



Citation for published version:

Olender, RT, Roy, S, Jamieson, HA, Hilmer, SN & Nishtala, PS 2024, 'Drug Burden Index is a Modifiable Predictor of 30-Day-Hospitalization in Community-Dwelling Older Adults with Complex Care Needs: Machine Learning Analysis of InterRAI Data', *Journal of Gerontology: series A - Medical Sciences*.
<https://doi.org/10.1093/gerona/glae130>

DOI:

[10.1093/gerona/glae130](https://doi.org/10.1093/gerona/glae130)

Publication date:

2024

Document Version

Peer reviewed version

[Link to publication](#)

Publisher Rights

CC BY

University of Bath

Alternative formats

If you require this document in an alternative format, please contact:
openaccess@bath.ac.uk

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Drug Burden Index is a Modifiable Predictor of 30-Day-Hospitalization in Community-Dwelling Older Adults with Complex Care Needs: Machine Learning Analysis of InterRAI Data.

Robert T. Olender MRes* ¹, Sandipan Roy PhD ², Hamish A. Jamieson PhD ³, Sarah N. Hilmer, PhD ⁴, Prasad S. Nishtala PhD ⁵

*Corresponding Author

¹ Department of Life Sciences, University of Bath, UK (rto20@bath.ac.uk)*

² Department of Mathematical Sciences, University of Bath, UK (sr2081@bath.ac.uk)

³ Department of Medicine, University of Otago, Christchurch, New Zealand (Hamish.jamieson@otago.ac.nz)

⁴ Kolling Institute, Faculty of Medicine and Health, Northern Clinical School, The University of Sydney and Northern Sydney Local Health District, St Leonards, New South Wales, Australia (sarah.hilmer@sydney.edu.au)

⁵ Department of Life Sciences & Centre for Therapeutic Innovation, University of Bath, UK (pn403@bath.ac.uk)

Word Count (Abstract): 246.

Word Count (Main text, excl. figure legends and references): 3953.

Number of data elements in the main text: 5 (2 tables, 3 figures).

Abstract

Background: Older adults (≥ 65 years) account for a disproportionately high proportion of hospitalization and in-hospital mortality, some of which may be avoidable. Although machine learning (ML) models have already been built and validated for predicting hospitalization and mortality, there remains a significant need to optimise ML models further. Accurately predicting hospitalization may tremendously impact the clinical care of older adults as preventative measures can be implemented to improve clinical outcomes for the patient.

Methods: In this retrospective cohort study, a dataset of 14,198 community-dwelling older adults (≥ 65 years) with complex care needs from the Inter-Resident Assessment Instrument database was used to develop and optimise three ML models to predict 30-day-hospitalization. The models developed and optimized were Random Forest (RF), XGBoost (XGB), and Logistic Regression (LR). Variable importance plots were generated for all three models to identify key predictors of 30-day-hospitalization.

Results: The area under the receiver operating characteristics curve for the RF, XGB and LR models were 0.97, 0.90 and 0.72, respectively. Variable importance plots identified the Drug Burden Index and alcohol consumption as important, immediately potentially modifiable variables in predicting 30-day-hospitalization.

Conclusions: Identifying immediately potentially modifiable risk factors such as the Drug Burden Index and alcohol consumption is of high clinical relevance. If clinicians can influence these variables, they could proactively lower the risk of 30-day-hospitalization. ML holds promise to improve the clinical care of older adults. It is crucial that these models undergo extensive validation through large-scale clinical studies before being utilized in the clinical setting.

Keywords: Artificial intelligence, Logistic Regression, Decision tree, Predictive modelling, Hospitalization

Introduction

Older adults aged ≥ 65 years are a growing population, which accounts for the highest proportion of hospitalizations and in-hospital deaths[1] and exhibits the highest multimorbidity[2]. These factors pressure healthcare systems, older adults requiring additional care and medical resources. For older adults, hospitalization should be avoided unless necessary[3]. Hospitalization increases the chances of patient complications, such as hospital-acquired pneumonia[4], hospital-acquired incontinence[5], deep vein thrombosis[6], pulmonary embolism[7], pressure ulcers[8], falls and related injuries[9], delirium[10]. Identifying patients at high risk of hospitalization can provide opportunities to intervene to prevent unnecessary admissions and to facilitate and resource care for individuals who need treatment in the hospital.

Traditional statistical approaches are parsimonious, have several limiting *a priori* assumptions and do not give insight into the importance of each variable for predicting the outcome. Machine Learning (ML) models do not suffer these drawbacks[11]. There is an immediate need to develop accurate predictive models to identify high-risk individuals and factors associated with an increased risk of unfavourable clinical events, such as mortality and hospitalization[12]. ML approaches have been shown to produce highly accurate models predicting clinical outcomes such as mortality[13] and delirium[14] from older adults' patient data. It should be noted that ML models are not expected to replace traditional statistical approaches or clinical acumen but rather become an additional tool in health service planning and the armamentarium of a skilled clinician.

The true power of ML models lies in identifying modifiable factors highly associated with unfavourable clinical events such as hospitalization. A non-modifiable risk factor, such as sex or age, can provide insight into the likelihood of an unfavourable clinical event. However, while helpful for planning health services or prioritizing patients for clinical review, this information is of little relevance to individual clinical management. On the contrary, it has been shown in multiple studies that identifying modifiable risk factors provides great clinical insight to clinicians, ultimately leading to a lowered risk of unfavourable clinical events[15-17]. Inappropriate medication use, defined as the use of medications where the current harm outweighs the benefit for the individual, is a modifiable risk factor closely associated with increased hospitalization rates and mortality in older adults[18, 19]. The Drug Burden Index (DBI), a validated metric, quantifies an individual's exposure to anticholinergic and sedative medications[20]. The DBI is a practical measure of cumulative risk of medication-related functional impairment in older adults[21], which is important clinical consideration when identifying inappropriate polypharmacy. Given that modifiable risk factors such as the DBI can be identified, this can directly inform clinical care of older adults[22], improving clinical outcomes and minimising the risk of unfavourable clinical events.

This study assesses the importance of several risk factors in predicting 30-day-hospitalization in older adults aged 65 years and over with complex care needs. Identifying modifiable risk factors associated with hospitalization could tremendously impact geriatric care and future direction regarding models of care to reduce unnecessary hospitalizations and prescribing guidelines in older adults[23].

This study aimed to:

1. Develop three ML classification models to predict 30-day-hospitalization.

2. Evaluate three ML classification models in terms of discriminatory power.
3. Identify important modifiable risk factors in predicting 30-day-hospitalization.

Three ML classification models were developed as part of this study: Random Forest (RF), XGBoost (XGB), and Logistic Regression (LR). RF is a widely used ML approach which combines the output of multiple decision trees to reach a single result[24]. XGB is a gradient-boosting algorithm. While RF trains multiple trees in parallel and outputs the most common outcome, XGB creates a sequential ensemble of improved tree models to predict the outcome[25]. LR describes the relationship between a dependent binary outcome variable and several independent input variables[26].

Methods

The Academic Ethics and Integrity Committee at the University of Bath has approved this project (Form No: 6738). The dataset utilized in this study was the InterRAI Home Care Assessment System repeat assessment at baseline. InterRAI is a collection of instruments utilized internationally to provide clinicians with insights into a patient's individual care requirements. In New Zealand, the Home Care assessment (InterRAI-HC) is employed to assess individuals with complex care needs looking to enter publicly funded aged residential care, while the shorter Contact assessment is utilized for those seeking home-based support services. Both assessments encompass a range of questions that cover various aspects, including medical, social, and functional well-being, to provide a comprehensive evaluation. The InterRAI-HC assessment includes 236 questions spanning 20 domains. Data collection is performed by assessors specifically trained and assessed by the Ministry of Health New Zealand, ensuring high data collection quality. Further yearly quality assessments ensure consistency [27]. More detailed information concerning InterRAI can be found at <https://interrai.org/>.

Participant Selection

For the current study, from InterRAI-HC, we isolated a retrospective condensed dataset pertaining to a cohort of community-dwelling older adults aged ≥ 65 years with complex care needs, focusing on extracting key demographic and phenotypic data with minimal missing values. InterRAI participants included in this study exhibit high levels of morbidity, with over 20% of participants hospitalized 30 days prior to assessment. The assessment date for the patients was between 01/06/2012 and 30/06/2014. The timeframe and the fact that all participants are from the same country increases the homogenous nature of the sample in terms

of clinical management. The full dataset contained 105,502 assessments of 70,159 participants and 597 variables[28]. The condensed dataset, published in previous literature, contained 14,198 participants and 26 variables [29]. The condensed dataset contained zero missing values. **Figure 1** shows the participant selection flowchart. As all variables within the dataset are categorical, the summary in **Table 1** (Supplemental Material) describes them in terms of relative frequencies. The primary outcome was 30-day-hospitalization, defined as any hospitalization related to any clinical event within 30 days. Hospital admission data was obtained from the complete InterRAI dataset. The baseline assessment determined the 30 day hospital admission window. Questions A12, A14, N4 and S2 from the ‘interRAI Home Care Assessment Form’ refer to hospitalization. The study contained several exclusions. Firstly, 6,404 assessments were conducted on participants who did not live at home. Participants not living at home represent a different cohort, with higher levels of multimorbidity, different factors influencing hospitalization due to different functional and clinical support available in the nursing home, and a higher prevalence of advance care directives limiting hospital care. Secondly, in our analyses, we included participants who had undergone more than one interRAI assessment to analyse a homogenous population and mitigate potential selection bias.

Figure 1. InterRAI Participant selection flowchart.

[Figure 1 uploaded as a separate JPG file.]

Note. DOD – Date of Death, DOA – Date of Admission, ARC – Admission to Residential Care.

DBI Calculations

The DBI data was obtained from the New Zealand Pharms dataset between 2012-2014, which is linked to interRAI[30]. Pharms contains information regarding the drug name, dose, daily dose, base units, strength, frequency, therapeutic group, quantity prescribed and dispensed and

the provider type. Hospitalization data was obtained from the National Minimum Dataset, which contains information regarding the hospitalization start date, end date and event type.

The DBI was calculated as follows;

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

Where D is the daily dose taken (estimated from dispensing data), and MDD is the minimum daily dose licenced for adults in New Zealand. The equation above considers all formulations of one medication. The patient's DBI is the sum of the DBI's calculated for each medication they are dispensed.

Data Preparation

The dataset was unbalanced concerning 30-day hospitalization, with 2,857 having a hospitalization and 11,341 not having a hospitalization. Therefore, SMOTE (Synthetic Minority Oversampling Technique) was utilized to oversample the minority class. This was done to minimise the impact of an unbalanced dataset which could obscure underlying patterns and associations, potentially leading to misleading conclusions. After SMOTE, the dataset contained 22,864 observations. To assess predictive performance, the dataset was split, 70:30, into a training ($n = 15,867$) and validation cohort ($n = 6,997$), respectively. For 11,523 observations, the 30-day hospitalization flag was positive and 11,341 negative. All variables from the condensed dataset were included in the analysis; these can be seen in **Table 1**.

ML Model Development and Validation

Variables selection was based on demographic variables and variables deemed clinically relevant for predicting short term hospitalization in the available literature[31-38]. Initially, all variables were converted to factors, and a reference factor level for each variable was set. The ‘hospitalization’ variable was converted from a 4-level factor to a binary factor representing 30-day hospitalization as a Y/N. DBI was refactored into one of two sub-groups (0-1 considered low and >1 high), in line with previous literature[20, 30, 39]. Three classification models were developed and validated during the project: LR, RF, and XGB. The same seed (‘7895’) was used for all models. A full binomial model was run using all variables using 100 times repeated cross-validation (2 repeats) for the LR model. For the RF model, Mtry was optimized to 6, and the remaining hyperparameters were left at default. For the XGB model, the independent variables in the training and validation dataset were one-hot encoded. The model was tuned using a tuning grid, optimising for nrounds, max_depth, eta, gamma, colsample_bytree, min_child_weight and subsample. All three models utilized all baseline variables. The LR, RF and XGB models underwent 100 times repeated cross-validation (2 repeats) using the ‘Nimbus’ high-performance computing unit at the University of Bath. Model performance was evaluated using Area Under the Receiver Operating Characteristics curve (AUC-ROC), accuracy, balanced accuracy, sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and F1 Score. All results have been presented in interpretable formats, ensuring benefit to the clinician. All models were built and evaluated in R version 4.3.0. The ML code has been deposited in a GitHub repository: https://github.com/RobertOlender/ML_InterRAI_Hospitalization_28092023

Variable Importance

Variable importance plots were generated to visualize the importance of each variable in predicting the 30-day-hospitalization variable correctly. To achieve this, the change in accuracy in out-of-bag samples is obtained through permutation. For each variable, a reference level was set to establish the baseline, allowing better interpretation of the plots for the direction of effect.

Results

Of the three ML models, as per **Table 2**, the RF model showed the greatest discriminatory power, predicting 30-day-hospitalization with an accuracy of 92% (95%CI: 0.9143, 0.9273). The XGB and LR models achieved a predictive accuracy of 82% (95%CI: 0.8144, 0.8327) and 67% (95%CI: 0.6570, 0.6795), respectively. The RF model significantly outperformed both XGB and LR models in terms of AUC-ROC (0.97, 0.90, 0.72, respectively), sensitivity (0.93, 0.78 and 0.69, respectively) and NPV (0.93, 0.81 and 0.66, respectively).

The confusion matrix (**Table 3**) provides insight into which cases the model classified as true positives, true negatives, false positives and false negatives. The RF model achieved the highest overall accuracy, classifying 6,269 cases of 30-day-hospitalization correctly. The RF model classified 229 cases as false-negatives and 309 as false-positives. In models predicting clinical events for preventative purposes, it is preferred for a model to have a higher false-positive than false-negative rate. This is because it is imperative not to miss high-risk patients at risk of 30-day-hospitalization. Both the XGB and LR models had a higher PPV than NPV.

The top 20 most important variables for predicting the 30-day-hospitalization are displayed in **Figure 2**. It should be noted that variable importance plots represent the aggregated importance scores by factor level, meaning the plot shows the top 20 most important variable levels out of a total of 84 variable factor levels. Additionally, all variables have a reference factor set, which marked by an “*” in **Figure 2**, suggest this variable factor level was important for predicting lack of 30-day-hospitalisation.

Figure 2. Variable Importance Plots for Three Models (A. Random Forest B. XGBoost C. Logistic Regression) Predicting 30-day-hospitalization. Only the top 20 most important variables are displayed. Variables marked with an “*” represent the variable’s reference level. For a complete list of variables included in the models, please refer to Table 1.

[Figure 2 uploaded as a separate JPG file.]

Note. Arbitrary scale for interpretability and comparability.

In all three models, the variable importance statistics show the DBI as important in predicting 30-day-hospitalization. In the RF model, high DBI was the 10th most important variable. In the XGB model, low DBI was the 5th most important variable (predicting lack of 30-day-hospitalization). In the LR model, high DBI was the 10th most important variable. Alcohol consumption was the most important variable in determining 30-day-hospitalization. Other important variables include fall history, mobility, and ADL (Activities of Daily Living).

The RF model achieved the highest AUC-ROC, followed by XGB and LR; 0.971, 0.895, and 0.724, respectively. All three ML models showed good discriminatory power. However, the RF model proved particularly powerful. AUC-ROC curves can be seen in **Figure 3**.

Figure 3. AUC-ROC of the three cross-validated ML models (A. Random Forest B. XGBoost C. Logistic Regression) for predicting 30-day-hospitalization.

[Figure 3 uploaded as a separate JPG file.]

Note. AUC-ROC – Area Under the Receiver Operating Characteristics Curve, 95% CI – 95% Confidence Interval.

Discussion

The potential applications of ML in geriatric medicine are vast and transformative. Accurately predicting unfavourable clinical outcomes such as 30-day-hospitalization will allow clinicians to prioritise high-risk patients. By leveraging ML models that identify patients at high risk of 30-day hospitalization, clinicians can gain actionable insights into the modifiable risk factors affecting each patient. This, in turn, allows health systems to identify patients in need of urgent clinical review, and healthcare professionals to tailor their individual patient care strategies, aiming to enhance patients' chances of a favourable outcome and effectively reduce the likelihood of hospitalization.

In this study, we developed three ML models to predict 30-day hospitalization in older adults with complex care needs. Our RF model emerged as the most effective, achieving a high AUC-ROC of 0.97 and accuracy of 92%. The XGB and LR models also performed commendably, with AUC-ROC scores of 0.90 and 0.72, respectively. These results compare favourably with several recent studies aimed at similar objectives. For example, *Bories et al., 2022* developed and optimized three ML models to predict hospitalization due to bleeding in a sample of 7,462 participants prescribed oral anticoagulants. In their study, the RF, XGB, and Support Vector Machine models achieved accuracy levels of 0.64, 0.68, and 0.64, respectively[40]. *Verdu-Rotellar et al., 2022* utilized a multivariable logistic regression model to predict 30-day hospitalization in a sample of 811 participants, achieving AUC-ROC scores of 0.73 and 0.89 in validation and derivation cohorts, respectively[41]. Our RF and XGB models, in particular, appear to show superior discriminatory power when compared to these recently published models. For instance, *Friz et al., 2022* predicted 30-day readmission in 3,079 participants using an adaptive boosting model, gradient boosting model, XGB, and RF, with AUC-ROC scores of 0.803, 0.782, 0.776, 0.786, respectively. Notably, all of these models outperformed the

traditional LACE (Length of hospitalization, Acuity, Comorbidities, Emergency department visits) index, which achieved an AUC-ROC of 0.504[42]. Several other clinical outcomes have been predicted using RF, XGB and LR models in recent literature, including but not limited to thrombolysis[43], 3-month giant cell arthritis flare-up[44], adverse events within 30 days of emergency department admission[45], and complications within 30 days of hospital admission[46]. The models presented in the current study outperform most models from recent literature. High model performance can be attributed to several factors such as the high quality of data on which the models were trained, and the carefully selected predictors which have been linked to short term hospitalizations in previous literature. In summary, both our RF and XGB models demonstrate good discriminatory power and may offer significant advantages in predicting hospitalizations in older adults. Nevertheless, external validation in a cohort representative of the general population of older adults remains a crucial next step to confirm these promising findings.

Our ML models identified DBI and alcohol consumption as important variables for predicting 30-day-hospitalization in older adults. Identifying these two variables is particularly interesting to clinicians, as they are potentially immediately modifiable risk factors, while acknowledging that for some people, deprescribing and reducing alcohol consumption can take weeks or even years to complete. Regarding the DBI, deprescribing—reducing or eliminating medications with anticholinergic or sedative effects where the harm outweighs the benefit for the individual—is a clinically sound strategy, but it is often a challenging task that has been met with limited success[47]. A study by *Nishtala et al., 2009*, showed that pharmacist-recommended dose changes for DBI-contributing drugs resulted in significantly decreased DBI[48]. Regarding alcohol consumption, a link between alcohol consumption and hospitalization has been documented in the literature. *Sacco et al., 2015* showed that rates of alcohol-related

hospitalizations are increasing for older adults. The group recommended that training healthcare professionals to combat this issue is crucial[31]. In a study by *Kohli et al., 2020*, alcohol-related and alcohol-withdrawal hospitalizations have led to increased length-of-stay, higher treatment costs and greater functional decline[32]. Additionally, rates of alcohol consumption among older adults (particularly females) have been shown to increase from 1997 to 2014 in the USA[33]. This is relevant given that female gender ranked as the 6th most important variable in the RF model developed in the current study. InterRAI quantifies alcohol consumption as the highest number of drinks in any “single sitting” in the last 14 days. Patients identified as high-risk should be specifically advised and educated on the negative effects of alcohol consumption on their health outcomes.

In contrast to the potentially immediately modifiable DBI and alcohol consumption, our models also identified several risk factors that are modifiable with comprehensive geriatric assessment and rehabilitation but are less likely to be reduced in a timeframe that affects 30-day hospitalization. Fall history ranked as the 7th and 2nd most important variable in the RF and XGB models and 1st in the LR model. *Vaishya et al., 2020* linked falls with hospitalization and concluded that ensuring safe living environments is vital to preventing falls[35]. Impaired mobility ranked as the 4th most important variable in the LR model and the 8th most important variable in the XGB model. *Fisher et al., 2013* identified mobility as a physical biomarker for overall health and 30-day readmission [37]. ADL (Activities of Daily Living) ranked as the 1st and 5th most important variable in the XGB and LR models, respectively. This is supported by a study by *Nguyen et al., 2021*, in which ADL impairment was associated with increased readmission in a cohort of patients with heart failure[34]. Most of the less immediately-modifiable risk factors identified in our study have been linked with hospitalization in other literature, further supporting the variables identified by the models in this study. Gender is the

6th and 4th most important variable in the RF and XGB models, respectively. In a study by *Gjestsen et al., 2018*, gender, particularly male, was associated with a higher hospitalization rate [36].

Impact of our Study on the Clinical Care of Older Adults

Hospitalization, while sometimes unavoidable, carries inherent risks for older adults. A hospital stay can catalyse a cascade of additional complications for many older adults, including hospital-acquired pneumonia, delirium, falls, and functional decline. Thus, proactive measures to mitigate these risks—whether through judicious prescribing, lifestyle modifications, or closer outpatient monitoring—are crucial. In this context, ML models serve as a powerful ally for clinicians. They offer data-driven insights that can inform more personalized, precise, and preventive care strategies, helping to avert hospital admissions whenever possible and, consequently, the cascade of complications that can accompany them. In this study, we have developed and optimized three ML models for predicting 30-day-hospitalization using the InterRAI dataset, which is widely considered the gold standard due to its high data quality[49]. Additionally, we identified DBI and alcohol consumption as important variables that are potentially immediately modifiable, in predicting 30-day-hospitalization. Other risk factors, such as functional independence, mobility, falls may be modifiable over time, through comprehensive geriatric assessment and rehabilitation. As this field of study grows, large-scale studies deploying highly discriminatory ML models in external cohorts of older adults representative of the general population are needed. Identifying patients early will allow clinicians to proactively minimise the risk to the patient, ensuring a high standard of geriatric care and improving public health.

Limitations and Strengths

This study has several limitations. Firstly, the dataset used to train and validate the models concerns people with complex care needs from New Zealand, bringing concerns about the generalisability to other older adult populations. Secondly, while our models underwent internal validation, they have not been validated in an external cohort of patients. However, we believe the RF model is appropriate for external validation, exhibiting a high accuracy, AUC-ROC and NPV. Third, the 30-day hospitalization outcome does not differentiate between emergency and elective admission. Fourth, short-term mortality rate in the study population was not incorporated into the models, therefore not accounting for the competing risk of death. Finally, The unbalanced and relatively small dataset size can cause generalisability concerns. While the dataset was balanced for the primary outcome variable, it was not balanced for other variables. Large-scale external validation studies utilising these models are necessary.

This study also had several strengths. Firstly, interRAI is an exceptionally high-quality dataset concerning older adults[49]. All the geriatric assessments on which the dataset is based are carried out by a healthcare professional trained to carry out the assessment. Secondly, the analysed interRAI dataset contained no missing values, so there was no need to employ data imputation techniques. Third, we performed 100 repeated cross-validations with two repeats for each ML model, minimising the effects of model overfitting. Finally, we have fully documented our research, reporting multiple key model evaluation metrics. We have shared the complete R scripts in a GitHub repository to facilitate future external validation studies.

Conclusion

As clinical databases continue to expand and evolve in complexity, so too does the potential of ML in enhancing geriatric care. A central application of these advanced tools lies in the identification of modifiable risk factors associated with 30-day hospitalization—a critical

concern for clinicians dedicated to the well-being of older adults. As shown in our study, immediately modifiable risk factors such as the DBI and alcohol consumption are of high clinical relevance, as clinicians can influence these variables and proactively lower the risk of 30-day-hospitalization. Early recognition of these risk factors allows for timely and targeted interventions, aiming to actively minimise patients' risk of hospitalization.

Declaration of Sources of Funding

This work was supported by the University Research Studentship Award, project code EA-PA1231. The funding body played no part in the design, execution, analysis and interpretation of data or writing of the study.

Acknowledgements

Sources of Data

We acknowledge the teams at TAS (Te Whatu Ora – Health New Zealand) and the New Zealand Ministry of Health for their support in extracting and providing the administrative datasets for this study.

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Study supervisor: PN. Study concept and design: RO, SR, PN. Acquisition of subjects and/or data: PN, HJ. Analysis and interpretation of data: RO, SR, PN, SH. Preparation of manuscript:

RO,

SR,

HJ,

PN, SH.

Sponsor's Role

The funding body had no influence on the design, methods, subject recruitment, data collection, analysis and preparation of the paper.

References

1. Dixon T, Shaw M, Frankel S, Ebrahim S. Hospital admissions, age, and death: retrospective cohort study. *BMJ*. 2004 May 29;328(7451):1288.10.1136/bmj.38072.481933.EE
2. Kingston A, Robinson L, Booth H, Knapp M, Jagger C, project M. Projections of multi-morbidity in the older population in England to 2035: estimates from the Population Ageing and Care Simulation (PACSim) model. *Age Ageing*. 2018 May 1;47(3):374-80.10.1093/ageing/afx201
3. Lee EA, Gibbs NE, Fahey L, Whiffen TL. Making hospitals safer for older adults: updating quality metrics by understanding hospital-acquired delirium and its link to falls. *Perm J*. 2013 Fall;17(4):32-6.10.7812/TPP/13-065
4. Burton LA, Price R, Barr KE, McAuley SM, Allen JB, Clinton AM, et al. Hospital-acquired pneumonia incidence and diagnosis in older patients. *Age Ageing*. 2016 Jan;45(1):171-4.10.1093/ageing/afv168
5. Mudge AM, McRae P, Hubbard RE, Peel NM, Lim WK, Barnett AG, et al. Hospital-Associated Complications of Older People: A Proposed Multicomponent Outcome for Acute Care. *J Am Geriatr Soc*. 2019 Feb;67(2):352-6.10.1111/jgs.15662
6. Jean-Luc Bosson JL, Marie Antoinette Sevestre, Joel Belmin, Laurence Beyssier, Antoine Elias, Alain Franco, Philippe Le Roux. Deep vein thrombosis in elderly patients hospitalized in subacute care facilities: a multicenter cross-sectional study of risk factors, prophylaxis, and prevalence. *Archives of Internal Medicine*. 2003;163:2613-8
7. John A. Heit MOF, Tanya M. Petterson, Christine M. Lohse, Marc D. Silverstein, David N. Mohr, L. Joseph Melton. Relative Impact of Risk Factors for Deep Vein Thrombosis and Pulmonary Embolism. *Archives of Internal Medicine*. 2002;162:1245-8
8. Mona Baumgarten DJM, A. Russell Localio, Sarah H. Kagan, Robert A. Lowe, Bruce Kinosian, John H. Holmes, Stephanie B. Abbuhl, William Kavesh, and Althea Ruffin. Pressure Ulcers Among Elderly Patients Early in the Hospital Stay. *Journal of Gerontology*. 2006;61A(7):749–54

9. Deandrea S, Bravi F, Turati F, Lucenteforte E, La Vecchia C, Negri E. Risk factors for falls in older people in nursing homes and hospitals. A systematic review and meta-analysis. *Arch Gerontol Geriatr.* 2013 May-Jun;56(3):407-15.10.1016/j.archger.2012.12.006
10. Marcantonio ER. Delirium in Hospitalized Older Adults. *N Engl J Med.* 2017 Oct 12;377(15):1456-66.10.1056/NEJMcp1605501
11. Rajula HSR, Verlato G, Manchia M, Antonucci N, Fanos V. Comparison of Conventional Statistical Methods with Machine Learning in Medicine: Diagnosis, Drug Development, and Treatment. *Medicina (Kaunas).* 2020 Sep 8;56(9).10.3390/medicina56090455
12. Olender RT, Roy S, Nishtala PS. Application of machine learning approaches in predicting clinical outcomes in older adults - a systematic review and meta-analysis. *BMC Geriatr.* 2023 Sep 14;23(1):561.10.1186/s12877-023-04246-w
13. Rose S. Mortality risk score prediction in an elderly population using machine learning. *Am J Epidemiol.* 2013 Mar 1;177(5):443-52.10.1093/aje/kws241
14. Matsumoto K, Nohara Y, Sakaguchi M, Takayama Y, Fukushige S, Soejima H, et al. Delirium Prediction Using Machine Learning Interpretation Method and Its Incorporation into a Clinical Workflow. *Applied Sciences.* 2023;13(3).10.3390/app13031564
15. Turan TN, Al Kasab S, Nizam A, Lynn MJ, Harrell J, Derdeyn CP, et al. Relationship between Risk Factor Control and Compliance with a Lifestyle Modification Program in the Stenting Aggressive Medical Management for Prevention of Recurrent Stroke in Intracranial Stenosis Trial. *J Stroke Cerebrovasc Dis.* 2018 Mar;27(3):801-5.10.1016/j.jstrokecerebrovasdis.2017.10.017
16. Meng X, Brunet A, Turecki G, Liu A, D'Arcy C, Caron J. Risk factor modifications and depression incidence: a 4-year longitudinal Canadian cohort of the Montreal Catchment Area Study. *BMJ Open.* 2017 Jun 10;7(6):e015156.10.1136/bmjopen-2016-015156
17. Chandrasiri A, Dissanayake A, de Silva V. Health promotion in workplaces as a strategy for modification of risk factors for Non Communicable Diseases (NCDs): A practical example from Sri Lanka. *Work.* 2016 Oct 17;55(2):281-4.10.3233/WOR-162413

18. Davies LE, Spiers G, Kingston A, Todd A, Adamson J, Hanratty B. Adverse Outcomes of Polypharmacy in Older People: Systematic Review of Reviews. *J Am Med Dir Assoc*. 2020 Feb;21(2):181-7.10.1016/j.jamda.2019.10.022
19. Li Y, Zhang X, Yang L, Yang Y, Qiao G, Lu C, et al. Association between polypharmacy and mortality in the older adults: A systematic review and meta-analysis. *Arch Gerontol Geriatr*. 2022 May-Jun;100:104630.10.1016/j.archger.2022.104630
20. Sarah N. Hilmer DEM, Eleanor M. Simonsick, Ying Cao, Shari M. Ling, B. Gwen Windham, Tamara B. Harris, Joseph T. Hanlon, Susan M. Rubin, Ronald I. Shorr, Douglas C. Bauer, Darrell R. Abernethy. A Drug Burden Index to Define the Functional Burden of Medications in Older People. *Archives of Internal Medicine*. 2007;167:781-7.10.1001/archinte.167.8.781
21. Liu BM, Kouladjian O'Donnell L, Redston MR, Fujita K, Thillainadesan J, Gnjdic D, et al. Association of the Drug Burden Index (DBI) exposure with outcomes: A systematic review. *J Am Geriatr Soc*. 2024 Feb;72(2):589-603.10.1111/jgs.18691
22. Fujita K, Hooper P, Masnoon N, Lo S, Gnjdic D, Etherton-Beer C, et al. Impact of a Comprehensive Intervention Bundle Including the Drug Burden Index on Deprescribing Anticholinergic and Sedative Drugs in Older Acute Inpatients: A Non-randomised Controlled Before-and-After Pilot Study. *Drugs Aging*. 2023 Jul;40(7):633-42.10.1007/s40266-023-01032-6
23. Pritchard C, Ness A, Symonds N, Siarkowski M, Broadfoot M, McBrien KA, et al. Effectiveness of hospital avoidance interventions among elderly patients: A systematic review. *CJEM*. 2020 Jul;22(4):504-13.10.1017/cem.2020.4
24. Breiman L. Random Forests. *Machine Learning*. 2001:5-32
25. Tianqi Chen CG. XGBoost: A Scalable Tree Boosting System. *Machine Learning*. 2016.10.1145/2939672.2939785
26. Stoltzfus JC. Logistic regression: a brief primer. *Acad Emerg Med*. 2011 Oct;18(10):1099-104.10.1111/j.1553-2712.2011.01185.x
27. Schluter PJ, Ahuriri-Driscoll A, Anderson TJ, Beere P, Brown J, Dalrymple-Alford J, et al. Comprehensive clinical assessment of home-based older persons within New Zealand: an

epidemiological profile of a national cross-section. Australian and New Zealand Journal of Public Health. 2016;40(4):349-55.10.1111/1753-6405.12525

28. Jamieson HA, Nishtala PS, Scrase R, Deely JM, Abey-Nesbit R, Hilmer SN, et al. Drug Burden Index and Its Association With Hip Fracture Among Older Adults: A National Population-Based Study. *J Gerontol A Biol Sci Med Sci*. 2019 Jun 18;74(7):1127-33.10.1093/gerona/gly176
29. Nishtala PS, Allore H, Han L, Jamieson HA, Hilmer SN, Chyou TY. Impact of Anticholinergic Burden on Cognitive Performance: A Cohort Study of Community-Dwelling Older Adults. *J Am Med Dir Assoc*. 2020 Sep;21(9):1357-8 e3.10.1016/j.jamda.2020.03.027
30. Nishtala PS, Narayan SW, Wang T, Hilmer SN. Associations of drug burden index with falls, general practitioner visits, and mortality in older people. *Pharmacoepidemiol Drug Saf*. 2014 Jul;23(7):753-8.10.1002/pds.3624
31. Sacco P, Unick GJ, Kuerbis A, Koru AG, Moore AA. Alcohol-Related Diagnoses in Hospital Admissions for All Causes Among Middle-Aged and Older Adults: Trends and Cohort Differences From 1993 to 2010. *J Aging Health*. 2015 Dec;27(8):1358-74.10.1177/0898264315583052
32. Kohli M, Charilaou P, Rousseau CP, Menezes R, Sanon M. Health care utilization in geriatric patients admitted with alcohol withdrawal from 2005 to 2014. *Am J Drug Alcohol Abuse*. 2020 Jul 3;46(4):478-84.10.1080/00952990.2020.1725539
33. Breslow RA, Castle IP, Chen CM, Graubard BI. Trends in Alcohol Consumption Among Older Americans: National Health Interview Surveys, 1997 to 2014. *Alcohol Clin Exp Res*. 2017 May;41(5):976-86.10.1111/acer.13365
34. Nguyen TV, Dang HT, Burns MJ, Dao HH, Nguyen TN. Impairment in activities of daily living and readmission in older patients with heart failure: a cohort study. *BMJ Open*. 2021 Feb 22;11(2):e044416.10.1136/bmjopen-2020-044416
35. Vaishya R, Vaish A. Falls in Older Adults are Serious. *Indian J Orthop*. 2020 Feb;54(1):69-74.10.1007/s43465-019-00037-x
36. Gjestsen MT, Bronnick K, Testad I. Characteristics and predictors for hospitalizations of home-dwelling older persons receiving community care: a cohort study from Norway. *BMC Geriatr*. 2018 Sep 3;18(1):203.10.1186/s12877-018-0887-z

37. Fisher SR, Kuo YF, Sharma G, Raji MA, Kumar A, Goodwin JS, et al. Mobility After Hospital Discharge as a Marker for 30-Day Readmission. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*. 2012;68(7):805-10.10.1093/gerona/gls252
38. Ofori-Asenso R, Liew D, Martensson J, Jones D. The Frequency of, and Factors Associated with Prolonged Hospitalization: A Multicentre Study in Victoria, Australia. *J Clin Med*. 2020 Sep 22;9(9).10.3390/jcm9093055
39. Best O, Gnjjidic D, Hilmer SN, Naganathan V, McLachlan AJ. Investigating polypharmacy and drug burden index in hospitalised older people. *Intern Med J*. 2013 Aug;43(8):912-8.10.1111/imj.12203
40. Bories M, Bouzille G, Cuggia M, Le Corre P. Drug-Drug Interactions with Oral Anticoagulants as Potentially Inappropriate Medications: Prevalence and Outcomes in Elderly Patients in Primary Care and Hospital Settings. *Pharmaceutics*. 2022 Jul 5;14(7).10.3390/pharmaceutics14071410
41. Verdu-Rotellar JM, Abellana R, Vaillant-Roussel H, Gril Jevsek L, Assenova R, Kasuba Lazic D, et al. Risk stratification in heart failure decompensation in the community: HEFESTOS score. *ESC Heart Fail*. 2022 Feb;9(1):606-13.10.1002/ehf2.13707
42. Polo Friz H, Esposito V, Marano G, Primitz L, Bovio A, Delgrossi G, et al. Machine learning and LACE index for predicting 30-day readmissions after heart failure hospitalization in elderly patients. *Intern Emerg Med*. 2022 Sep;17(6):1727-37.10.1007/s11739-022-02996-w
43. Velagapudi L, Mouchtouris N, Schmidt RF, Vuong D, Khanna O, Sweid A, et al. A Machine Learning Approach to First Pass Reperfusion in Mechanical Thrombectomy: Prediction and Feature Analysis. *J Stroke Cerebrovasc Dis*. 2021 Jul;30(7):105796.10.1016/j.jstrokecerebrovasdis.2021.105796
44. Venerito V, Emmi G, Cantarini L, Leccese P, Fornaro M, Fabiani C, et al. Validity of Machine Learning in Predicting Giant Cell Arteritis Flare After Glucocorticoids Tapering. *Front Immunol*. 2022;13:860877.10.3389/fimmu.2022.860877
45. Sax DR, Mark DG, Huang J, Sofrygin O, Rana JS, Collins SP, et al. Use of Machine Learning to Develop a Risk-Stratification Tool for Emergency Department Patients With Acute Heart Failure. *Ann Emerg Med*. 2021 Feb;77(2):237-48.10.1016/j.annemergmed.2020.09.436

46. Ren SS, Zhu MW, Zhang KW, Chen BW, Yang C, Xiao R, et al. Machine Learning-Based Prediction of In-Hospital Complications in Elderly Patients Using GLIM-, SGA-, and ESPEN 2015-Diagnosed Malnutrition as a Factor. *Nutrients*. 2022 Jul 24;14(15).10.3390/nu14153035
47. Jamieson H, Nishtala PS, Bergler HU, Weaver SK, Pickering JW, Ailabouni NJ, et al. Deprescribing anticholinergic and sedative drugs to reduce polypharmacy in frail older adults living in the community: a randomized controlled trial. *J Gerontol A Biol Sci Med Sci*. 2023 Jan 24.10.1093/gerona/glac249
48. Prasad S, Nishtala SNH, Andrew J, McLachlan, Paul J, Hannan and Timothy F. Chen. Impact of Residential Medication Management Reviews on Drug Burden Index in Aged-Care Homes. *Drugs Aging*. 2009;26:677-86.10.2165/11316440-000000000-00000
49. Hogeveen SE, Chen J, Hirdes JP. Evaluation of data quality of interRAI assessments in home and community care. *BMC Med Inform Decis Mak*. 2017 Oct 30;17(1):150.10.1186/s12911-017-0547-

Captions for Tables and Illustrations

Table 1 (Supplemental Material):

Table 1. Baseline participant characteristics of the condensed InterRAI dataset. Percentage rounded to 1 significant figure.

*Note. *The Drug_Burden_Index is defined as: (Low = 0-1, High = >1)*

Table 2:

Table 2. Model Evaluation Statistics for the cross-validated RF, XGB, and LR Models Predicting 30-day-hospitalization.

Note. PPV – Positive Predictive Value. NPV – Negative Predictive Value.

Table 3:

Table 3. Confusion Matrix for the cross-validated RF, XGB and LR Models Predicting 30-day-hospitalization.

Note. RF- Random Forest, XGB – XGBoost, LR – Logistic Regression.

Table 4 (Supplemental Material):

Table 4. ML Sensitivity Analysis.

*Note. *alcohol_consumption was the most important variable in the RF model **ADL was the most important variable in the XGB model ***fall_history was the most important variable in the LR model.*

Figure 1:

Figure 1. InterRAI Participant selection flowchart.

Note. DOD – Date of Death, DOA – Date of Admission, ARC – Admission to Residential Care.

Figure 2:

Figure 2. Variable Importance Plots for Three Models (A. Random Forest B. XGBoost C. Logistic Regression) Predicting 30-day-hospitalization. Only the top 20 most important variables are displayed. Variables marked with an “” represent the variable’s reference level. For a complete list of variables included in the models, please refer to Table 1.*

Note. Arbitrary scale for interpretability and comparability.

Figure 3:

Figure 3. AUC-ROC of the three cross-validated ML models (A. Random Forest B. XGBoost C. Logistic Regression) for predicting 30-day-hospitalization.

Note. AUC-ROC – Area Under the Receiver Operating Characteristics Curve, 95% CI – 95% Confidence Interval.

Table 2. Model Evaluation Statistics for the cross-validated RF, XGB, and LR Models Predicting 30-day-hospitalization.

Model	Accuracy (95% CI)	Balanced Accuracy	Sensitivity	Specificity	PPV	NPV	F1 Score
RF	0.9210(0.9143, 0.9273)	0.9206	0.9344	0.9068	0.9134	0.9293	0.9238
XGB	0.8237(0.8144, 0.8327)	0.8227	0.7814	0.8639	0.8451	0.8061	0.8120
LR	0.6683(0.6570, 0.6795)	0.6677	0.6908	0.6446	0.6716	0.6646	0.6811

Note. PPV – Positive Predictive Value. NPV – Negative Predictive Value.

Table 3. Confusion Matrix for the cross-validated RF, XGB and LR Models Predicting 30-day-hospitalization.

RF			XGB			LR			
		Reference				Reference			
Prediction	Y	N	Prediction	Y	N	Prediction	Y	N	
Y	3,261	309	Y	2,592	475	Y	2,411	1,179	
N	229	3,008	N	725	3,015	N	1,079	2,138	

Note. RF- Random Forest, XGB – XGBoost, LR – Logistic Regression.