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ORIGINAL RESEARCH ARTICLE

Predicting the Risk of Adverse Drug Reactions in Older Inpatients: External Validation of the GerontoNet ADR Risk Score Using the CRIME Cohort

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Abstract

Background Adverse drug reactions (ADRs) in older people are often preventable, indicating that screening and prevention programs aimed at reducing their rate are needed in this population.

Objective The aim of this study was to externally validate the GerontoNet ADR risk score and to assess its validity in specific subpopulations of older inpatients.

Methods Data from the prospective CRIteria to assess appropriate Medication use among Elderly complex patients (CRIME) cohort were used. Dose-dependent and predictable ADRs were classified as type A, probable or definite ADRs were defined according to the Naranjo algorithm, and diagnostic accuracy was tested using receiver operating characteristic (ROC) analyses. Sensitivity and specificity were calculated for a cut-off point of 4.

Results The mean age of the 1075 patients was 81.4 years (standard deviation 7.4) and the median number of drugs was 10 (range 7–13). At least one ADR was observed in 70 patients (6.5%); ADRs were classified as type A in 50 patients (4.7%) and defined as probable or definite in 41 patients (3.8%). Fair diagnostic accuracy to predict both type A and probable or definite ADRs was found in subpopulations aged <70 or ≥80 years with heart failure, diabetes, or a previous ADR. Good accuracy to predict type A ADRs was found in patients with a low body mass index (BMI; >18.5 kg/m^2) and a Mini-Mental State Examination (MMSE) score of >24/30 points, as well as in patients with osteoarthritis. The cut-off point of 4 points yielded very good sensitivity but poor specificity results in these subpopulations.

Conclusion This study suggests that the GerontoNet ADR risk score might represent a pragmatic approach to identifying specific subpopulations of older inpatients at increased risk of an ADR with a fair to good diagnostic accuracy.

Key Points

This study provides evidence that the GerontoNet ADR risk score might identify specific subpopulations of older inpatients at risk of adverse drug reactions.

The findings from this study suggest that the GerontoNet ADR risk score could be adopted within routine clinical care for older patients belonging to these specific subpopulations.

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1 Introduction

Adverse drug reactions (ADR) are an important problem in older hospitalized patients because they are quite common [1], often preventable [2], and associated with increased morbidity and healthcare utilization [3]. Identifying patients at risk of an ADR could help in directing additional time and resources towards this risk group in order to potentially prevent ADRs. Several models have been developed to predict the risk of older inpatients experiencing an ADR. In a recent review, Stevenson and colleagues showed that these models have a poor to modest performance, and they also underlined the need for further work to assure their external validity [4]. Lavan and Gallagher [5] recently pointed out that it is unlikely for a single tool to accurately predict every ADR in every older patient due to the numerous contributing factors to ADR occurrence and the heterogeneity of the older population. They suggest ADR risk prediction strategies to focus on ADRs in older patients with a particular illness or clinical characteristic.

The GerontoNet ADR risk score has been developed based on data from the medical literature and on secondary analysis of the Italian Group of Pharmacoepidemiology in the Elderly (GIFA) database comprising 5936 older hospitalized patients. It was validated to have fair predictive performance (area under the curve [AUC] 0.70, 95% confidence interval [CI] 0.63–0.78) in 483 older patients from four hospitals in Europe (as part of the GerontoNet cohort) [6], but poor predictive performance (AUC 0.62, 95% CI 0.57–0.68) in 513 older patients admitted to a university teaching hospital in Ireland [7]. The aim of the present analyses was to validate the GerontoNet ADR risk score in subpopulations of the prospective CRIteria to assess appropriate Medication use among Elderly complex patients (CRIME) [8] cohort and to assess its validity in subgroups of older patients with specific diseases or clinical characteristics.

2 Methods

2.1 CRIteria to Assess Appropriate Medication Use Among Elderly Complex Patients (CRIME) Study and Population

The CRIME study [8] was initiated to assess prescribing patterns in older adults hospitalized in Italy and to produce recommendations for pharmacological prescribing in older complex patients. This multicenter observational study was performed in three academic hospitals in Italy (Catholic University of the Sacred Heart Rome, University of Perugia, and University of Ferrara) and four centers of the Italian National Institute of Health and Science on Aging (situated in Ancona, Cosenza, Fermo, and Rome). Patients admitted to geriatric and internal medicine acute care wards between June 2010 and May 2011 were consecutively recruited, with the only inclusion criteria being age of at least 65 years and a willingness to participate.

Participants were assessed within 24 h of admission and were followed daily until discharge, in-hospital death, or transfer to another ward. Questionnaire data were collected by clinical staff and/or external research staff, who used direct observation, clinical records, and interviews with the patients, family, friends or formal service providers as the information source. Drugs were coded according to the Anatomical, Therapeutic and Chemical (ATC) codes [9]. The 30-item Mini-Mental State Examination (MMSE) score (range 0–30 points) was used to evaluate patients' cognitive status, and a cut-off of >24/30 points was adopted to identify cognitively intact participants [10].

2.2 Adverse Drug Reactions (ADRs)

According to the World Health Organization definition, an ADR is defined as "one which is noxious and unintended, and which occurs at doses used in man for prophylaxis, diagnosis or therapy" [11]. For each suspected ADR, a study physician coded its type and causality with drug use. ADRs were classified as type A (dose-dependent and predictable) or type B (unrelated to the known pharmacology of the drugs), and causality assessment was evaluated using the Naranjo algorithm [12]. The relationship between drug use and ADRs was classified as definite (score of 9–12), probable (score of 5–8), possible (score of 1–4), or doubtful (score of 0). When more than one ADR was observed in the same patient, only the first ADR was taken into account.

2.3 GerontoNet ADR Risk Score

The GerontoNet ADR risk score ranges from 0 to 10 points and consists of six variables, each of which was assigned a score based on the strength of its association with ADRs: presence of 4 or more comorbid conditions (1 point), renal failure (1 point), heart failure (1 point), liver disease (1 point), number of drugs (1 point when between 5 and 7; 4 points when 8 or more), and a history of ADRs (2 points).

To count the number of comorbid conditions present, a set of 50 medical diagnoses were checked in the CRIME study, including cardiovascular, endocrine, genitourinary, musculoskeletal, neurological, and malignant diseases. We defined renal failure as having an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 body surface area for at least 3 months. The eGFR was computed using the four-variable Modification of Diet and Renal Disease Study formula [13]: 186 × (serum creatinine in mg/

dl)$^{-1.154}$ × (age)$^{-0.203}$ × (1.210 if black) × (0.742 if female). We defined liver disease as any disorder of the liver with doubling of transaminases in comparison with the normal limit on admission, while heart failure was defined as the inability of the heart to keep up with the demands on it and, specifically, failure of the heart to pump blood with normal efficiency. Clinical diagnoses were recorded by the study physicians, who gathered information from the patients and the attending physicians and carefully assessed medical histories and clinical documentation.

2.4 Statistics

Descriptive data were presented as mean (standard deviation [SD]), median (first to third quartile) or number (percentage), where appropriate. Patients with an observed ADR were compared with patients without any observed ADR using Chi square tests. Diagnostic accuracy of the GerontoNet ADR risk score (to predict ADRs definitely or probably caused by drugs used during the hospital stay, and type A ADRs) was tested using receiver operating characteristic (ROC) analyses. Performance was defined as excellent when AUC = 0.90–1.00, good when AUC = 0.80–0.89, fair when AUC = 0.70–0.79, poor when AUC = 0.60–0.69, and failed when AUC is <0.60. Sensitivity and specificity were calculated for a cut-off point of 4. Analyses were performed using SPSS software version 23.0 (IBM SPSS Statistics for Windows; IBM Corporation, Armonk, NY, USA), and statistical significance was indicated by a p value <0.05; all p values were two-tailed.

3 Results

3.1 Patient Characteristics

Of 1123 participants in the CRIME study, 1075 had complete data to compute the GerontoNet ADR risk score and were included in the present analyses. Their mean age (SD) was 81.4 years (7.4), and the median (first to third quartile) number of drugs used during the hospital stay was 10 (range 7–13). Table 1 provides further details about the characteristics of these patients at hospital admission. Additionally, it was reported that 505 patients (47.0%) were widowed, while 498 patients (46.3%) were married or cohabiting, 49 patients (4.6%) were living in nursing homes or residences for the elderly, and 263 patients (24.5%) were living alone.

During the hospital stay, a total of 87 ADRs were observed in 70 patients (6.5%). Cardiovascular complications ($n = 20$) represented the most frequent ADRs, followed by metabolic/endocrine ($n = 15$), gastrointestinal ($n = 13$), neuropsychiatric ($n = 13$), dermatologic/allergic ($n = 9$), and hematologic ($n = 8$) complications. The first (or only) observed ADR was defined as probable or definite, according to the Naranjo algorithm, in 41 patients (3.8%), and classified as type A in 50 patients (4.7%). Patients who experienced a probable or definite ADR during the hospital stay were more likely to have younger age, heart failure, be female, or have experienced an ADR in the past compared with the remaining sample. Patients who experienced a type A ADR were more likely to have younger age, heart failure, renal failure, use five or more drugs during the hospital stay, or have experienced an ADR in the past compared with those without type A ADRs. Patients with an ADR during admission had a median hospital stay of 13 days (range 8–18) compared with 10 days (range 7–14) in patients without observed ADRs ($p = 0.002$).

3.2 GerontoNet ADR Risk Score

The median GerontoNet ADR risk score was 5 points (range 3–6). The most frequently identified variables were the presence of four or more comorbid conditions ($n = 761$; 71%) and the use of eight or more drugs ($n = 742$; 69%). The GerontoNet ADR risk score was significantly higher for patients in whom an ADR was observed that was probably or definitely related to drug use (median 6, interquartile range [IQR] 5–8) or that was type A (median 7, IQR 5–8) compared with the score for patients without observed ADRs probably or definitely related to drug use or type A (both median 5, IQR 3–6; $p = 0.008$ and $p = 0.002$, respectively); 796 patients (74%) scored ≥4 points on the GerontoNet ADR risk score.

ROC analyses to evaluate the diagnostic accuracy of the GerontoNet ADR risk score yielded an AUC of 0.64 (95% CI 0.55–0.74) to predict ADRs probably or definitely related to drug use, and an AUC of 0.69 (95% CI 0.60–0.77) to predict type A ADRs. Table 2 reports AUC values in subpopulations of the CRIME cohort. Fair diagnostic accuracy to predict both type A and probable or definite ADRs was found in subpopulations aged <70 or ≥80 years with heart failure, diabetes, or a history of any previous ADR. Good diagnostic accuracy to predict type A ADRs was found in patients with a low body mass index (BMI; >18.5 kg/m^2) and an MMSE score >24/30 points, as well as in patients with osteoarthritis. The suggested cut-off point of 4 points on the GerontoNet ADR risk score yielded very good sensitivity but very poor specificity results in these subpopulations (with the exception of patients with four or fewer drugs during the hospital stay).

Table 1 Comparison of descriptive characteristics in patients with and without an ADR in the CRIME cohort [$N = 1075$]

Characteristic	Total no. of patients (%) [$N = 1075$]	No. of patients without an ADR (%; Naranjo ≥5) [$N = 1034$]	No. of patients with an ADR (%; Naranjo ≥5) [$N = 41$]	p value	No. of patients without a type A ADR (%) [$N = 1025$]	No. of patients with a type A ADR (%) [$N = 50$]	p value
Age, years				0.018			0.001
<70	55 (5.1)	49 (4.7)	6 (14.6)		47 (4.6)	8 (16.0)	
70–79	358 (33.3)	345 (33.4)	13 (31.7)		345 (33.7)	13 (26.0)	
≥80	662 (61.6)	640 (61.9)	22 (53.7)		633 (61.8)	29 (58.0)	
Sex				0.048			0.346
Female	597 (55.5)	572 (55.3)	25 (61.0)		566 (55.2)	31 (62.0)	
Male	478 (44.5)	462 (44.7)	16 (39.0)		459 (44.8)	19 (38.0)	
BMI, kg/m^2 (data for 84 patients missing)				0.617			0.632
<18.5	38 (3.8)	36 (3.8)	2 (5.3)		36 (3.8)	2 (4.4)	
18.5–24.9	394 (39.8)	382 (40.1)	12 (31.6)		377 (39.9)	17 (37.8)	
25–29.9	365 (36.8)	351 (36.8)	14 (36.8)		351 (37.1)	14 (31.1)	
≥30	194 (19.6)	184 (19.3)	10 (26.3)		182 (19.2)	12 (26.7)	
ADL impairments				0.490			0.397
≥1	391 (36.4)	374 (36.2)	17 (41.5)		370 (36.1)	21 (42.0)	
0	684 (63.6)	660 (63.8)	24 (58.5)		655 (63.9)	29 (58.0)	
MMSE score				0.968			0.163
>24	346 (41.3)	330 (41.4)	16 (41.0)		322 (40.8)	24 (51.1)	
Number of comorbidities				0.081			0.074
0–3	314 (29.2)	307 (29.7)	7 (17.1)		305 (29.8)	9 (18.0)	
≥4	761 (70.8)	727 (70.3)	34 (82.9)		720 (70.2)	41 (82.0)	
Clinical diagnosis							
Hypertension	815 (75.8)	780 (75.4)	35 (85.4)	0.145	773 (75.4)	42 (84.0)	0.166
Heart failure	295 (27.4)	278 (26.9)	17 (41.5)	0.040	275 (26.8)	20 (40.0)	0.042
COPD	389 (36.2)	375 (36.3)	14 (34.1)	0.782	372 (36.3)	17 (34.0)	0.742
Diabetes mellitus	323 (30.0)	306 (29.6)	17 (41.5)	0.104	302 (29.5)	21 (42.0)	0.059
Osteoarthritis	343 (31.9)	327 (31.6)	16 (39.0)	0.319	327 (31.9)	16 (32.0)	0.988
Liver disease	28 (2.6)	26 (2.5)	2 (4.9)	0.351	25 (2.4)	3 (6.0)	0.123
Renal failure (eGFR <60 mL/min)	510 (47.4)	487 (47.1)	23 (56.1)	0.258	479 (46.7)	31 (62.0)	0.035
Number of drugs taken during the hospital stay				0.064			0.040
≥5	995 (92.6)	954 (92.3)	41 (100)		945 (92.2)	50 (100)	
Previous ADR				0.011			0.000
Yes	203 (18.9)	189 (18.3)	14 (34.1)		180 (17.6)	23 (46.0)	
No	872 (81.1)	845 (81.7)	27 (65.9)		845 (82.4)	27 (54.0)	

ADR adverse drug reaction, *BMI* body mass index, *ADL* activities of daily living, *MMSE* Mini-Mental State Examination, *eGFR* estimated glomerular filtration rate, *COPD* chronic obstructive pulmonary disease, *CRIME* CRIteria to assess appropriate Medication use among Elderly complex patients

4 Discussion

The GerontoNet ADR risk score was developed in 2010 as a simple method of identifying patients who are at increased risk of an ADR in a population of geriatric inpatients [6]. However, a later observational study showed that the GerontoNet ADR risk score missed almost 40% of those at risk of an ADR, showing poor performance (AUC 0.62, 95% CI 0.57–0.68) in 513 older patients admitted to a university teaching hospital in Ireland [7]. However, it has to be noted that the study population, as well as the evaluation, assessment, and reliability of the identified ADRs, were different compared with the GerontoNet study validation group. In addition, the ADR prevalence was much higher in the Irish study.

Table 2 Diagnostic accuracy of the GerontoNet ADR risk score to predict ADRs in subpopulations of the CRIME cohort

Characteristic	AUROC (95% CI)	Cut-off ≥4		AUROC (95% CI)	Cut-off ≥4	
		Se	1-Sp		Se	1-Sp
Age, years						
<70	0.74 (0.51–0.98)	83.3	59.2	0.78 (0.60–0.97)	87.5	57.4
70–79	0.49 (0.33–0.64)	61.5	71.6	0.54 (0.36–0.72)	61.5	71.6
≥80	0.72 (0.61–0.84)	90.9	76.1	0.75 (0.65–0.85)	89.7	76.0
Sex						
Female	0.69 (0.56–0.81)	80.0	72.7	0.70 (0.59–0.80)	80.6	72.6
Male	0.57 (0.43–0.70)	81.3	75.1	0.67 (0.54–0.81)	84.2	74.9
BMI, kg/m^2						
<18.5	0.66 (0.23–1.00)	100.0	83.3	0.87 (0.71–1.00)	100.0	83.3
18.5–24.9	0.63 (0.48–0.79)	83.3	69.1	0.63 (0.50–0.77)	82.4	69.0
25–29.9	0.58 (0.41–0.75)	71.4	75.2	0.64 (0.47–0.81)	71.4	75.2
≥30	0.69 (0.50–0.88)	90.0	79.3	0.73 (0.57–0.89)	91.7	79.1
ADL impairments						
≥1	0.64 (0.52–0.77)	83.3	76.1	0.68 (0.58–0.79)	86.2	75.9
0	0.65 (0.51–0.80)	76.5	69.8	0.70 (0.56–0.84)	76.2	69.7
MMSE score						
>24	0.76 (0.64–0.88)	93.8	73.3	0.81 (0.71–0.91)	91.7	73.0
Number of comorbidities						
0–3	0.65 (0.46–0.83)	71.4	57.0	0.65 (0.48–0.82)	66.7	57.0
≥4	0.63 (0.52–0.74)	82.4	80.9	0.70 (0.60–0.80)	85.4	80.7
Clinical diagnosis						
Hypertension	0.64 (0.54–0.74)	82.9	75.5	0.69 (0.60–0.78)	83.3	75.4
Heart failure	0.73 (0.60–0.86)	94.1	92.8	0.77 (0.66–0.88)	95.0	92.7
Chronic obstructive pulmonary disease	0.58 (0.43–0.73)	85.7	80.0	0.73 (0.61–0.86)	94.1	79.6
Diabetes mellitus	0.75 (0.64–0.86)	100.0	82.0	0.78 (0.68–0.89)	95.2	82.1
Osteoarthritis	0.77 (0.64–0.91)	87.5	68.2	0.81 (0.69–0.93)	93.8	67.9
Liver disease	0.69 (0.63–0.74)	72.5	57.1	0.67 (0.62–0.73)	67.5	61.9
Renal failure (eGFR <60 mL/min)	0.66 (0.53–0.79)	87.0	84.2	0.67 (0.55–0.79)	83.9	84.3
Number of drugs taken during the hospital stay						
≥5	0.62 (0.52–0.72)	80.5	79.4	0.67 (0.58–0.76)	82	79.3
Previous ADR						
Yes	0.75 (0.64–0.86)	100	87.8	0.72 (0.62–0.82)	100	87.2
No	0.55 (0.44–0.66)	70.4	70.7	0.54 (0.43–0.66)	66.7	70.8

AUROC area under receiver operating characteristics, *CI* confidence interval, *Se* sensitivity, *Sp* specificity, *BMI* body mass index, *ADL* activities of daily living, *MMSE* Mini-Mental State Examination, *eGFR* estimated glomerular filtration rate, *ADR* adverse drug reaction, *CRIME* CRIteria to assess appropriate Medication use among Elderly complex patients

A recent systematic review of the ADR risk prediction models suggested that the GerontoNet ADR risk score, similar to three other models that were developed in the meantime, is not yet suitable for use in clinical practice [4, 14–16]. This finding underlined the need for either identification of new risk factors to be added to the score, or for validation of the GerontoNet ADR risk score in different subpopulations of older patients. We admit that adaptation of the GerontoNet score and addition of new variables would be interesting in further assessing the predictive ability of the score. Furthermore, a comparison of the GerontoNet score with other predictive ADR risk scores might certainly be the subject of further research, and therefore useful for daily practice. However, in view of the limitations of the existing geriatric ADR risk prediction models, the best way to proceed would be prospective collection of a new large data set with judicious ADR ascertainment for the purpose of re-evaluation of ADR risk factors in complex older patients. The challenge for future research is to integrate valuable information obtained by

existing instruments and methodologies in a complete and global approach, targeting all potential factors involved in the onset of ADR. However, in this paper we opted for a different scope, i.e. assessing the predictive values of the original GerontoNet score in certain subpopulations of older inpatients, according to our objective, to validate the GerontoNet risk score in different populations and settings, as indicated previously [6].

With the present analyses, we have shown that the GerontoNet ADR risk score has fair to good diagnostic accuracy to predict ADRs probably or definitely related to drug use, as well as type A ADRs, in several subpopulations of a hospitalized cohort of older patients admitted to geriatric and internal medicine wards from seven Italian hospitals.

Moreover, fair diagnostic accuracy to predict both ADRs probably or definitely related to drug use, as well as type A ADRs, was found in subpopulations aged <70 or ≥ 80 years with heart failure, diabetes, or a history of a previous ADR. The findings of fair diagnostic accuracy with AUC 0.70–0.79 in the respective subpopulations might be important for clinical practice, given the fact that, in particular, patients older than 80 years with multiple comorbidities (i.e. heart failure, diabetes) and a history of a previous ADR, may benefit from timely detection of a higher risk of ADRs [17].

In addition, good diagnostic accuracy to predict type A ADRs was found in patients with low BMI and an MMSE $>24/30$ points, and in patients with osteoarthritis. BMI might be a relevant determinant in the development of ADR. In particular, low BMI is associated with a reduced proportion of body fat, meaning that the volume of distribution for lipid soluble drugs is reduced, leading to increased drug concentrations [18]. Cognitive competency of an older patient might be very important in order to adequately take a patient's medication history and perform medication review and reconciliation. Cognitively impaired patients are at risk of underreporting of ADRs. On the contrary, older patients without cognitive impairment are expected to provide accurate information, compared with their cognitively impaired counterparts, in regard to previous history of ADRs, a variable of the GerontoNet ADR risk score that has been assigned 2 points based on the strength of its association with ADRs [19]. Osteoarthritis is one of the most prevalent conditions in older people and a leading cause of chronic disability and long-term use of non-steroidal anti-inflammatory drugs (NSAIDs), opioids and related analgesics. The use of NSAIDs in older people has been associated with a high risk of ADRs [20]. In addition, some opioids, such as morphine, due to renally cleared metabolites, may increase the risk of ADRs and should be used with caution among older adults. In this particular patient subpopulation, the GerontoNet ADR risk score appears to be sufficiently diagnostically accurate in identifying patients who are at increased risk of an ADR [21].

The suggested cut-off point between 3 and 4 points on the GerontoNet ADR risk score yielded very good sensitivity but very poor specificity results in these subpopulations (with the exception of patients with four or fewer drugs during the hospital stay). This finding, although important for the detection of patients with an effectively high risk of ADRs, might, at the same time, result in many patients who are not at risk of an ADR being categorized as having an increased risk and then being subjected to further investigation.

ADRs can have an impact on healthcare utilization as patients with an ADR had significantly longer hospital stays than patients without ADRs [22]. Moreover, increased length of stay may also increase the risk of older patients to acquire other hospital conditions, which may further exacerbate their situation. With this finding we additionally underline the importance of timely detection of ADRs among older inpatients.

In the current study, we did not conduct the assessment of ADR risk based on the individual drug classes because the pattern of drug use may change across settings over time. In addition, the unique distinction between drugs in certain 'classes' can be difficult because drugs with similar therapeutic effects may have different safety profiles. In addition, the overall prevalence of patients with an observed ADR was relatively low in this hospitalized cohort (3.8% with an ADR probably or definitely related to drug use and 4.7% with a type A ADR) compared with the prevalence reported in other studies, i.e. up to 26% [7] of patients experiencing an ADR during the hospital stay, which, to a certain extent, might affect the generalizability of our findings. Several underlying causes might account for this relatively low prevalence. First, the vast majority of patients were admitted to a geriatric ward; it has been found that geriatric medical consultation is associated with lower prescription of potentially inappropriate medications and thereby potentially less ADRs [23]. Second, prescribing patterns and epidemiology of disease burden may vary across countries [24, 25]. The ADR prevalence in the Italian GIFA cohort was, likewise, relatively low at 6%. Third, the high number of cognitively impaired patients in our cohort may have caused an underreporting of ADRs. Indeed, the presentation of an ADR in older adults is often atypical and non-specific, which further complicates its recognition. The ADR may therefore mistakenly be ascribed to the onset of a new medical problem or an already existing diagnosis. Moreover, under-recognition and under-documentation of previous ADRs in everyday clinical practice may negatively influence the success of a predictive score. Finally, data on the description of ADRs

Table 3 Diagnostic accuracy of the GerontoNet ADR risk score to predict both ADRs probably or definitely related to drug use and type A ADRs in subpopulations of older inpatients with specific diseases or clinical characteristics

Fair diagnostic accuracy; AUC = [0.70; 0.79]
Age ≥80 years
Heart failure
Diabetes
History of any previous ADR
Good diagnostic accuracy; AUC = [0.80; 0.89]
Low BMI (>18.5 kg/m^2)
MMSE score of >24/30 points
Osteoarthritis

ADR adverse drug reaction, *AUC* area under the curve, *BMI* body mass index, *MMSE* Mini-Mental State Examination

experienced before admission were not collected and therefore we cannot exclude that ADRs detected during hospital stay may represent a recurrence of a former ADR.

ADRs in older adults are mostly preventable as the majority are type A (due to an exaggerated response to the expected action of the drug) and dose-related, indicating that the need for screening and prevention programs aimed at reducing the rate of iatrogenic illness are necessary in this population. In an attempt to improve ADR recognition in older adults, its diagnosis should routinely be part of the broader diagnostic approach. In older patients taking drugs, the differential diagnosis should always include the possibility of adverse drug effects. Safe drug use goes along with global assessment of the clinical and functional parameters of patients, and that integration of skills from different healthcare professionals are needed to address medical complexity of older adults.

5 Conclusions

This study provides evidence that the GerontoNet ADR risk score might represent a pragmatic and useful approach to identifying specific subpopulations of older patients at increased risk of an ADR with a fair to good diagnostic accuracy. Moreover, these findings may suggest that the GerontoNet ADR risk score could be adopted and implemented within routine clinical care for older patients belonging to these specific subpopulations (Table 3).

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Compliance with Ethical Standards

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Conflicts of interest Mirko Petrovic, Balamurugan Tangiisuran, Chakravarthi Rajkumar, Tischa van der Cammen and Graziano Onder declare that they have no conflicts of interest directly relevant to the content of this study.

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