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External validation of the 80+ score and comparison with three clinical scores identifying patients at least 75 years old at risk of unplanned readmission within 30 days after discharge

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Summary

AIM OF THE STUDY: A potentially avoidable readmission is an unplanned readmission occurring within 30 days of discharge. As 20% of hospitalised elderly patients are rehospitalised as an unplanned readmission, it is necessary to identify with a clinical score those patients who are at risk of readmission and need discharge interventions as a priority. The main objective of this study was to externally validate and compare the 80+ score with the three other scores predicting the risk of unplanned readmission.

METHODS: We conducted a retrospective case-control study using a clinical data warehouse. The study included patients hospitalised between 1 September 2014 and 31 October 2015 in an 800-bed university hospital. We included patients aged 75 and over. Cases were readmitted at the emergency department within 30 days after the index discharge. Controls were not readmitted as an emergency within 30 days. Four clinical scores (80+ score, LACE index, HOSPITAL score, TRST) were externally validated. Discrimination of the scores was assessed by calculating the area under the receiver operating characteristic curves (AUC). Calibration was assessed with a Hosmer-Lemeshow χ^2 test.

RESULTS: We included 438 patients. For discrimination, the 80+ score, the LACE index, the HOSPITAL score and the TRST had AUCs of 0.506 (95% confidence interval [CI] 0.413–0.546), 0.534 (95% CI 0.459–0.591, 0.517 (95% CI 0.466–0.598) and 0.589 (95% CI 0.524–0.654), respectively. The Hosmer-Lemeshow χ^2 tests had p-values of 0.44, 0.43, 0.11 and 0.49, respectively.

CONCLUSION: In our study, the 80+ score was externally validated and showed less favourable discrimination than the three other scores in this population.

Key words: elderly, clinical score, unplanned readmission, external validation

Introduction

The elderly (people over 75 years of age or those over 65 with comorbidities) are at high risk of potentially avoidable hospital readmission. A potentially avoidable readmission is an unplanned readmission caused by known morbidities and occurring within 30 days of discharge [1]. About 20% of elderly inpatients are subject to potentially avoidable readmission [2]. As there is no consensus on a classification of avoidable readmissions [3, 4], all unplanned readmissions are considered. These readmissions are deleterious for the elderly: a readmission increases the risk of dependence and functional or psychosocial decline [5]. Moreover, they increase the risk of decompensation of other comorbid conditions, thus increasing the frailty of elderly patients [6]. In the United States, costs associated with these readmissions amount to 17.5 billion dollars [7]; it is therefore, a public health priority to reduce readmission rates of the elderly.

According to the French Ministry of Health, it is neither "necessary nor efficient to intervene for every patient" aged 75 and over to reduce the readmission rate [8]. Therefore, it is crucial to develop and apply tools to identify patients at risk of readmission and then to set up interventions. Clinical scores are tools that make it possible to identify elderly inpatients at risk of readmission.

In the literature, there are many scores that identify elderly inpatients at risk of readmission [9]. Among these, the LACE index, created in 2010 [10], the HOSPITAL score, 2010 [11] or the Triage Risk Screening Tool (TRST), 2003 [12] can easily be calculated from data in medical records and are widely used. The purpose of this study was to implement the chosen score in the hospital's medical soft-

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ware, in order to generate an automatic alert on high-risk patients.

In 2015, Alassaad et al. constructed a clinical score including iatrogenic factors (prescription of drugs for peptic ulcer, opioid drugs or non-tricyclic antidepressants) [13]. This focus on iatrogenic factors is interesting, as 10 to 30% of readmissions are drug-related [14], and iatrogenic factors can be eliminated by adjusting the prescription. This "80+ score", which focuses on iatrogenic factors, must be compared with already existing scores focusing on demographic and sociological factors or comorbidities: the LACE index [10], the HOSPITAL score [11] and the TRST [12].

Clinical scores require internal and external validation. Internal validation means testing the score in the population used to create it. It describes the performance of the score (calibration and discrimination). Then, prior to general application, the score has to be externally validated – tested in a new population that ensures the reproducibility of the score. According to the TRIPOD statement [15], external validation may use types of participants different from the development population. Thus, we choose to externally validate the LACE and HOSPITAL scores, which were developed in general adult population, on an elderly population.

Unlike the LACE index [10], the HOSPITAL score [11] and the TRST [12], the 80+ score has not been externally validated to date.

The main objective of this study was to carry out an external validation of the 80+ score and to compare it with the three other scores.

Materials and methods

Study design

We used the patient data from a monocentric, retrospective, matched, case-control study using the clinical data warehouse [16] of a French university hospital, the Hôpital européen Georges Pompidou. This is a teaching hospital of 795 beds with 24 clinical departments (15 medical wards and 9 surgical units). The clinical information system is coupled with a clinical data warehouse, which makes reuse of healthcare data and clinical research possible. The main objective of the first study was to research iatrogenic risk factors for unplanned readmissions.

Participants

Elderly patients are people over 75 years of age or those over 65 with comorbidities; in order to avoid the inclusion

of patients between 65 and 75 years old without comorbidities, we included only patients over 75 years old. Patients were admitted to hospital, in a medical or surgical ward, between 1 October 2014 and 30 September 2015. Cases were elderly patients who experienced an unscheduled readmission within 30 days after the index discharge. Readmissions had to be via the accident and emergency department (AED) to be considered unscheduled. The patients were either discharged after the AED visit or hospitalised. The control group consisted of elderly patients who had not had any unscheduled readmissions during the 30 days after the index discharge. All controls who died during the index hospitalisation were excluded. Cases and controls were randomly matched for sex and age. We excluded all patients lost to follow-up who were potentially dead after the index admission.

Study size

The sample size of our study was calculating according to Collins et al. [17]. They suggested that, to externally validate prognostic models, a minimum of 100 events and ideally 200 (or more) events are required.

Presentation of the four scores (table 1)

A clinical score is a tool that can be used by hospital practitioners to guide medical interventions. They are built with a series of variables corresponding to medical background, and sociological, biological or clinical observations. For each variable, the patient is attributed a number of points. Points are added up, giving the final value of the score. The scoring system ranges from a minimum to a maximum, where the likelihood of readmission increases with the calculated value of the score.

The 80+ *score* [13] is a point score system used for risk estimation that was developed at the Uppsala University Hospital in 2015. It includes seven variables and ranges from -2 to 10. A patient with a score greater than 3 has an 80% risk of readmission. The 80+ score was internally validated in a prospective randomised control trial [13] and showed good performances, with a c-statistic of 0.72 (95% confidence interval [CI] 0.66–0.77) and a good calibration. However, to our knowledge, this score has never been externally validated, unlike the other three scores.

The LACE index [10] is a point score initially conceived in Ontario, Canada in 2010. It ranges from 0 to 44. A patient with a score greater than 10 is considered at high risk for unplanned hospital readmission. This score was derived and validated in a prospective cohort study. This internal

Table 1: Items comprising	each of the four scores.
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Score 80+	LACE index	HOSPITAL	TRST		
Estimated glomerular filtration rate (eGFR)	Lengths of hospitalisation	Haemoglobin level at discharge	History of cognitive impairment		
Level of social support	Acuteness of the admission Discharge from an Oncology unit		Difficulty walking/transferring or recent falls		
Pulmonary disease (asthma or chronic ob- struction pulmonary disease)		Sodium level at discharge			
Malignant disease	Comorbidities of patients	Procedures during hospital stay	Taking five or more medications		
Prescription of a drug for peptic ulcer or gastro-oesophageal reflux disease		Index admission type			
Prescription of an opioid drug	AED admissions	Number of hospital admissions during the previous year	AED use in previous 30 days or hospitali- sation in previous 90 days		
Prescription of an antidepressant drug (except tricyclic antidepressant)		Length of hospitalisation			

AED = accident and emergency department; TRST = Triage Risk Screening Tool

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validation showed good discrimination, with a c-statistic of 0.684 [10].

The HOSPITAL score [18], developed in Massachusetts, USA in 2013, is a score built with seven variables forming the acronym HOSPITAL. The score ranges from 0 to 13. A patient is considered at high risk of readmission when he or she has a score equal or greater than 7. The HOSPI-TAL score was internally validated in a retrospective cohort study [18] and showed good performances with a c-statistic of 0.71.

The TRST [12] is a five-item clinical prediction, a rule designed for rapid administration by the triage nurse in an AED after minimal training; it was developed in Cleveland, USA in 2003. The score ranges from 0 to 5. A patient is at high risk of readmission if the score is greater than 2. The TRST was internally validated in a prospective cohort study [12] and showed a good performances with an area under the receiver operating characteristic curve (AUC of the ROC curve) of 0.72 for readmissions at 30 days.

The table 2 shows the differences between the development data and our validation data in setting, eligibility criteria and outcome.

Data collection

All patient data and medical history records were retrieved using the clinical data warehouse. An ethics committee approved the study protocol (CERHUPO, CDW 2015 0023).

For biological data (estimated glomerular filtration rate [eGFR], haemoglobin and sodium levels), the last available analyses before discharge were chosen. For medication data (drug for peptic ulcer, opioid, non-tricyclic antidepressant and polypharmacy), we used the prescription at discharge.

For other data, all available medical records were analysed to find the patient's medical background (pulmonary and malignant disease, Charlson index and history of hospital admission), mental and physical state of the patient (cognition, falls, staff recommendation) and procedures performed during the hospitalisation.

Medical records are completed by healthcare professionals. It is recognised that in medical records, doctors enumerate comorbidities and do not always record specific data that are unknown. We therefore considered that the absence of a specific piece of information (such as asthma, cancer history) in the medical report meant the absence of the condition.

Statistical analysis

For data management, the outliers were corrected after a second check of the medical record: when an outlier was detected, the medical record was read to confirm the variable. The missing data of qualitative variables were imputed according to the context. For example, elderly patients usually live at home, and not in a nursing home. Thus, if it was not mentioned that the patient lived in a nursing home, he or she was assumed to be living at home. The data were then corrected. The quantitative variables were imputed by the median (less than 20% of missing data) or by multiple imputation (more than 20% of missing data).

All scores were calculated by adding the points of each given variable. Cases and controls were analysed for each variable of each score. The qualitative variables were compared using Pearson's χ^2 test. A univariate analysis was performed with a t-test to compare scores between the two groups.

Discrimination is the ability of the score to separate cases from control groups. To determine the discriminatory ability of the scores, the c-statistic was calculated. The c-statistic gives the probability that a randomly selected patient has a higher score than a patient not -readmitted. A value below 0.5 indicates that the score has poor discriminatory ability. A score has a good discrimination when the c-statistic ranges from 0.7 to 1. It has fair discrimination when ranging from 0.5 to 0.7. The graphic representation of the c-statistic is the receiving operating characteristic (ROC) curve. The ROC curves of the four scores were drawn, and the areas under the curve (AUCs) were calculated.

Calibration shows the ability of the model to generate probabilities that match the observed rates. We used the Hosmer-Lemeshow χ^2 test to assess the calibration of the selected scores. If the p-value is greater than 0.05, the score has a good calibration.

We then estimated the sensitivity, the specificity, the positive predictive value, the negative predictive value, the positive likelihood ratio and the negative likelihood ratio. Analyses were performed with the R software (R version 3.3.2), with a significance level of $\alpha = 0.05$.

Results

From 1 September 2014 to 31 October 2015, 6574 elderly patients meeting our criteria were admitted to the hospital. Within 30 days after discharge of the index admission, 456 patients (6.4%) were readmitted, and 6118 were not. These 456 patients were randomly matched with 456 controls among the 6118 patients, creating 456 case-control pairs. Of those 456 pairs, 237 controls were lost during follow-

Table 2: Differences between development data and validation data.

Criteria	Development data			Validation data	
	Score 80+	LACE	HOSPITAL	TRST	
Setting	Internal medicine wards in Uni- versity Hospital, Sweden	Medical or surgical services of 11 hospitals, Canada	Medical wards of two hos- pitals, USA	Two urban, academic AED	Medical or surgical wards of an university hospital, France
Eligibility criteria	Patients aged 80 years and old- er, acutely admitted	Adult patients discharged to the community	Adult inpatients (length of stay of more than 24 hours)	Patients aged 65 years and older, with AED visit, dis- charged home	Patients aged 75 years and older, discharged home
Outcome	Unplanned readmission (AED visit or readmission) or death during the 12-month follow-up period	Unplanned readmission to hospital or death within 30 days of discharge	30 day potentially avoid- able readmission	AED visit, hospital admission or nursing home admission at 30 and 120 days	Unplanned readmission (AED visit or readmission) within 30 days of dis- charge

AED = accident and emergency department; TRST = Triage Risk Screening Tool

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up, resulting in a final pool of 219 pairs. The flow of participants is described in figure 1.

Patient characteristics

A total of 438 patients were included, whom 52% were women. The mean age was 84.4 years (standard deviation [SD] 5.90). On admission, 46% of the patients were in a re-



lationship, 51% were single (3% missing values). The patients' baseline characteristics are listed in table 3.

Score results

Using a t-test, the means of the scores were compared between cases and controls (table 4). The 80+ score, the LACE index and the HOSPITAL score had p-values of 0.87, 0.24 and 0.60, respectively, meaning that there was no significant difference between cases and controls. In contrast, for the TRST, the mean score of the cases was significantly different from the mean score of the controls (p <0.001).

Diagnostic values of the scores

The discrimination was calculated with the AUC of the ROC curve (table 5). The 80+ score had the lowest AUC (0.506) and TRST had the highest (0.589; fig. 2).

The calibration was estimated with the Hosmer-Lemeshow χ^2 test (table 6).

The LACE index had the highest sensitivity (61%, 95% CI 55–68%) and the HOSPITAL score had the lowest sensitivity (21%, 95% CI 16-27%). The HOSPITAL score had the highest specificity (80%, 95% CI 75–85%) and the LACE index had the lowest specificity (44%, 95% CI 38–51%; table 7).

Table 3: Patient characteristics.

Variables	n (100%) or mean (±SD)	% missing values
Age (year)	84.4 (±5.9)	0
Gender		0
Female	229 (52%)	
Male	209 (48%)	
Marital status		3%
Single	225 (51%)	
In a relationship	201 (46%)	
Living situation		4%
Living alone	169 (39%)	
Living with someone	248 (57%)	
Place of residence		1%
Nursing home	33 (8%)	
Private home	397 (91%)	
Charlson index	2.64 (±1.92)	2%
Length of stay (days)	8.49 (±7.5)	0
Admission type		0
Planned	287 (66%)	
Unplanned	151 (34%)	
Ward type		0
Medical ward	286 (65%)	
Surgical ward	152 (35%)	
Discharge		1%
Discharge home	316 (72%)	
Transfer	120 (27%)	
Primary diagnosis at discharge		0
Cardiovascular	120 (27%)	
Oncological	64 (15%)	
Respiratory	41 (9%)	
Gastrointestinal	38 (9%)	
Kidney/Urological	35 (8%)	
Other	140 (32%)	
Number of medications at discharge	7.5 (±3.8)	2%

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Discussion

Main results

In our study, the new 80+ score showed an AUC of the ROC curve of 0.506. Thus it has not demonstrated better discrimination than the three other scores.

The TRST performed best in identifying elderly patients at risk for readmission within 30 days of discharge. Even though they showed fair calibration, the 80+ score, the HOSPITAL score and the LACE index had not strong enough discriminatory power. The four scores had all previously been internally validated. In our study we observed

Table 4. Score results	able 4	Score	results.	
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Variables	Cases	Controls	p-value
n = 430	– readmission n (%)	no readmission n (%)	
	80+ score		
eGFR			
>90 ml/min	37 (44)	47 (56)	0.28
60–89 ml/min	70 (50.4)	69 (49.6)	0.93
30-59 ml/min	85 (52.5)	77 (47.5)	0.53
<30 ml/min	27 (50.9)	26 (49.1)	0.89
Social support			
Living alone or with spouse	196 (48.2)	211 (51.8)	0.46
Nursing home	23 (74.2)	8 (25.8)	0.007
Pulmonary disease (yes)	32 (43.2)	42 (56.8)	0.24
Malignant disease (yes)	93 (51.1)	89 (48.9)	0.77
Drug for peptic ulcer or GORD	96 (46.6)	110 (53.4)	0.36
Opioid drug	41 (58.6)	29 (41.4)	0.15
Non-TCA-antidepressant drug	43 (59.7)	29 (40.3)	0.10
Total, mean (SD)	2.83 (1.69)	2.80 (1.75)	0.650
	LACE index		
Length of stay			
1 day	17 (58.6)	12 (41.4)	0.35
2 days	48 (54.5)	40 (45.5)	0.39
3 days	21 (43.8)	27 (56.2)	0.39
4–6 days	48 (48.5)	51 (51.5)	0.76
7–13 days	58 (50)	58 (50)	1
≥14 days	27 (46.6)	31 (53.4)	0.60
Admitted via AED	138 (47.9)	150 (52.1)	0.48
Charlson index, mean (SD)	16.3 (1.29)	16.06 (1.31)	0.072
No. of AED visits			
0	73 (44.8)	90 (55.2)	0.18
1	177 (52.7)	69 (47.3)	0.51
2	22 (44)	28 (56)	0.40
3	16 (55.2)	13 (44.8)	0.58
≥4	31 (62)	19 (38)	0.09
Total, mean (SD)	11.92 (4.16)	11.45 (4.3)	0.240
H	OSPITAL score		
Low haemoglobin level at discharge	133 (50.6)	130 (49.4)	0.85
Discharge from an oncology service	22 (45.8)	26 (54.2)	0.56
Low sodium level at discharge	39 (52)	36 (48)	0.73
Procedure during hospital stay	97 (47.5)	107 (52.5)	0.48
Index admission type (urgent)	137 (47.6)	151 (52.4)	0.41
No. of hospital admissions during the previous year			
0–1	97 (44.2)	123 (55.9)	0.08
2–5	101 (56.1)	79 (43.9)	0.10
>5	21 (55.3)	17 (44.7)	0.52
Length of stay ≥5 days	112 (48.7)	118 (51.3)	0.69
Total, mean (SD)	4.48 (2.37)	4.36 (2.45)	0.606
	TRST		
Cognitive impairment	44 (60.3)	29 (39.7)	0.08
Difficulty walking, falls	54 (61.4)	34 (38.6)	0.03
Polymedication	174 (51.9)	161 (48.1)	0.48
History of AED visit or hospitalisation	72 (52.9)	64 (47.1)	0.49
AED staff recommendations	123 (54.9)	101 (45.1)	0.14
Total, mean (SD)	2.13 (1.11)	1.78 (1.11)	0.00086**

AED = accident and emergency department; eGFR = estimated glomerular filtration rate; GORD = gastro-oesophageal reflux disease; SD = standard deviation; TCA = tricyclic antidepressant; TRST = Triage Risk Screening Tool ** p <0.001

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that the calibration and validation of these four scores were not as good as had been reported in the internal validation studies. One of the possible reasons for this difference was the selection of our patients, who were all alive 30 days after discharge, whereas most of these other studies also included deaths, meaning that patients in our study were in a better health. Indeed, in a validation study of the LACE index, performed at the Department of Medicine for the Elderly Cambridge University Hospital [19], the LACE index also showed poor performances in predicting readmission, but better performance in predicting death. This supports the hypothesis that these scores perform better at identifying both patients at risk of readmission and at risk of dying.



Table 5: Discriminatory ability of the four scores analysed with c-statistics

The HOSPITAL score, an easy-to-use score, was externally validated in a large international (USA, Canada, Switzerland, Israel) retrospective cohort study [11] of 121,136 patients, and showed very good calibration and discrimination. Our study included only 219 control-case pairs, and therefore probably did not have the same statistical power. The HOSPITAL score was also validated in a Swiss population of patients aged 50 years old and older [20]. In this second validation study, with a population more similar to ours, showed very good calibration (p = 0.89) and discrimination (c-statistic = 0.72). It was a prospective cohort study and the first outcome was either death or unplanned readmission within 30 days, whereas our primary outcome was only unplanned readmission within 30 days after discharge. As we had an older population (inpatients 75 years and older vs 50 years and older for Aubert et al. [20]), the death rate might have been higher. Moreover, Cooksley et al. [21] have shown that the discriminatory power of HOSPITAL and LACE scores decreased with increasing age.

The 80+ score is a recent clinical score identifying elderly patients at risk of readmission. Its strength is that it takes into account medication. Thus, if the prescription is adjusted during the hospitalisation, the risk of readmission is decreased. The same applies to the TRST, which takes into account the number of drugs, so that the prescription can also be adjusted according to the benefit-risk balance of the treatment. Conversely, the LACE index and the HOS-PITAL score do not take into account prescriptions. They focus on admission characteristics (index admission type, length of stay and history of hospitalisation). In a recent systematic review, Pedersen et al. identified length of stay and comorbid conditions as risk factors for readmission [22]. Thus, some drugs have an impact on the benefit-risk ratio, in favour of risk, when administered to elderly patients. There are lists of potentially inappropriate medica-

Score	AUC
80+ score	0.506 (0.413–0.546)
LACE index	0.534 (0.459–0.591)
HOSPITAL score	0.517 (0.466–0.598)
TRST	0.589 (0.524–0.654)

AUC = area under the receiver operating characteristic curve; TRST = Triage Risk Screening Tool

Table 6: Calibration of the four scores analysed with the Hosmer-Lemeshow χ^2 test.

Score	X ²	Degrees of freedom	p-value
80+ score	7.89	8	0.44
LACE index	23.56	23	0.43
HOSPITAL score	15.75	10	0.11
TRST	3.44	4	0.49

TRST = Triage Risk Screening Tool

Table 7: Metrological characteristics.

	80+ score	LACE index	HOSPITAL score	TRST	
Cut-off	>3	>10	>6	>2	
Sensitivity	0.31 (0.24–0.37)	0.61 (0.55–0.68)	0.21 (0.16–0.27)	0.37 (0.31–0.43)	
Specificity	0.69 (0.63–0.75)	0.44 (0.38–0.51)	0.80 (0.75–0.85)	0.74 (0.68–0.80)	
PPV	0.50 (0.41–0.58)	0.52 (0.46–0.58)	0.52 (0.41–0.62)	0.59 (0.50–0.67)	
NPV	0.50 (0.44–0.55)	0.54 (0.46–0.61)	0.50 (0.45–0.56)	0.54 (0.48–0.60)	
LR-P	0.99 (0.74–1.30)	1.1 (0.94–1.29)	1.07 (0.74–1.54)	1.42 (1.07–1.88)	
LR-N	1.01 (0.89–1.14)	0.87 (0.70–1.09)	0.98 (0.89–1.08)	0.85 (0.75–0.97)	

PPV = positive predictive value; NPV = negative predictive value; LR-P = likelihood ratio-positive; LR-N = likelihood ratio negative

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tions (PIMs) [23–25], although the results of studies on PIMs and readmissions are conflicting. A study showed that the prescription of PIMs had no effect on readmission [26], but another study showed that the prescription of benzodiazepines, some of which (long-acting benzodiazepines) are listed as PIMs, was associated with a higher readmission risk (odds ratio 1.23) [27]. This might explain the lower performance of the 80+ score.

When the 80+ score was internally validated, it showed better discriminatory ability than in our study. This difference may be due to the difference of population in the two studies. Alassaad et al. [13] included patients aged 80 years and older and acutely admitted to an internal medicine ward at a university hospital, whereas we included patients aged 75 years and older admitted (acutely or not) to medical and surgical wards.

Limitations

We acknowledge that our study has limitations. It was a single-centre retrospective case-control study. Sex and age were matched in order to select the controls and obtain a relatively homogeneous population. Matching on length of stay or comorbidities, which are items of the LACE and HOSPITAL scores, would not have improved the power of the study. All the data were retrieved from an electronic database and we made the assumption that if a specific condition was not in the medical record, it was absent. Therefore, it is less powerful than a prospective study with a questionnaire where each variable of the score would be filled in with either a negative or positive answer. In the same way, we excluded elderly under 75 years old, i.e., we ignored patients aged 65 to 75 years with comorbidities. Deaths within 30 days and patients lost to follow-up were not included. Another limitation due to the use of an electronic database is that we did not consider readmissions that did not originate from an AED visit or that occurred in another hospital. It could explain why the readmission rate was relatively low (6.4%).

Recommendations for further research

In the cohort of this study, the 80+ score showed poorer discrimination than the three other scores. All the four scores analysed showed less ability to identify potentially avoidable readmission of elderly patients than in other studies found in the literature. One of the perspectives of this study would be to identify patients at risk of readmission using the TRST and then set a medication reconciliation protocol with case and control groups and finally assess the efficiency of such interventions in a population at risk.

Disclosure statement

No financial support and no other potential conflict of interest relevant to this article was reported.

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