than those who had their DBI=0 (OR= 3.42, 95% CI: 1.6–7.3; P= 0.001). The DBI category significantly predicts 7-day readmission (P=0.002), the area under the curve for the ROC curve was 0.65 (95% CI: 0.58 - 0.71; P<0.001). For 14-day readmissions, patients with a DBI >1, compared with DBI=0, had a reported higher Odds Ratio (OR = 2.19, 95% CI: 1.1–4.4; P= 0.025). However, the DBI category prediction power for 14-day readmission was not significant (P=0.069). DBI failed to show an association with 30- and 90-day readmissions. The adjusted estimated marginal difference for LOS of patients with DBI>1 vs. DBI=0 was 2.7 (95%CI: 0.89 – 4.5; P=0.003).
Conclusion: DBI was a statistically significant tool to predict 7-days unplanned readmission. DBI was not a statistically significant predictor for readmission over longer periods. Higher DBI was associated with a longer LOS.
Impact on Practice Statements: Readmission within seven days of a patient's discharge can be predicted by the DBI, and a longer hospital stay was also associated with higher DBI. Accordingly, the hospital teams can consider reporting DBI scores and performing tailored discharge plans for patients who are at risk for seven days of unplanned readmission.

Keywords: Patient-centred Care, Drug Burden Index, Readmission, Length of Hospital Stay.

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Authors' contributions
The participation of each author corresponds to the criteria of authorship and contributorship emphasized in the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals of the International Committee of Medical Journal Editors. Indeed, all the authors have actively participated in the redaction, the revision of the manuscript, and provided approval for this final revised version.

Ethics approval
A detailed study protocol was submitted to the Northern Health and Social Care Trust (NHSCT) research governance for consideration. The committee did not have any issues regarding performing this research, and permission was granted to perform the study under the hospital quality improvement scheme.

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Conflict of interest
The authors declare that there is no conflict of interest regarding the publication of this article.

1. INTRODUCTION

Healthcare providers often use tools to support the assessment of appropriate medication use. Many specialized tools have been developed to target selected pharmacological groups of medicines. Several tools have focused on medicines with anticholinergic properties, for example, Anticholinergic Burden Classification (ABC) score (1); Anticholinergic Drug Scale (ADS) (2); Anticholinergic Risk Scale (ARS) (3); Anticholinergic Activity Scale (AAS) (4); Anticholinergic Load Scale (ACL) (5). Other scales have focused on sedative properties, e.g., The Scale of Sedative Load (6,7), Analgesic Ladder and Sedative Load (8), and the effect of central nervous system medication use (9–11).

The Drug Burden Index (DBI) was developed in 2007. It combines the two important features of sedative and anticholinergic effects(12). Since the DBI tool was published, many researchers have assessed its value in predicting health outcomes and using various study designs.

A negative association between high DBI scores and physical function has been detected through the following instrumental measurements: Aging and Body Composition (ABC) score (12), The Established Populations for Epidemiological Studies of the Elderly summary performance scale (13), Instrumental Activities of Daily Living (IADLs) scale (14,15), Barthel Index (15,16) and the Timed Up and Go (TUG) test (14). Recently, the association between DBI and nutrition status has been investigated, where malnutrition was found to be 2.21 times higher for every one-unit increase in DBI score (17).

In contrast, no consistent relationship was demonstrated with other physical function measurements. Wilson and colleagues (18) demonstrated no statistically significant associations between increasing DBI and impairment of grip strength, walking speed, or reaction time. High risk prescribing (as measured by the DBI score) was shown, however, to contribute to worsening frailty status in community-dwelling men (19), and lower DBI scores have been associated with better neurological health performance at discharge as measured by the Glasgow Coma Scale (GCS) (20).

Discussions continue regarding the association between DBI and fall-related hospital admissions. Researchers in Australia (21) concluded that no association existed, while an earlier study in New Zealand (22) concluded that DBI was associated with higher odds of fall-related hospitalization. Wilson and colleagues (23) reported that DBI was significantly and independently associated with the annual number of falls for older people living in residential aged care facilities. A similar conclusion confirmed that medication-related fall risk is associated with DBI (24).On the other hand, Kenya and colleagues reviewed risk factors for falls and measures of medication exposure. They found no significant association between falls risk with DBI (25).

The association between DBI and the health-related quality of life is inconsistent across different tools. For example, higher DBI scores were associated with lower five dimensions, five levels of the European group health-related quality of life utility measure, EQ-5D5L utility scores, but not Dementia (DE) Quality of life (QOL) measures as DEMQOL-Proxy-Utility or DEMQOL-Self-Report-Utility scores(17).

There is also a discussion on whether DBI can predict 30- and 90-day post-discharge hospital readmission and Length of hospital stay (LOS) during the readmission. Some researchers have shown DBI not to be a significant independent contributor to the prediction of 30 and 90 days post-discharge rehospitalization when other variables are controlled for (26,27). Other researchers have concluded that 'Readmitted patients were more likely to have a higher DBI' (28). Regarding LOS, some researchers found that DBI was an independent, significant predictor of longer LOS (16,20,27), while others have reported no association between increasing DBI and LOS (21,26).

2. AIM OF THE STUDY

The aim of the present study was to evaluate the impact of DBI on the prediction of unplanned hospital readmissions at 7, 14, 30- and 90-days post-discharge in a population of hospitalized patients in Northern Ireland. A further aim was to investigate the association between LOS and DBI score within this patient population.

3. METHODS

The study design was a cross-sectional, retrospective audit of data collected to investigate the risk factors for early acute hospital readmission of patients in the Antrim Area Hospital, a medium-sized teaching hospital (426-bed) within the Northern Health and Social Care Trust (NHSCT) in Northern Ireland. Anonymised, administrative Hospital Episodes Statistics (HES) records for 8575 adult patients admitted as acute or unscheduled medical admissions during 2011 were available for analysis. Full details of prescribed medications and doses were available for 5060 patients after application of exclusion criteria, i.e., patients

who died during their hospital stay, patients discharged directly from Accident & Emergency (A&E), or patients discharged to another hospital. A random sample of 1000 records was generated through SPSS version 18 for carrying out the present analysis.

The British National Formulary (BNF) and the Monthly Index of Medical Specialities (MIMS) were used to identify drugs with anticholinergic or sedative properties. For the present study, specific drug-related information, such as dose, route, and frequency of administration, were extracted from the original data set.

The DBI was calculated as follows (12):

$$DBI = \sum \frac{D}{D + \delta}$$

D: the daily dose of anticholinergic or sedative drug

δ: the minimum efficacious daily dose as recommended by the BNF version 61.

The standard tables of sample sizes required for logistic regression were reviewed to confirm a sufficient sample size (n=1000) and determine the desired statistical power. The later tables rely on the statistical power $\alpha = 0.05$ and $1 - \beta = 95$ percent (29,30).

To create and develop binomial logistic regression models, variables were first checked for normal distribution and were assessed to detect contribution to the outcome (readmission rate at 7, 14, 30, and 90 days). Student t-tests and chi-square or Fisher exact tests were used to determining associations. Variables that showed univariate unadjusted P values of less than 0.25 were considered for regression prediction modeling. Binomial logistic regression (backward stepwise) was used to eliminate independent predictors with non-statistically significant contributions (i.e., P-value more than 0.05). DBI, as a categorical independent predictor (31), had the following subgroups: DBI =0, which was coded to be the reference; the other two subgroups were low DBI exposure (DBI >0<1) and high DBI exposure (DBI >1).

Overall statistical significance tests for models were carried out to evaluate the quality of the logistic regression results (i.e., model fit). The Omnibus Test of Model Coefficients (32) was used, and the Hosmer and Lemeshow goodness of fit test (33). Moreover, Bootstrapping (34) was used to confirm statistically significant results for each predictor coefficient (B). Discriminative ability testing was carried out through Receiver Operating Characteristic (ROC) curve analysis (35,36). To detect the optimum cut off point, the Youden's index (j) formula was used (37,38)

j =Sensitivity (true positives) + Specificity (true negatives) – 1

Correlation between variables in the final model were obtained through the Pearson correlation coefficient (r), where the relationship was considered small if $0.1<|r|<0.3$, medium if $0.3 < |r| < 0.5$ and strong if $|r|> 0.5$.

Analysis of covariance (ANCOVA) was performed to determine whether LOS (in days) differed based on the three levels of DBI exposure (DBI=0, DBI>0<1, and DBI>1). To detect the predictive association between DBI and the index LOS (measured in the number of days), negative binomial regression was used, as the data showed an over-dispersed count, i.e. conditional variance exceeded the conditional mean (39). The Akaike's Information Criterion (AIC) and Bayesian Information Criterion (BIC) were used to compare the goodness of fit.

4. RESULTS

4.1. Demographic characteristics of the study population

Table 1 highlights the demographic characteristics of the study population. The majority of discharged patients (84%) were prescribed at least one high alert medicine, i.e., medicines considered by the hospital as high-risk medicines for medication-related problems. The most commonly prescribed high alert medicines were antiplatelet, opioids, and beta-blockers (36.8%, 27.4%, and 27.5%, respectively). Approximately two-thirds of the population were prescribed central nervous system medications (70.7%). Table 2 lists patient medication on discharge.

Unplanned readmission rates at 7, 14, 30 and 90 days were 5.4%, 9.0%, 15.0% and 28.8% respectively. Using univariate unadjusted analysis, DBI showed an association (P<0.25) with 7- and 14-day readmission. It failed to show any association with 30- and 90-day readmission (Table 3). Accordingly, multivariate analysis was performed only for the 7- and 14-day readmission periods.

4.2. Drug burden index and 7-day readmission

The final logistic regression model revealed that both lengths of index hospital stay and the DBI were significant variables for predicting hospital readmission within seven days (Table 4).

Table 1: Main characteristics of the study population (n=1000)

Characteristic	Number (%) or Mean + Standard Deviation
Gender	
Male	429 (43 %)
Female	571 (57%)
Age (years)	**68.8 ± 8.8**
18 - 30	62 (6.2 %)
31 - 45	94 (9.4 %)
46 – 65	231 (23.1%)
> 65	613 (61.3%)
Charlson comorbidity index (CCI)	**3.17 ± 0.9**
0	84 (8.4%)
1-2	160 (16%)
3-4	254 (25.4%)
> 4	502 (50.2%)
Length of index hospital stay	**6.04 ± 7.6**
> 2 days	631 (63.1%)
≤ 2 days	369 (36.9%)
Drug Burden Index	**2.2 ± 1.6**
DBI Non-exposure (DBI = 0)	115 (11.5%)
DBI exposure (DBI > 0)	885 (88.5%)
DBI >0 and <1	162 (16.2%)
DBI ≥ 1	723 (72.3%)
Number of medications per patient	**8.2 ± 5.0**
1-3 medicines	279 (27.9%)
4-9 medicines	329 (32.9%)
10-14 medicines	283 (28.3%)
15 medicines or more	109 (10.9%)
Method of Discharge	
Normal discharge	818 (81.8%)
Nurse-led discharge	181 (18.1%)
Self-discharge	1 (0.1%)
Discharge to nursing home	
Yes	106 (10.6%)
No	894 (89.4%)

The probability of the Wald statistic within the final model showed that the odds of readmission within seven days for patients who had received high doses of sedative and/or anticholinergic medicines (i.e., DBI >1) were 3.42 times higher than for those patients who had no exposure (OR= 3.42, 95% CI: 1.6–7.3; P= 0.001). Also, when considering the sub-group DBI=0 as a reference, patients who were exposed to low doses of sedative and/or anticholinergic medicines (i.e., DBI >0 and < 1) had an odds ratio (OR) of 1.52. However, this ratio failed to demonstrate statistical significance (95% CI: 0.71 – 3.3; P= 0.29).

Bootstrapping indicated the following statistical contribution of predictors within the final model: LOS (P=0.001), DBI >1 (P=0.001), DBI >0<1 (P= 0.29). The overall model was statistically significant using the Omnibus Test of Model Coefficients (P<0.001). The Hosmer and Lemeshow goodness of fit test was not statistically significant (P= 0.32), indicating no evidence of poor fit.

The resultant risk factor model constructed a receiver operating characteristic (ROC) curve (Figure 1). The area under the curve (AUC) for the ROC curve (ROC AUC) was 0.65 (95% CI: 0.58 - 0.71; P<0.001), indicating that the model's discrimination ability was modest but statistically significant.

According to the highest Youden's index (j) value, the optimum cut-off was set at a predicted probability score of 0.04 (predicted probability score range 0.01-0.20), which yielded 94.4% sensitivity (true positive) and 30.8% specificity (true negative).

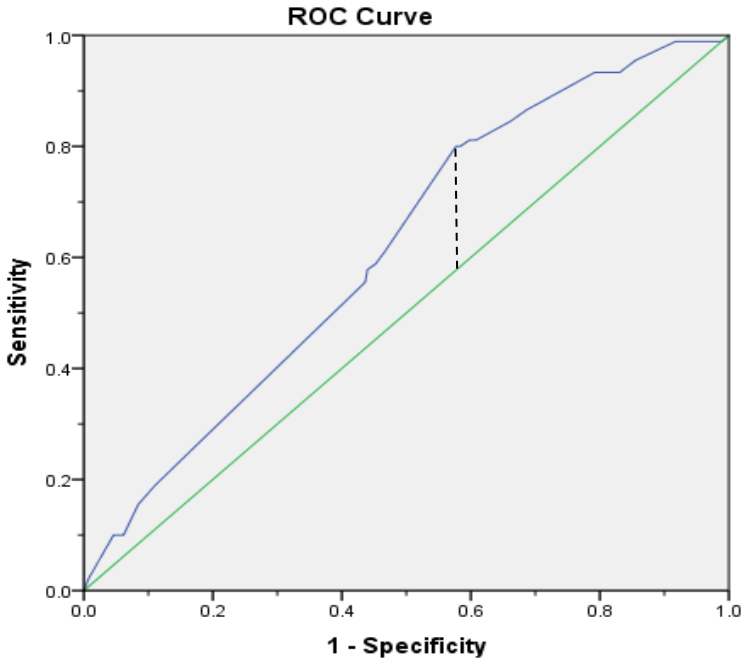

Figure 1: Area under the curve for logistic regression model for 7-day post-discharge readmission (Solid blue line: ROC curve; solid green line: chance level; Vertical black dashed line: (J) maximum value of Youden's index for the ROC curve.

Table 2: Medication on discharge, n= number of patients (% of sample size).			
BNF medication chapter (organ systems)			
Gastrointestinal	559 (55.9%)	Malignant	30 (3%)
Cardiovascular	665 (66.5%)	Nutrition	320 (32%)
Respiratory	267 (26.7)	Musculoskeletal	114 (11.4%)
Central nervous system	707 (70.7%)	Eye	95 (9.5%)
Infection	342 (34.2%)	ENT	62 (6.2%)
Endocrine	399 (39.9%)	Skin	81 (8.1%)
Gynaecology	86 (8.6%)	Anaesthesia	3 (3%)
High-alert medicines (840 patients received at least one high alert medicine)			
NSAIDs	52 (5.2%)	Digoxin	75 (7.5%)
Diuretic	260 (26%)	Prednisolone	134 (13.4%)
ACE inhibitors/ARB	230 (23%)	Anti-platelet	368 (36.8%)
Antidepressant	240 (24%)	Anticoagulant	108 (10.8%)
Lithium	5 (0.5%)	Antiepileptic	98 (9.8%)
Beta blockers	274 (27.4%)	Antidiabetics	126 (12.6%)
Opiates	275 (27.5%)	Potassium	26 (2.6%)

4.3. Drug burden index and 14-day readmission

Length of hospital stay at index admission and Charlson comorbidity index (CCI) was found to be statistically significant predictors using the regression model. Even though the high DBI sub-group (DBI>1), when compared to the non-exposure sub-group (DBI=0), showed a statistically significant impact (P=0.025), the combined DBI variable showed only a trend toward readmission prediction (P=0.069) as shown in Table 5. Patients with high DBI (i.e. DBI >1) had higher OR for 14-day readmission compared with non-exposed patients (OR = 2.19, 95% CI: 1.1– 4.4; P= 0.025). The OR for patients with low exposure (i.e., DBI >0 and <1) was not statistically significantly different when compared with no exposure (OR = 1.42, 95%CI: 0.75 – 2.7; P=0.28).

Bootstrapping demonstrated the following statistical contribution for predictors within the final model: LOS (P=0.007), CCI (P=0.021), DBI >1 (P=0.032), DBI >0 and < 1 (P=0.3). The overall model was statistically significant, i.e., the Omnibus Test of Model Coefficients (P=0.002). The Hosmer and Lemeshow goodness of fit test was not statistically significant (P=0.29), indicating no evidence of poor fit.

The ROC curve shown in Figure 2 illustrates the discriminative ability of the regression model for the 14-day readmission data. Based on the area under the curve, the model prediction ability was modest but statistically significant (C=0.62, 95% CI: 0.56-0.67; P<0.001). According to the highest j value (Youden index), the optimum cut-off point was found at the predicted probability score of 0.09 (predicted probability score range 0.02 - 0.24), which yielded 80% sensitivity and 42.3% specificity.

The DBI showed a statistically significant medium correlation with the CCI (r=0.36; P<0.001) and a statistically significant but lower correlation with LOS at index admission (r=0.14; P<0.001)

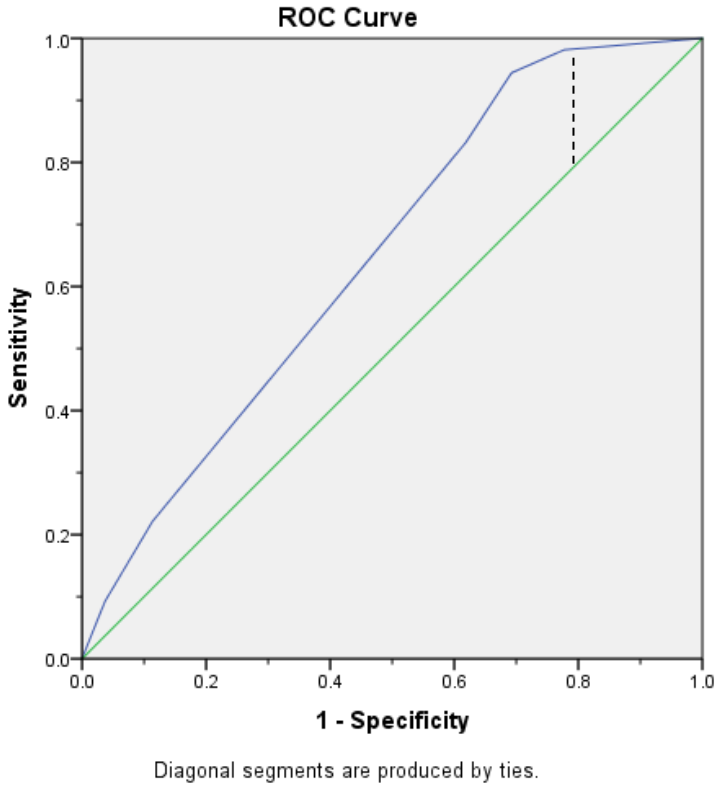

Figure 2: Area under the curve for logistic regression model for 14-day post-discharge readmission (Solid blue line: ROC curve; solid green line: chance level; Vertical black dashed line: (J) maximum value of Youden's index for the ROC curve.

4.4. Association of DBI with the length of hospital stay

Figure 3(a) shows the analysis of covariance for the association of the mean length of hospital stay (LOS) and the DBI. The unadjusted estimated marginal difference for LOS of patients with DBI>1 and DBI=0 was 3.8 days (95%CI: 1.9 – 5.6; P<0.001) after adjustment for age, gender, Charlson comorbidity index, nursing home status and discharge during weekend days. (Figure 3.b) the difference was 2.7, i.e., statistical significance was retained (95%CI: 0.89 – 4.5; P=0.003).

Table 6 displays the association between LOS-based and DBI. Findings of the final negative binomial regression model indicated that for every unit (0.1) DBI scores increase (as a

continuous independent variable), there would be a predicted 6.7% increase in LOS days. The adjusted Incidence Rate Ratio (IRR) was 1.067 (95% CI: 1.02 – 1.12; P =0.005). When patients with a DBI score of 0 (as a categorical independent variable) were considered as the reference subgroup, the adjusted IRR for the high DBI subgroup was 1.77 (95% CI: 1.4-2.2; P<0.001), and it was 1.54 (95% CI: 1.2-2.0; P=0.002) for the low DBI subgroup.

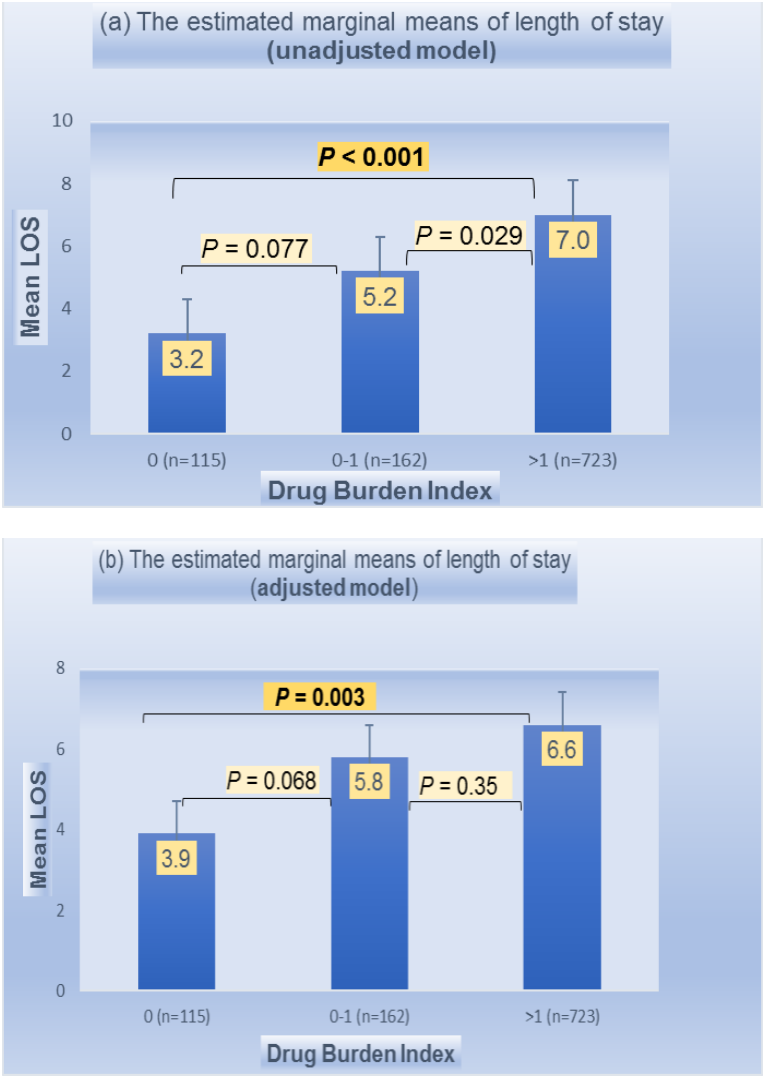

Figure 3: Analysis of covariance for the association of adjusted means of length of hospital stay in days with Drug Burden Index subgroups. Error bars show 95% confidence interval. Adjusted model for age, gender, Charlson comorbidity index, nursing home status and discharge during weekend days.

5. DISCUSSION

In the present work, the impact of DBI on readmission and LOS at the index admission were investigated retrospectively. A high proportion of patients (88.5%) in the present cohort had been prescribed anticholinergic and/or sedative medicines (i.e., DBI>0). In the literature, one study reported that the proportion of elderly hospitalized patients with DBI>0 was 78.8% (40), while other studies documented these proportions to be 69.9% (18) and 52% (16). Studies that were carried out in a community-dwelling patient population, however, showed lower proportions of exposure to anticholinergic and/or sedative medicines, i.e., 38% (26), 37% (14), and 34% (41).

The mean DBI for the study population was 2.2 (SD± 1.6), higher than in other studies that utilized the index. For example, studies carried out in Australia reported a mean DBI of 0.60 (SD± 0.66) (18,42), 0.58 (SD± 0.64) (43), 0.22 (SD± 0.42) (44) and 0.18 (SD ± 0.35) (14). Studies in the USA reported mean DBI scores of 1.55 (SD± 1,26), 1.00 (SD± 0.92) (28) and 0.18 (SD ± 0.35) (12). Studies in Finland had mean DBI values of 0.45 (SD± 0.59) and 0.27 (SD± 0.49) (27). Another study in the UK reported that the median DBI was 0.48

Table 3: Univariate unadjusted analysis to detect association between variable and readmissions at different time intervals.

Variables relating to the reference admission	7 days *P* value	14 days *P* value	30 days *P* value	90 days *P* value
Gender	0.17* [a]	0.59 [a]	0.64 [a]	0.058* [a]
Age (in years)	0.69 [b]	0.26 [b]	0.070* [b]	0.049* [b]
Charlson comorbidity index	0.18* [b]	0.035* [b]	<0.001* [b]	< 0.001* [b]
Drug Burden Index	0.021*	0.215* [b]	0.63 [b]	0.300 [b]
Length of stay (≤ 2 days; >2 days)	0.074* [a]	0.005* [a]	<0.001* [a]	< 0.001* [a]
Discharge on weekend day	0.42 [a]	0.29 [a]	0.38 [a]	0.87 [a]
Discharge to nursing home	0.9 [a]	0.38 [a]	0.98 [a]	0.56 [a]
Primary diagnosis (ICD chapters)				
- Infection	1.0 [c]	1.00 [c]	0.78 [c]	0.42 [a]
- Neoplasm	1.0 [c]	1.00 [c]	1.000 [c]	0.34 [a]
- Blood	0.27 [c]	0.22* [c]	0.17* [c]	0.045* [a]
- Endocrine	0.71 [c]	0.54 [c]	0.72 [a]	0.68 [a]
- Mental health	1.0 [c]	1.00 [c]	1.00 [c]	0.33 [c]
- Nervous system	0.68 [c]	1.00 [c]	0.60 [c]	0.34 [a]
- Eye, Ear and other similar factors	1.0 [c]	1.00 [c]	1.00 [c]	0.51 [c]
- Circulatory	0.66 [a]	0.98 [a]	0.48 [a]	0.95 [a]
- Respiratory	0.88 [a]	0.46 [a]	0.36 [a]	0.80 [a]
- Digestive	0.19* [a]	0.92 [a]	0.44 [a]	0.47 [a]
- Skin	0.19* [c]	0.64 [c]	0.48 [c]	1.00 [c]
- Musculoskeletal	0.39 [c]	0.50[c]	1.00 [c]	0.97 [c]
- Genitourinary	0.80 [c]	0.23* [a]	0.41 [a]	0.98 [a]
- Pain, symptoms, not elsewhere classified	0.17* [a]	0.11* [a]	0.37 [a]	0.50 [a]
- Injury/Poisoning	1.0 [c]	0.75 [c]	0.15* [a]	0.08* [a]

a Chi square test.
b independent sample t-test
c Fisher's Exact Test
* Significant contribution at P<0.25

(IQR 0.0-1.0) (16). In a recently published cluster-randomized clinical trial, there was no significant reduction in DBI exposure in older adults at 3-months follow-up when comparing home care systems and computerized clinical decision support systems (17). Patients in the current study were hospitalized, while most other studies were carried out in community settings or residential care facilities. Differences in prescribing habits and the differences in the minimum recommended daily doses (δ) that different medicinal product information agencies list offer possible explanations for differences across different countries.

It is widely accepted for sample size calculations that a minimum of ten events for each variable should be used with logistic regression models (30,45–49). In the present study, all logistic regression models were well more than this 10:1 ratio.

The age range (>18 years) of the population (n=1000). Many previous studies tended to target more homogenous patient groups with smaller sample sizes. For those studies that

Table 4: Multivariable logistic regression for 7-day readmission predictors.

Variable	B (SE)		Odds ratio	95% CI		*P* value
				Lower	Upper	
Length of stay	1.41	0.39	4.08	1.90	8.76	<0.001*
DBI category						0.002*
DBI (0)			1 (reference)			
DBI (>0 and <1)	0.42	0.39	1.52	0.71	3.28	0.29
DBI ≥1	1.23	0.38	3.42	1.61	7.27	0.001*
Constant	-4.16	0.39	0.016			<0.001*

Variable(s) entered at step 1: Length of hospital stay, Drug Burden index, Charlson comorbidity index, gender, primary diagnosis of: skin related disorders, pain and symptoms (not elsewhere classified), digestive system disorders.
* Statistically significant P<0.05

targeted hospitalized patients, one study was conducted in critically ill patients >65 years at a neuroscience intensive care unit(n=112), mean DBI was not reported (20),
while another used data for patients (>60 years) admitted to a geriatric medicine unit, (n=362), median DBI was 0.48 (16). Data for patients who were admitted with hip fractures and scheduled for surgery (aged >65 years, n=71, DBI range for the anticholinergic component was 0.0 – 1.75) were analyzed in another study (50). A study that targeted only vulnerable patients was carried out in the USA, in which the population was aged >65 years, n=229, mean DBI was 1.55 (28).

The present study findings indicate that DBI could predict 7-day readmission. The relationship between DBI and rehospitalization was not unexpected due to the well-known side effects of anticholinergic and sedative medicines (51),(52). However, this ability was attenuated when the 14-day readmission rates were considered (Tables 4, 5). In both time intervals receiving a DBI > 1 was associated with a statistically significant higher OR for readmission when compared with non-exposed patients. Logistic stepwise regression was carried out to take account of possible confounders, e.g., CCI (33,53), together with bootstrapping to ensure that the prediction model was robust. Model discrimination testing was also performed.

Similar to the present findings, other studies have found that DBI is not a significant independent predictor of 30 and 90 days post-discharge rehospitalization when controlling for other variables (26,27). In one study which examined the association between DBI and 30-day readmission rate, the authors stated that 'Readmitted patients were more likely to have higher DBI' (28). In this latter study, which was carried out in a vulnerable elderly patient population (n=229; >65years), the 30-day readmission dataset was not, however, controlled and/or adjusted for other variables or confounders (28).

A higher DBI score was also associated with a longer LOS in the index admission (Figure 3); this is in line with results from three other studies (16,20,27). Other researchers (26) found that higher DBI was associated with a longer hospital stay in univariate analysis. The adjusted regression model was not shown as a significant independent predictor for a longer hospital stay. Another study (21) concluded that there was no association between increasing DBI and length of hospital stay. However, the latter study reviewed the impact of the DBI on LOS values of more than ten days, while in the present study and other studies, which confirmed an association, the impact of DBI was detected when LOS was less than ten days. LOS was a significant predictor for both 7- and 14-days readmission in the present work, while CCI was a significant predictor for 14 days of readmission. This was not unexpected, as many previous studies have confirmed that both variables are powerful predictors for hospital readmissions (54–61).

The present study has a number of limitations. Firstly, data for the present study were obtained from a single hospital (Antrim Area Hospital), which may limit the generalizability of the results. Secondly, due to the retrospective approach taken in this research, some data were not available, e.g., change in DBI during hospitalization between admission and

Table 5: Multivariable logistic regression for 14-day readmission predictors.

Variable	B (SE)		Odds ratio	95% CI		*P* value
				Lower	Upper	
Length of stay	**0.72**	**0.27**	**2.06**	**1.20**	**3.52**	0.008*
Charlson comorbidity index	**0.32**	**0.14**	**1.37**	**1.05**	**1.80**	0.023*
DBI category						**0.069**
DBI (0) Reference			**1 (reference)**			
DBI (>0 and <1)	**0.35**	**0.33**	**1.42**	**0.75**	**2.67**	**0.28**
DBI ≥1	**0.79**	**0.35**	**2.19**	**1.10**	**4.36**	0.025*
Constant	**-4.01**	**0.39**	**0.28**			<0.001*

Variable(s) entered at step 1: length of hospital stay, Drug Burden index, Charlson comorbidity index, gender, primary diagnosis of: blood, genitourinary, pain and symptoms, not elsewhere classified.
***Statistically significant P<0.05**

Table 6: Association between length of hospital stay and drug burden index.

Adjusted model [a]						
	B	SE	P value	IRR	95% CI	
					Lower	Upper
DBI continuous score	0.065	0.0023	0.005	1.067	1.02	1.11
DBI = 0	0			1 (Reference)		
DBI >0 and<1	0.43	0.14	0.002	1.54	1.17	2.01
DBI ≥ 1	0.57	0.12	<0.001	1.77	1.40	2.24

CI= confidence interval. B=coefficient estimates. SE= Standard Error. IRR= incidence rate ratio.
[a] Negative binomial regression model adjusted for age, gender, Charlson comorbidity index, nursing home status and discharge on weekend days.

discharge. Moreover, information available was limited regarding the duration of treatment with the anticholinergic and/or sedative medicines. Reasons for readmissions were not available for all cases. Therefore it was not feasible to assess the possible relationship between DBI and specific readmission categories, e.g., fall-related readmission or delirium-related readmission. The DBI calculation was based on medical records, which may not accurately reflect the true medication exposure.

6. CONCLUSION

The present study demonstrated that patients who were prescribed high doses of anticholinergic and/or sedative medications (DBI > 1), despite their disease conditions, were at a greater risk of short interval hospital readmission (7-day and 14-day) compared with those who were not prescribed such medicines (DBI=0). As an independent variable, DBI could significantly predict 7-day readmission rates. DBI demonstrated no significant role in the prediction of 30-day and 90-day readmissions. Length of hospital stay was associated with a higher DBI as an independent variable.

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